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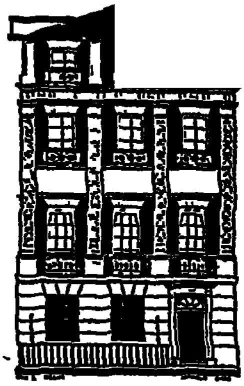

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HOW A LAWYER THINKS *

LORD RADCLIFFE
P C, G B E, M A Oxfd
A LORD OF APPEAL IN ORDINARY

MANY people are becoming more and more vexed by e problem of communication There seems some son, to think that, as our technical mastery of the ans of communication increases, there is a correponding decrease in our power to employ those means in y way that is worthy of their possibilities Whether his is more than a coincidence I do not know What is any rate worthy of remark is that we still appear to nderstand each other so little

If we lived in a less complicated less interdependent rm of society, the want of understanding might be of particular importance Earlier societies have got on, ten happily enough, with a minimum of common nderstanding between their different classes and ections Retrospect may to some extent flatter English ciety of an earlier age, but it was probably rather ceptionally fortunate in the range of common feeling at united it, despite huge barriers or gaps It would not ave been altogether nonsense to talk of a common ulture informing that earlier society less misleading han it might be to talk of it today Most of what now ok like the prevailing causes—a general and dominant ligious faith, a still unbroken association with the land, e influence of insularity, the sheer effect of a simple cial organism—have ceased to operate, even though me of the institutions that were founded upon them ay still survive And at a period when our complex lationships make it essential that we should understand ch other or perish, we understand each other, perhaps, ss and less

If you do not have common ideas, you cannot have a mmon speech That is, if the words that a speaker es either do not mean the same thing to his listener they mean to him, or, more simply, do not mean anything to the listener at all, there is either misunderstanding or no understanding In either event there is o communication in any valuable sense of the word t is hard enough for the specialist to realise this , but at ast he is conscious of some necessity for a free translation, if he is to make himself generally understood ut the realisation is harder yet, I believe, for the man f general literary education—the man, let us say, whose ducation was directed towards or culminated in the arts egree at a university. For the conceptions which were planted in him by that form of education, itself erived from the common culture of the older Europe, ssume a certain fixed relationship between words and eas, and assume moreover that, because of that lationship, words, properly combined, are an adequate ehicle for the expression of ideas Deny him the alidity of that assumption and he becomes something a lost man in the modern world That sovereign strument for communicating ideas, which he thought bridge between his own and other minds, becomes only ne more of those esoteric jargons in which specialists ell the sign language of their tribe Puffs of smoke on he hill, knife markings on a tree, rock carvings of a rgotten pictogram And, since many of the leading en in our public and professional life have been raised s the products of a literary general education of this nd, and there are even some who think it a good thing hat they should have been, it is no wonder that the roblem of communicating meaning, or, to put it another ay, the problem of expounding ideas, is today thought of as a serious one For these men may understand each other, if they listen, but it is very doubtful whether they possess the ability to make themselves at all generally understood

Essentially the problem is not one that turns upon a relationship between leader and led or between those who prophesy and those who are prophesied to We live, of course, in a managerial age, and management—political social, or industrial—is very largely the art of communicating ideas in a persuasive form But everyone has always lived in a managerial age of some kind It distorts the problem to think of communication in terms of "putting things over," an amiable method of getting one's own way So understood, the art of communication appears as little more than one of the techniques of public relations It seems to me much more fruitful to approach the problem as a search for a modern art of generating ideas by a free exchange of them We ought to try to gather together at any rate the cultured classes—pass the phrase for the moment without assuming that it is necessarily priggish—from the isolation which the specialisation of learning is tending to bring about Because this isolation is a harmful thing and it is something of a new phenomenon in European life It is a very natural product of two things which press upon us all today—the lack of any agreed curriculum of general education, and the great additions to specialised knowledge in so many fields, which give so few of us enough time to put our noses outside our own books It is natural enough, under prevailing conditions but more and more its effect will be that even the professional classes will understand each other's concepts and language less and less, and the common ground of enlightened opinion on which so many people have stood firmly in the past will shrink to a negligible plot So let us be upon our guard against this new threat of Enclosures !

* * *

This is rather too grave an introduction for the simple reflections that are to follow But my own professional training has been in the discipline of the Law , and when the Royal Society of Medicine did me the honour of inviting me to deliver the Lloyd Roberts lecture, adding considerately, "the subject is not necessarily medical," I thought to myself that it is sometimes more interesting to know how a thing works than what it does How does a lawyer work ? It might make some contribution to the mutual understanding between Medicine and Law if I were to reflect a little upon the main influences that govern a lawyer's way of thought Any worthwhile profession sets its mark upon a man just as surely as the ancient callings did—sets its mark upon his mouth and his hands and his eyes, and speaks a little through his voice But apart from the physical uniform, it imposes too, certain patterns of ideas or modes of thought, and unless these are fairly understood the language which is their vehicle of expression remains a foreign language People used to speak of the three learned professions, the Church, Medicine, and the Law. Now university research has so much extended that Learning itself has become a profession . But how far do we understand each other today, where we hope to go, and where we would like to stand ?

* * *

I believe that one of the noteworthy things about the lawyer in our present age is that the system of knowledge which constitutes his learned study is not itself a progressive one Progressive, of course, is an equivocal term But the world today is humming with the murmur of those who study and apply the expanding sciences and who see before them an unconfined field of experiment and discovery Physics, Chemistry, Biology I suppose that there can be few people who feel themselves to have reached some mastery of those subjects who do not feel at the same time that the work of the past was only a preliminary to the almost unpredictable developments of the future. Now to live and work in a world of that kind, which by the very terms of its existence is a revolutionary world, must be intensely exciting. And the excitement of those who understand what is going on communicates itself to the general public. You may have guessed already what I am going to hint at, that it does not communicate itself to me. I wish that it did. It is a depressing experience to attend some great ceremonial procession with the crowd waving and cheering madly and to feel cut off from the whole thing, neither able to see the procession nor to share the excitement. It is obvious, indeed, that the great advances in what for want of a better word I will call the scientific sciences are going to modify, even to revolutionise, the conditions under which human life has to be lived. But it is not equally obvious that the alteration of those conditions will alter in any important way the terms of the human dilemma itself. No doubt an expedition will reach the Moon in due course, or some inhabited constituent of the solar system, but suppose none of the inhabitants has ever got further than writing the *Iliad* or *Hamlet* or *King Lear* or *Don Quixote*?

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* The Royal Society of Medicine's Lloyd Roberts lecture for 1955, delivered on Nov 30, and published with the society's permission

I speak as if the lawyer were the contemplative philosopher of the present day. He is not at all, at any rate in this country. Law is not a reflective calling it can hardly afford to be, since its essential function lies in the discovery and application of practical rules which have to be treated for the sake of appearances as if they were universals. But all the same there is something rather unusual, something which might be characterised as introverted, about a profession in which the range of learning is, in effect, closed and in which a principle is the more treated as valid the more it can be shown to be ancient and long-established. Such a background should favour a certain conservatism and a certain detachment of outlook. It should favour, too, an almost desperate humanism as the best justification of our, perhaps, dying art. On the whole I think that this is what our background does. But since the lawyer revolutionary is himself a recurrent figure in the historical process, I take it that there is something in the legal discipline which produces by reaction the extreme antithesis of the normal type.

* * *

You cannot be a good lawyer unless you can cultivate good historical sense. The more you try to understand the reason or principle that lies behind any branch of our jurisprudence, the more you are forced to see that it is not Reason in itself but a decent rationalisation of attitudes, moral or social, which belong to the history of our society. When I was a young man I used to get rather embarrassed by this. I used to think that it rather lowered the status of Law and of our learning in it. Now I do not feel quite the same way. It seems to me that the life of man in society is so complex a thing that good social habit which has some root in the past, which is nourished by the emotional association of history, is a more valuable possession for the individual than a mastery of a dialectic which may be intellectually more satisfying. Not all of us in fact know much about history and very few of us know as much as we should but nevertheless I think it true as a generalisation that to the lawyer the history and the historical development of his country convey a more vivid sense of living and practical reality than they do to others who follow other callings. We are so often forced to see the present in its true light as a point of time in a continuous process which does not itself pause for time. That is a strength at least it should give a certain richness at the expense of a certain soberness, of tone.

* * *

Most people think of the lawyer as a great arguer. Argument is, I suppose, the most typical weapon of the lawyer's armoury. How much it governs his real thinking seems to me worthy of some analysis, since it may help to show how ambiguous a word "argument" is. On the one hand, undoubtedly, the administration of law consists in the application of principles to particular combinations of circumstances. The combinations are regarded as new, the principles as given or at any rate as demonstrable by deductive reasoning based upon other principles. Deductive logic therefore plays a large part in the legal process, being employed alike by the advocate to present his argument and by the judge to support his decision. The decision as arrived at is arrived at, accordingly, as a demonstrated necessity and this use of the logical process, which those trained in it have been taught to regard as infallible, satisfies the general conception of what we need of justice, that it should be certain, impartial, and, above all, impersonal. We can say of the lawyer, then, that he is a person who is conditioned by his training to marshal the expression of his thoughts in the form of logical reasoning.

Away from the Law Courts, this habit does not tend to make the lawyer a good controversialist. His method smacks too much of scholastic debate in the Middle Ages, in which it was essential to success that one contestant should never allow the other to get away for one moment with a single uncertain premise. If he did, there was no breaking the chain of unchallengeable deductions that would soon be tied to it. So he cried *At distinguo*, and pulled the other back to the beginning. It was a good discipline for those who can attribute to words precise and definite meanings. But public controversy needs an altogether looser rein. It requires the impressionist technique. What is important is not so much where the other man gets to what matters more is the significant effect produced by the whole arrangement. And to achieve the effect a few striking passages may be much more compelling than the logical consistency of the whole.

But the interesting thing is that, though all lawyers instinctively resort to deductive reason to demonstrate their conclusions, it is in practice by no means the strongest part of their equipment. A professor of logic would find in even famous judgments some sad howlers—the undistributed middle, transference of meaning in the use of the same word, questions begged until they are in rags. And not only the professor of logic. Ask an intelligent member of the public to make a critical study of some well-known judgment and to give his comments. He would find much to admire—a good, if rather desiccated, style of prose, clarity of exposition, economy of expression and a reassuring air of detachment but what I do not believe that he would be impressed or convinced by is the reasoning itself. I do not say that he would fault it as the professor might, but I think that his readiness to be satisfied with the result of a trial would arise more from his satisfaction with the judge himself, the conduct of the proceedings, and the treatment of the witnesses, than from any feeling that the considerations which were ultimately held to be the determining ones were based upon the kind of reasoning that he would himself be convinced by in the critical decisions of his own life. In particular, the distinctions upon which the result seems to turn often present themselves as somewhat unreal, not so much as points of substance as fine points of verbal distinction.

Now most lawyers would find an answer to this kind of criticism, although they are not very ready to offer it. If it was offered more often and more explicitly it would help to a better general understanding of what is the true structure of legal reasoning and might mitigate the impression, quite widespread, that law must seem much more convincing to lawyers than it does to the outside world The thing to be admitted is that Law is not in any sense an exact science, indeed it is not in the modern sense of the word a science at all Its material consists of the conduct and the affairs of living human beings in all the complexity of their relations, and its art consists in the application of certain generalisations styled principles, to a particular combination of circumstances These generalisations are themselves half moral half practical in each case the compound is produced more by perception than by rule It is a mistake to suppose that logic based on verbal propositions can ever be much of a guide for this purpose, and I have the impression that lawyers more or less unconsciously accept that their formal process is not their real one The real process the mastery of which constitutes the abiding fascination of administering law, proceeds by the method of selection and arrangement Once the picture has been composed by the artist there is indeed something inevitable in the resulting impression but, of course, the art has lain in the justness of the selection and the firm outline of the pattern

* * *

Perhaps you will allow me to illustrate what I am saying by an extract taken from a well known judgment in the House of Lords by one of the greatest exponents of the legal art that this country has known The speaker is Lord Macnaghten , the period 1888 the setting a late-Victorian, foggy, lamplit Christmas Eve at Paddington , the subject a Gladstone bag lost at the station by a certain Mrs Bunch Mrs Bunch is now at grapples with the Great Western Railway as to which of them is to bear the burden of the loss This is how Lord Macnaghten deals with the problem

"Your Lordships are familiar with the evidence in this case, and I do not propose to repeat it It is enough to say that on the 24th of December 1884 at 4 20 p m Mrs Bunch came to Paddington with a Gladstone bag and some other luggage, meaning to travel with her husband by the 5 p m train to Bath, that on her arrival at the station her luggage was received by a porter in the employment of the company, and taken by him to the platform for the purpose of the journey, and that the Gladstone bag was last seen on the platform with the same porter a few minutes afterwards From that time all trace of the bag is lost The porter and the bag both vanish from the scene It was suggested by the learned counsel for the appellants, by way of explanation, that the porter was possibly one of a number of men picked up by the company for the day to meet the pressure of Christmas traffic But I may observe, in passing, that so far as the public was concerned, there was apparently nothing to distinguish the casual helper of whom little if anything, was known, from the regular and trusted servants of the company

"On these bare facts standing alone it seems to me that there would be evidence upon which the County Court judge might reasonably find for the plaintiff even if the company were not under the liability of common carriers as regard the lost bag

"But then it was contended with much earnestness that it ought to have been inferred from the circumstances of the case and from Mrs Bunch's conduct that at the time of the loss the bag was not in the custody of the company for the purpose of the journey It was said that Mrs Bunch *came to the station too soon—that* she came before the train was drawn up—that she broke the journey, if the journey is to be taken as having begun—and left the bag in the charge of a porter who was then not acting as the servant of the company within the scope of his authority as such, but acting as her agent in his individual capacity, and that if this was not what she meant, it was an attempt on her part to saddle the company with a liability which they were not bound to undertake

"It seems to me that there is no substance in any of these objections Mrs Bunch, no doubt, came to the station somewhat early But the one thing that railway companies try to impress on the public is to come in good time And considering the crowd likely to be attracted by cheap fares during the Christmas holidays, and the special bustle and throng on Christmas Eve it does not seem to me that Mrs Bunch came so unreasonably early as to relieve the company who received the luggage from the ordinary obligations flowing from that receipt It is impossible to define within the extreme limits on both sides the proper time for arrival Everything must depend upon the circumstances of the particular case But, among those circumstances, the least important, as it seems to me is the time when the train is drawn up at the departure platform That is as everybody knows, a very variable time And it is a matter over which the passenger has no control, and of which he can have no notice before he comes to the station

"Then I think that there is nothing in the conversation which took place between Mrs Bunch and the porter Mrs Bunch s question was a very natural one The answer which she received was just what might have been expected Nine women out of ten parting with a travelling bag on which they set any store would have asked the same question In ninety-nine times out of a hundred the same answer would be returned I do not think that this conversation altered the relation between the parties in the least degree It seems to me almost absurd to treat it as a solemn negotiation by which the lady abdicated such rights as she possessed against the Great Western Railway Company and constituted this ephemeral and evanescent porter in his individual *capacity the sole custodian of her Gladstone bag*

"Nor can it, I think, be said that Mrs Bunch broke the journey by leaving the platform to meet her husband and get her ticket To take a ticket is a necessary incident of a railway journey It is at least, a very common incident in railway travelling for persons, who intend to travel in company, whether they be members of the same family or not, to meet by appointment in the railway station from which they mean to start, and it is certainly not unusual in such a case for the purchase of tickets to be deferred until the meeting takes place . "

"It was said that if everybody acted as Mrs Bunch acted in this case, railway companies would require an army of porters, and that it would be almost impossible for them to carry on their business I quite agree, but I am not much impressed by that observation I apprehend that if all travellers acted precisely alike, if everybody arrived at a station for a particular journey at precisely the same moment, though the time of arrival were the fittest that could be imagined, there would be no little confusion, and perhaps some consternation among the railway officials Whatever may be the result of your Lordship's judgment, there is no fear that it will have the effect of making everybody act alike Things will go on just as usual The fidgety and the nervous will still come too soon , the unready and the unpunctual will still put off their chance of arrival till the last moment, and the prudent may have their calculations upset by the many accidents and hindrances that may be met with on the way to the station And it is just because of the irregularity of individuals that the stream of traffic is regular and easily managed "

Now there are several things that might be said by way of commentary on this specimen of judicial reasoning I would like to draw your attention to one or two of them First, though this may seem merely an incidental comment, the style is very nicely fitted to the subject It is grave, without being portentous it is admirably detailed, without being finicky , and at the same time there is, I think, at the back of it a gleam of decorous amusement that these sober legal propositions have to be marshalled and weighed to solve the problem of Mrs Bunch and her Gladstone bag Next, these paragraphs which seem to be no more than a recital of facts or a rather quizzical glance at certain arguments, do in fact contain an exposition of legal principles—so much so that Mrs Bunch's case has become a leading case determining for good the kind of considerations that are to govern the loss of Gladstone and other bags at railway stations and the weight to be given to some of those considerations But the legal principles are, as it were, built into the factual structure of the story itself not imposed upon it, so that the story seems to arrange itself naturally round them and to take its form and order from their intrinsic logic (This quality of design is a quality common to all great artists, in whatever medium they work They speak as one having authority, not as one bound by other men's measure They do not labour at odds with their material A master of his art is a master of his means and under his hands formless mass glows to clear outline and coherent shape) And, lastly, the whole passage, though the careful simplicity of it is to some extent delusive, is irradiated by a vivid common sense, the most difficult of all qualities for the lawyer to incorporate into his work

I do not mean to level that as a cheap generalisation It is quite true that in every calling which is primarily intellectual it is easy to reason oneself away from common sense The Law is not singular in that respect, though its immediate application to the practical affairs of living throws its defects into the sharper relief But common sense is not itself the highest of human qualities nor is it the final arbiter in our affairs The lawyer's problem is not understood unless it is understood as a problem, never completely resolved, of keeping his conclusions sufficiently related to common sense without subordinating them to it Perhaps I could describe his process as away from common sense by way of reason and then back to common sense to test the conclusion And his difficulty is enlarged by the fact that the Law, for all its portentousness, for all that it must affect to deal with the issues of life and death, of honour and dishonour, of fortune and ruin, is condemned to make its survey over a limited field which covers always much less than the whole subject *This* consideration is admissible, *that* is excluded For *this* purpose the Court may learn of a man's motive, for *that* purpose it is to be treated as irrelevant The human heart may be the prime mover in most of the combinations of events that come before a court of law's review, but only a very limited acknowledgment can be permitted either of its existence or of its impulses There would be little worth honouring in the Law if it could not relate its judgments to a sense of morals, and yet we know that a court of law is not, and is not free to be, a court of ethics in itself

I do not criticise the ambiguity of attitude that is forced upon us by these limitations Nor, I think, do most lawyers No one could practise law without realising that some such limitation is unavoidable It is not the purpose of this lecture to rehearse the reasons Every case has to be seen as one step only in the process of administering justice, and administration creates its own necessities—of time, of good order, of what is in the true sense triable and what is not Law is essentially a generalisation—how can it provide even handed justice if it is not ?—and the rules and principles which we apply are the product of those generalisations So, although we must dispute as to the application of the rules and as to the qualifications upon them that ought to be recognised, I think that we are conditioned to acceptance of the idea that in the Law we practise an imperfect art, and that the judgments which we pass, however profoundly meditated, are valid only within the terms which we ourselves impose upon the insoluble complexity of life

* * *

It is not easy to explain this attitude to the lay world, since it is the lawyer's mystery

Ostensibly, the Law is portentous in its claims But I do not think that any lawyer who is either sensitive or sensible feels that he is portentous in himself, despite the terms of expression which his subject almost forces upon him Among the several forms of legal humour, much of it esoteric, you can sometimes notice a rather grim anger at the ambiguity of a position in which by the very condition of his calling the lawyer is prohibited from speaking, though he cannot be prevented from feeling Often such expressions pass for a merely macabre or even ghoulish brand of humour, of a kind that professions do indeed generate Sometimes they are , but so to write them off is, I think, to miss a quality of feeling that has always seemed to me an important part of the make up of a lawyer Let me try to make good an instance or two of this kind of irony

There is a record of an 18th century judge on assize at Stafford, who sentenced a man to death, as law then required, for uttering a forged bank note He charged him to prepare himself to leave this world for another where, said the judge, it was to be hoped that "through the merits and mediation of our blessed Redeemer he would experience that mercy which a due regard for the credit of the paper currency of this nation forbade him to hope for here " Of course, you may take that in more ways than one the bland 18th century philosophy of the Powers that-Be , a small, macabre, private joke , or, as I think, a sudden, Swiftian flash at man's unending inhumanity to man

Max Beerbohm attended Sir Charles Russell's famous cross examination of the forger Pigott during the sitting of the Parnell Commission There were the three Lords Justice, as aweful as only Victorian judges, perhaps, could be there was the pitiable Pigott, who was to kill himself a few days later, mumbling and stumbling in his exposure and there was Sir Charles Russell, the most overwhelming man of his period, addressing him " Come, Mr Pigott, strive to do yourself justice Remember you are face to face with my Lords ! " Portentousness ? mumbo-jumbo ?—or one brief commentary on the whole judicial scene ?

Few lawyers can be quite easy in the reflection that the rights of a litigant who can afford to spend money on the presentation of his case are more readily safe guarded than the rights of one who cannot " The gates of the Courts of Justice are open to rich and poor alike ", one judge has said, " so are the doors of the Ritz Hotel " The comment in different dress is much older than the Ritz but I doubt if it will ever be repeated just as a joke

On one occasion, which has now passed into history, a few sentences on the same theme are said to have done much to bring about a major change in the law of the country Up to the middle of the last century there were no divorce courts marriage could be dissolved at law by one process only, the obtaining of a special Act of Parliament Few people had time, influence, or money enough to resort to this other persons whose marriages went astray and who desired a second union had the choice between the crime of bigamy and the scandal of open adultery In 1845 a labourer was prosecuted at Warwick Assizes on a charge of bigamy to which he pleaded guilty The judge, Mr Justice Maule, sentenced him in these words

"Prisoner at the bar, you have been convicted of the offence of bigamy, that is to say, of marrying a woman while you had a wife still alive—though it is true that she has deserted you and is living in adultery with another man You have therefore committed a crime against the laws of your country, and you have also acted under a very serious misapprehension of the course which you ought to have pursued You should have gone to the ecclesiastical court and there obtained against your wife a divorce *a mensa et thoro* You should then have brought an action in the courts of common law and recovered, as no doubt you would have recovered, damages against your wife's paramour Armed with these decrees you should have approached the legislature and obtained an Act of Parliament which would have rendered you free and legally competent to marry the person whom you have taken on yourself to marry with no such sanction It is quite true that these proceedings would have cost you many hundreds of pounds, whereas you probably have not as many pence But the Law knows no distinction between rich and poor The sentence of the Court upon you, therefore, is that you be imprisoned for one day, which period has already been exceeded, as you have been in custody since the commencement of the assizes."

The prisoner was released. Only a few years later the requirement of an Act of Parliament to dissolve marriage was abolished and our modern divorce court was set up under which divorce is obtained by judicial process.

* * *

I have the feeling that the lawyer's processes of thought, as I have presented them to you, are such as to make him rather a figure on the side-lines of the game as it is played today. But then Law itself, his native art, is coming to stand rather on the side lines of modern civilisation. His status is still a high one, but this eminence he owes in part to the very great value that was placed upon his calling in the earlier forms of our own society. He enjoys therefore an inherited prestige which is out of proportion to the current evaluation of the services which Law can render. The reason, I believe, lies in that change of attitude which is at once the cause and the consequence of the present age. There is not really much to be said for Law unless it is thought of as representing absolute standards of right and wrong, even at a far remove. But then that means that its fundamental rules, whatever they are, stand above and independent of social needs and aspirations of the day. The function of the lawyer, you might say, is to reconcile the demands of human nature to the acceptance of those rules. There are periods of historical development when men prize very highly such a service of reconciliation. I do not think that this is one of those periods. The vast possibilities of material change and advance have made men haughty to their institutions. Their institutions must serve them, absolutely, and they will not in any way serve their *institutions*. So be it: but a lawyer remains, first and last, an institutionalist, and the lawyer, his equipment a little rusty, his habit a little worn, not quite the tremendous figure of the past, stands compactly on one side, content to wait his turn.

DIETETIC TREATMENT OF PEPTIC ULCER

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FOR over a century the principal treatment of peptic ulcer has consisted in the restriction of the diet to "bland" foods. At one time a preliminary period of starvation was recommended (Leube 1876, Riegel 1903), but it has been more usual to start treatment with a diet of milk, eggs, and perhaps cream, and subsequently to add other soft and "non-irritating" foods (Lenhartz 1904, Sippy 1915, Hurst and Stewart 1929). Under the influence of Meulengracht (1934) the use of very limited diets has largely been abandoned, but most patients are still provided with a long list of foodstuffs which they are advised to avoid.

The value of a special diet has never been demonstrated by a controlled series of observations, and it must be presumed that its use is continued partly for reasons of tradition, partly on the theoretical grounds (ill supported in practice) that "bland" foods stimulate less secretion than other foods and do not "irritate" the ulcer physically, and partly because patients given a restricted diet tend to lose their pain. It is, however, now realised that the bouts of pain associated with the presence of an ulcer are nearly always self-limiting, and it is widely held that the duration of the bouts can be influenced by psychological means. Several workers have, therefore, questioned whether dieting has any specific effect. Nicol (1942) and Lawrence (1952) compared the results obtained by giving patients a full diet with those obtained by a standard ulcer regime, and neither found that the standard régime had any advantage.

The present investigation was planned to be a controlled trial of certain types of special dieting. In the first part of the investigation a comparison was made between the rate of healing of gastric ulcers in patients treated in hospital by two different diets; in the second, the frequency with which symptoms recurred and the ulcer remained unhealed was compared in two series of outpatients with gastric or duodenal ulcers who were recommended to adhere to different dietetic schedules.

Inpatients with Gastric Ulcers

The inpatient trial was part of a long-term investigation into factors affecting the rate of healing of gastric ulcers. The type of patients admitted for treatment and the general plan of the investigation have been described in detail elsewhere (Doll and Pygott 1952, 1954, Doll et al. 1956).

In order to obtain more information in a limited period, the effects of three different types of treatment have been assessed concurrently. The different treatments have been allocated to patients in such a way that the group of patients who have been given a specific treatment and the group not given it have each contained the same proportion of patients given each of the other treatments; hence, the value of each treatment can be assessed independently. In the present trial the contrasted methods of treatment were: (1) a standard ulcer diet, and an almost normal ward diet; (2) continuous intragastric milk drip, and no drip; and (3) advice to smokers to stop smoking, and allowing them to continue smoking.

With milk drip pain appeared to be relieved somewhat more quickly than without it, but no effect could be detected on the rate of healing of the ulcers (Doll et al. 1956). Insufficient patients have yet been advised to stop smoking for assessment of the value of this advice; no interaction has been observed between the advice and either of the two diets, and it is thought that any effect which may be attributable to it can be ignored in assessing the value of the diets.

TABLE I—COMPARABILITY OF PATIENTS ON ADMISSION WITH REGARD TO PRESENCE OF PAIN, BODY WEIGHT, AND SIZE OF ULCER

Characteristics	No. of patients on	
	Standard ulcer diet	Almost normal diet
Pain on admission		
Present	21	24
Absent	11	8
Initial weight		
Under 7 st.	2	3
7 st. –	8	7
8 st. –	8	7
9 st. –	2	4
10 st. –	8	3
11 st. +	4	5
Not recorded	0	3
Av. all patients (st., lb., oz.)	9, 0, 7	8, 13, 12
Initial size of ulcer niche (sq. mm.)		
10–24	9	8
25–49	9	7
50–99	7	7
100 +	7	10

TABLE VIII—RELIEF OF SYMPTOMS DURING INPATIENT TREATMENT FOR GASTRIC ULCER REPORTED IN VARIOUS STUDIES

No of patients	Treatment	Proportion pain free (%)	Proportion with occasional pain or dyspepsia (%)	Proportion with daily pain for 1 wk or longer (%)
16	Almost normal diet*	19	56	25
16	Standard bland diet (present investigation)*	44	38	19
40	Standard bland diet (Doll et al 1956)*	38	40	23
31	Standard bland diet (Doll and Pygott 1952)†	42	29	29

* Excluding patients treated with milk drip

† Excluding 1 patient with an ulcer niche initially less than 10 sq mm in profile

One other controlled trial of dietetic treatment has been reported

Lawrence (1952) treated 140 inpatients with gastric, duodenal, or jejunal ulcers by a modified Lenharz régime or by a "full convalescent" diet including "fried foods, cheese and pork pies" and without sieving or special preparation of vegetables or fruit Alternate patients received one régime, the remainder the other All patients were given the same drugs and (with certain exceptions equally distributed in the two treatment groups) were kept in bed until the ulcer was radiographically healed Healing of the ulcer was obtained in 93% of patients on both treatments, in average times of 58 days for those on the full diet and 64 days for those on the Lenharz diet Pain was abolished in 94% of patients on both treatments, in average times of 25 and 26 days respectively Lawrence noted that some patients on the full diet "were at first dubious of a régime so much at variance with their earlier instructions but their anxiety was allayed when it was explained to them that such food was required to inactivate their over potent gastric juice"

These results should not be interpreted as signifying that the pathogenesis of peptic ulcer is entirely unrelated to diet But specifically harmful or curative factors—if they exist—do not appear to have yet been adequately identified So far as the healing of ulcers is concerned, it may be concluded that there is no advantage to be gained from limiting the diet to "bland" foods—that is, not in the way that diet is commonly limited in hospital Even fried foods, which were excluded from both types of diet given to inpatients in the present investigation, were not harmful in Lawrence's study, and no harm could be demonstrated from allowing their use to outpatients in the present study

In both investigations inpatients on the standard ulcer diets had 2-hourly feeds, and patients on the more normal diets had snacks on waking, at mid-morning, and at bedtime While, therefore, patients on the more normal diets had two less feeds a day than the patients on the ulcer diets, they did not have as long intervals between food as many people have It may be concluded that strict 2 hourly feeds have no greater beneficial effect on the rate of healing of gastric ulcers than feeds at the longer intervals adopted for the control diets, but no evidence has been obtained about the value of snacks between meals

Whether "bland" foods and 2-hourly feeds were of value for the relief of pain is uncertain The small difference observed in part of the present investigation might have disappeared if a stronger attempt had been made to convince the patients that the unaccustomed diet was harmless

Summary

The value of the dietetic treatment of peptic ulcer by means of "bland" foods has been assessed on (1) 64 inpatients with gastric ulcers, and on (2) 80 outpatients with gastric ulcers and 50 outpatients with duodenal ulcers

The inpatients were divided into two equal groups, patients in one group were given the standard hospital ulcer diet, while in the other they were given an almost normal diet The diets were strictly supervised throughout

The results showed a slight but statistically insignificant advantage to the patients on the "almost normal" diet with regard to the proportion in whom the ulcers became completely healed (10/32, compared with 5/32) and the average amount healed for the whole group (70 3%, compared with 65 1%), and (if patients on milk drip are omitted) a significant advantage in the average amount of weight gained (5 lb 8 oz, compared with 2 lb 14 oz), on the other hand, they showed an appreciable advantage to the patients on the standard ulcer diet with regard to the proportion who reported themselves completely free of pain throughout treatment (17/32, compared with 9/32)

The outpatients were either advised to continue for a year on the standard ulcer diet with which they had previously been treated, or were advised to revert to a wholly normal diet At the end of a year the proportion who had remained free of pain and in whom the ulcer was radiographically healed was practically the same in the two groups (pain free 22% and 21%, ulcer healed 45% and 51%)

Dieting with "bland" foods does not increase the rate of healing of peptic ulcers

We are grateful to Dr F Avery Jones and Dr T D Kellock for referring patients to us for treatment, and to the dietitians and other members of the staff of the gastro enterological and radiological departments of the hospital for their assistance in the care and investigation of the patients

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Appendix

Inpatients on the standard ulcer régime were given the basic diet for the first 2 weeks of treatment and the convalescent diet for the subsequent two weeks

Basic diet Two hourly feeds from 6 A M to 10 P M

6 A M (if awake) teacupful of warm milk
8 A M one helping of fine oatmeal porridge made with milk
cornflakes and milk egg lightly boiled poached, scrambled or as
omelette Bread and butter with jelly marmalade, honey or syrup
Teacupful milk flavoured with weak tea
10 A M teacupful milk flavoured with 'Ovaltine,' 'Horlicks
or 'Milo Plain biscuits or rusks
NOON one helping of egg or cheese dish, fresh fish, tripe, brains,
or chicken Mashed potatoes sieved vegetable
2 P M one helping of milk pudding, ice cream, light sponge
pudding or jelly
4 P M teacupful milk flavoured with weak tea Bread and
butter with jelly jam, honey or syrup Sponge cake or plain biscuits
6 P M one helping of vegetable soup (made with milk), egg or
cheese dish, fresh fish tripe, brains or chicken Bread and butter
8 P M as at 2 P M
10 P M as at 10 A M

Convalescent diet Two hourly feeds from 6 A M to 10 P M

6 A M 10 A M and 10 P M feeds as in basic diet
8 A M one helping of fine oatmeal porridge and milk cornflakes
and milk, egg, boiled poached scrambled or as omelette grilled
bacon soft roes or fishcake Bread and butter with jelly marmalade,
honey or syrup Weak freshly made tea with teacupful of milk
NOON one helping of egg or cheese dish fresh fish tripe brains
chicken, rabbit, ham lamb, or mutton (minced if tough) Mashed
potato Sieved vegetable
2 P M one helping of milk pudding, ice cream light sponge
pudding or sieved fruit
4 P M weak freshly made tea with teacupful milk Bread and
butter with jelly, jam, honey, or syrup Sponge-cake or plain
biscuits

6 P M   first course as at midday
8 P M   as at 2 P.M

Inpatients on the almost normal diet were given the same diet throughout

Almost normal diet

6 A M (if awake) tea with milk and sugar as desired
8 A M one helping of egg boiled, poached, or scrambled, grilled bacon or fish Bread and butter with marmalade Tea with milk and sugar as desired
10 A.M milk drink, flavoured as desired, or 'Bovril' Biscuits
Noon One helping of any fish, offal, chicken or any meat Potato mashed or boiled Green or root vegetables or salad Milk or sponge pudding ice-cream jelly, or fruit
3 30 P M bread and butter with any jam, honey, or lemon curd. Cake or biscuits Tea with milk and sugar as desired
6 P.M one helping of cheese or egg dish, fish, or any meat Green or root vegetables or salad (or helping of soup, cheese and biscuits) Bread and butter Sweet as at noon.
9 P M as at 10 A M

Fried foods were excluded from all three diets

Outpatients advised to adhere to a gastric diet were given the convalescent schedule described above, save that the 2 P.M and 8 P M feeds were combined with the midday and evening meals and the 4 P M and 10 P M feeds were brought forward $^1/_2$–1 hour

THE INEFFECTIVENESS OF SPLINTING IN THE TREATMENT OF ABDUCTOR PARALYSIS AT THE SHOULDER

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FOR many years the application of an abduction splint has been a part of the accepted treatment of abductor paralysis at the shoulder (Jones and Lovett 1929)

The principle aims of splinting are as follows

(1) To relax the deltoid muscle and thereby to encourage its recovery

(2) To prevent the development of laxity in the capsule and ligaments of the shoulder-joint

(3) To prevent adduction contracture

(4) To prevent scoliosis

(5) To prevent or treat œdema of the upper limb

(6) To assist the patient in the performance of certain actions, such as feeding himself

We assess here the value of splinting, in relation to these aims, in the treatment of abductor paralysis caused at the shoulder by poliomyelitis

Material and Method

This study is based on all the adequately documented records of patients with poliomyelitis seen between 1946 and 1953 by one of two observers, Mr D M Brooks and one of us (W J W S) The records contained complete muscle charts, and paresis or paralysis of one deltoid muscle or of both was detected by clinical examination six weeks after the onset of paralysis This group comprised 129 patients with both deltoids affected, and 101 with one deltoid affected, making 230 patients and 359 affected muscles The two observers used the same technique of assessment of muscle power throughout Records were made of the following items

(1) The power of the deltoid muscle and of other muscles of the shoulder and upper arm six weeks after the onset of the paralysis and on a second occasion at least eighteen months later The Medical Research Council (1942) scale of muscle grading was used. We were particularly careful, in our assessment of the deltoid muscle, to observe that the movement produced was true scapulo humeral movement and that the deltoid muscle was producing it Up to 60° of abduction can be produced by scapular rotation alone, and true abduction at the scapulo humeral joint can occasionally be produced by the supraspinatus muscle in the presence of complete paralysis of the deltoid muscle

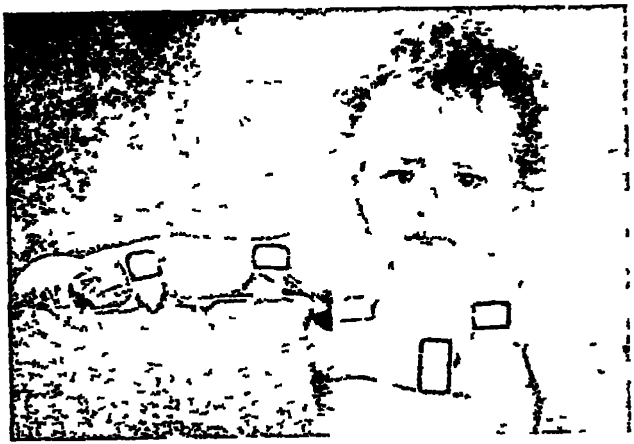

Fig 1—Standard abduction splint.

(2) The passive mobility of the shoulder joint, recorded as (*a*) normal, (*b*) laxity, in which the humeral head could be moved passively in the sagittal plane, (*c*) laxity subluxation, in which the humeral head could be moved passively in the vertical and sagittal planes, (*d*) mild contracture, in which total passive abduction of the upper arm was not full but was more than 90°, or (*e*) severe contracture, in which passive abduction was limited to less than 90°

(3) The duration of continuous or almost continuous respirator treatment and the existence of respiratory embarrassment that contra indicated the use of an abduction splint

(4) The presence of œdema in the upper limb

(5) The presence of scoliosis

(6) The duration of splinting in abduction

Treatment Groups

During the acute stage of poliomyelitis it was the usual practice, in the infectious diseases hospitals in which most of the patients were treated, to support an upper arm affected by poliomyelitis in abduction by suitably placed pillows or sandbags except where treatment in a respirator prevented this When a patient was admitted to the Royal National Orthopædic Hospital, one of the following regimes of treatment was prescribed

Group A, the deltoid muscle had been severely affected (*M.R C grade 0, 1, or 2*) 98 cases Splinting in abduction was continued either by an abduction splint (fig 1) when the patient was ambulant or sitting or by pillows when he was recumbent Adduction of the upper arm was allowed only during periods of active physiotherapy Splinting was continued for at least four months and in many instances for up to three years, the average time being twenty months This method was used in two-thirds of the patients admitted before 1950 but progressively less after this time

Group B, the deltoid muscle had been severely affected (*M R C grade 0, 1, or 2*) 118 cases No splinting in abduction was attempted A simple sling was used for comfort or convenience This group became relatively larger when a number of surgeons at the Royal National Orthopædic Hospital began to suspect that splinting in abduction was not essential for recovery of the deltoid muscle The admission of a patient to a bed in the charge of a surgeon who did or did not advocate splinting depended only on the chance vacancy at the time of request for admission When splinting was considered at all it was more likely to be prescribed where the initial deltoid grade was 0 rather than 1 and 2, and when the involvement was unilateral rather than bilateral

TABLE I—RECOVERY OF DELTOID MUSCLES IN GROUPS A (SPLINTED) AND B (UNSPLINTED)

—	Initial grade	Final grade						Total	Proportion showing recovery of 1 or more grades (%)
		0	1	2	3	4	5		
Group A (splinted)	0	71	6	5	2	—	—	84	15
	1	—	—	—	5	5	—	10	100
	2	—	—	—	1	3	—	4	100
Group B (unsplinted)	0	34	9	10	2	1	1	57	40
	1	—	—	2	19	5	2	28	100
	2	—	—	—	5	22	6	33	100

Group C, the deltoid muscle had been severely affected (M R C grade 0, 1, or 2) 17 cases Splinting in abduction was begun as in group A but, for various reasons, was discontinued before the fourth month These cases could not be considered as having been treated in either group A or B and were therefore analysed separately

Group D, the deltoid muscle had been severely affected (M R C grade 0, 1, or 2) and the patient had suffered respiratory weakness for which a mechanical respirator had been used 40 cases These patients could not wear an abduction splint, since there was not a free choice to splint in these cases, they were analysed separately

Group E, the deltoid muscle had been moderately or mildly affected (M R C grade 3 or 4) 86 cases No splinting in abduction was ever used after the sixth week in these cases

All the patients, whether splinted or not, were given similar treatment by passive movements to the shoulder-joint and by active exercises for the deltoid and other muscles of the upper limb (if working) up to, but not beyond, the point of fatigue

TABLE II—RECOVERY OF PARALYSED DELTOID MUSCLES IN GROUPS A AND B IN RELATION TO AGE

—	Age (yr)	Final grade						Total	Proportion showing recovery of 1 or more grades (%)
		0	1	2	3	4	5		
Group A (splinted)	0–4	41	2	1	2	—	—	46	11
	5–14	23	4	3	—	—	—	30	23
	15 or more	7	—	1	—	—	—	8	13
Group B (unsplinted)	0–4	12	2	3	1	—	1	19	37
	5–14	8	2	4	—	—	—	14	43
	15 or more	14	5	3	1	1	—	24	42

Recovery of Deltoid Muscle

The final grades reached by deltoid muscles in groups A and B are shown in table I There was little difference between the recovery in splinted and unsplinted cases when the deltoid muscle was acting at grade 1 or 2 at six weeks When the deltoid muscle was paralysed (grade 0) at six weeks, recovery was considerably better in the unsplinted than in the splinted cases Of the unsplinted muscles 40% (23 out of 57) showed some recovery compared with only 15% of the splinted muscles (13 out of 84) To test the validity of this conclusion analyses were made in relation to four other factors which might have influenced the recovery of the deltoid muscle

(1) *Age*—Muscle recovery in poliomyelitis is known to be more rapid and slightly greater in infants and children than in adults (Sharrard 1955) In the age distribution of groups A and B (table II) there is a predominance of children under the age of 15 in the splinted group (A) and of adolescents and adults in the unsplinted group (B) This might be expected to affect adversely the recovery in group B, but an analysis of the recovery of paralysed deltoid muscles in relation to age shows that *in each of the three age groups* 0–4, 5–14, and 15 or more, muscles in the unsplinted group recover more frequently than those in the splinted group There were too few cases in groups A and B with initial deltoid power of grade 1 or 2 to make a similar analysis by age

(2) *Calendar Differences*—An analysis was made of the recovery of paralysed deltoid muscles in groups A and B in relation to the year of onset of the paralysis This analysis was necessary because the decision by some surgeons to abandon splinting was made before 1949 and by others in 1949 or later In the early part of the period under review most of the cases were splinted, whereas later more of them were not splinted It seemed important to show that any differences in the recovery of patients in the two groups were independent of differences from one year to another in the type of patient or *in the general severity* of the poliomyelitis The results (table III) show that in each of the periods before 1949 and 1949–52 group B had the advantage over group A The only exception to this pattern in individual years was in 1948, where the numbers of patients in each group were small and the advantage of group A over group B was insignificant

TABLE III—RECOVERY OF PARALYSED DELTOID MUSCLES IN GROUPS A AND B IN RELATION TO YEAR OF ONSET OF PARALYSIS

—	Years of onset	Final grade						Total	Proportion showing recovery of 1 or more grades (%)
		0	1	2	3	4	5		
Group A (splinted)	Pre 1949	34	1	4	—	—	—	39	13
	1949–52	37	5	1	2	—	—	45	18
Group B (unsplinted)	Pre 1949	10	3	2	—	—	—	15	33
	1949–52	24	6	8	2	1	1	42	43

The recovery of paretic deltoid muscles (grade 1 or 2) generally showed a slight advantage in favour of group B, but there were too few muscles to allow a satisfactory comparison to be made in individual years

(3) *Distribution of Affection in Limbs*—H D Darcus (personal communication) has found that, in healthy people, specific exercise training given to one upper limb produces a training effect in the opposite upper limb The recovery of unilateral and bilateral cases in groups A and B was analysed to exclude the effect of different treatments applied to the opposite shoulder The results (table IV) indicate that, whatever treatment was being given to the opposite limb, the advantage was still with the unsplinted group (B)

(4) *Severity of Paralysis*—Among muscles that are still paralysed six weeks after the onset of poliomyelitis there are some, probably over 60% in all, that have been completely and irrevocably denervated by loss of all the anterior horn cells that supply them These muscles cannot recover A useful indication of the severity of the lesion affecting the motor nucleus of a given muscle, and hence its potentialities for recovery, can be obtained from an examination of the power of muscles supplied by the same spinal segments (Sharrard 1954)

A recovery index was calculated for each deltoid muscle It consisted of the sum of the grades of eight muscles that take some supply from the 5th and 6th cervical spinal nerve roots supraspinatus, infraspinatus,

TABLE IV—RECOVERY OF PARALYSED DELTOID MUSCLES IN GROUPS A AND B IN RELATION TO DISTRIBUTION OF AFFECTION IN ONE OR BOTH LIMBS

—	Distribution of affection	Final grade						Total	Proportion showing recovery of 1 or more grades (%)
		0	1	2	3	4	5		
Group A (splinted)	Unilateral	43	1	2	1	—	—	47	9
	Bilateral in same treatment groups	13	3	1	—	—	—	17	24
	Bilateral in different treatment groups	15	2	2	1	—	—	20	25
Group B (unsplinted)	Unilateral	4	2	1	—	—	1	8	50
	Bilateral in same treatment groups	27	5	7	2	—	—	41	34
	Bilateral in different treatment groups	3	2	2	—	1	—	8	63

TABLE V—RECOVERY OF PARALYSED MUSCLES IN GROUPS A AND B IN RELATION TO RECOVERY INDICES

—	Recovery index	Final grade						Total	Proportion showing recovery of 1 or more grades (%)
		0	1	2	3	4	5		
Group A (splinted)	0–9	56	—	—	—	—	—	56	0
	10–19	13	4	3	2	—	—	22	41
	20–29	2	2	2	—	—	—	6	67
Group B (unsplinted)	0–9	28	3	2	1	—	—	34	18
	10–19	5	2	7	1	1	—	16	69
	20–29	1	4	1	—	—	1	7	86

pectoralis major, teres major, subscapularis, biceps brachii flexor carpi radialis and pronator teres Table V analyses the recovery of paralysed deltoid muscles in relation to these indices and shows that, at all levels of the index, recovery in the unsplinted group B was superior to that in the splinted group A Similar analyses were made for deltoid muscles of initial grades 1 and 2 but with the small numbers available no consistent or significant advantage was seen in either treatment

Combined analyses were also made of recovery in relation to age and recovery index, distribution of paralysis and recovery index, and year of onset and recovery index The detailed results are not given here, since they only confirm the conclusions stated above

The final grades reached by deltoid muscles in groups C and D are shown in table VI Group C behaves rather more like group B than group A, though it is too small to show significant deviation from either

TABLE VI—RECOVERY OF DELTOID MUSCLES IN GROUP C (SPLINTED LESS THAN 4 MONTHS) AND IN GROUP D (UNSPLINTED WITH RESPIRATORY EMBARRASSMENT)

—	Initial grade	Final grade						Total	Proportion showing recovery of 1 or more grades (%)
		0	1	2	3	4	5		
Group C	0	8	3	2	—	—	—	13	38
	1 and 2	—	—	—	—	4	—	4	100
Group D	0	18	5	5	2	—	—	30	40
	1 and 2	—	—	3	3	3	1	10	100*

* The 3 cases with final grade 2 were initial grade 1

Recovery in group D appears to be as good as, or better than, in groups A or B, and detailed analysis showed this most clearly for paralysed deltoid muscles with low indices of recovery As regards paralysed muscles with all degrees of recovery index the proportion of group-D cases showing some improvement is 40% (12 out of 30), the same as in group B (23 out of 57) This group is interesting in showing that a position of adduction during the acute stage, though undesirable because of the liability of develop adductor contracture of the shoulder, does not seem to prejudice the ultimate recovery of the deltoid muscle

Conclusion—From these results it appears that splinting in abduction does not aid recovery of the deltoid muscle and may where the paralysis is severe actually discourage it

These results have received independent confirmation in a study of muscle recovery (Sharrard 1955) in which individual muscles of the upper and lower limb except the deltoid muscle and certain muscles in the shoulder region, showed identical curves of recovery In these the recovery was slower than the average in other muscles up to the sixth month but was greater at the tenth month Almost all the cases in that series were splinted, the late spurt of recovery coincided with the time when many of the splints were discarded

Laxity of Shoulder-joint

Without exception increased passive mobility of the shoulder-joint was present only if the deltoid muscle had remained paralysed Furthermore, the impression gained during the clinical examination of these cases was that laxity of the shoulder joint was often associated with severe paralysis of other muscles that play a part in holding the head of the humerus in the glenoid cavity A shoulder index was calculated for each case it consisted of the sum of the grades of eight muscles that act in this way deltoid supraspinatus infraspinatus, pectoralis major teres major, subscapularis, biceps brachii and long head of triceps

Any case in which the index was less than 10 was extremely likely to have a lax shoulder-joint, unless an adduction contracture had been allowed to develop during the acute stage of the poliomyelitis When the index was more than 14 laxity was uncommon, and when it was more than 24 laxity was never observed

TABLE VII—PASSIVE MOBILITY OF SHOULDER-JOINT IN GROUPS A AND B IN RELATION TO SHOULDER INDICES

Passive mobility	Shoulder index					
	0–9		10–19		20 –	
	A	B	A	B	A	B
Laxity-subluxation	31	10	3	—	—	—
Laxity	9	6	5	—	—	—
Normal	2	2	14	17	31	78
Mild contracture	1	2	2	1	—	2
Total	43	20	24	18	31	80

To assess the effect of splinting in abduction, cases in groups A and B at the same level of shoulder index were compared (table VII) At the critical index levels between 10 and 19 laxity subluxation and laxity were observed in 8 of the 24 splinted (group A) and in none of the 18 unsplinted (group B) Thus it may be that splinted cases suffer a double disadvantage not only do they recover less completely and hence become more likely to develop laxity at the shoulder-joint, but also, even with such muscle power as is regained, they may be more liable than unsplinted cases to develop laxity.

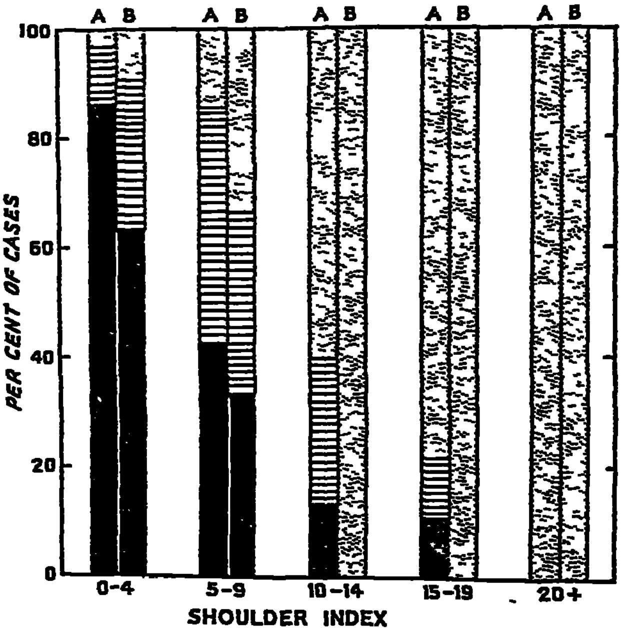

Fig 2—Relationship between shoulder index and laxity of the shoulder-joint in groups A and B *black*, laxity subluxation, *hatched*, laxity *stippled*, no laxity

The relationship between shoulder index and laxity, and the relative incidence of this condition in muscles in groups A and B are illustrated in fig 2

Conclusion —Splinting in abduction does not reduce or prevent laxity of the shoulder in the presence of weak scapulo-humeral muscles, but in some cases it increases it Lack of splinting does not increase laxity, which is primarily due to paralysis of muscles that help to maintain the head of the humerus in relation to the glenoid cavity

Adduction Contracture at Shoulder-joint

A mild adduction contracture was observed in 3 cases in group A (splinted), 5 cases in group B (unsplinted), and 1 case in group C (temporarily splinted)—an incidence of 3%, 4%, and 6% respectively In contrast to laxity, there was no evidence that contracture in these groups was related to the recovery index In group D (unsplinted, respiratory embarrassment), however, 18 shoulder-joints showed a severe contracture and 14 a mild contracture, a combined incidence of 80% (table VIII)

TABLE VIII—PASSIVE MOBILITY OF SHOULDER JOINT IN GROUP D IN RELATION TO DURATION IN TANK RESPIRATOR

Passive mobility	Time in respirator			
	<4 weeks	4–7 weeks	8 weeks or more	Total
Severe contracture	0	4	14	18
Mild contracture	4	10	0	14
Normal	6	2	0	8
Total	10	16	14	40

Since all the patients in this group had spent some time in a tank respirator, it is reasonable to infer that the limitation of movement was due to the position of adduction of the shoulder and to the fact that it was impossible to give adequate passive movements to the joints during the acute stage of the poliomyelitis Table VIII shows that the degree of contracture was related to the duration of more or less continuous respirator treatment Adduction contracture never increased or developed in a shoulder joint in any case in which it was not present at the initial examination six weeks after the onset of the paralysis No abnormality of passive movement of the shoulder was observed in group E (unsplinted, mildly affected)

Conclusion —Adduction contracture arises in cases in which the upper arm lies by the side and adequate passive movements cannot be maintained during the acute stage of the poliomyelitis, after the sixth week splinting in abduction is unnecessary to prevent a contracture from developing in a mobile joint

Scoliosis

In 39 patients the paralysis of one shoulder was severe (a recovery index of 9 or less) while the muscles of the opposite shoulder and in the remainder of the body showed no clinical paralysis Such a distribution of paralysis has been said to cause a thoracic scoliosis because of the unequal muscle pull on the two sides of the body exerted by muscles passing between the trunk and the upper limbs Not a single structural scoliosis was found even in cases examined six years after the onset of the paralysis, whether a splint had been worn or not In 10 cases a mild postural curvature of not more than 15° was present, in only 1 case was there a postural curvature of greater degree than this, and the curve was in the opposite direction to that which might have been anticipated from the site of the paralysis It was almost certainly due to the wearing of an abduction splint and disappeared a few weeks after the splint was discarded Eighteen other patients developed a structural scoliosis, in all of them the trunk muscles, especially the intercostal or lateral abdominal muscles, had been asymmetrically affected This confirms an observation first made by J I P James (personal communication)

Conclusion —Neither shoulder girdle paralysis nor splinting in abduction has any influence on the development or prevention of structural scoliosis in poliomyelitis

Œdema

No œdema was found in any upper limb in this series after the sixth week

Splinting as an Aid to Function

Whatever the eventual recovery of the deltoid muscle, the opinion of many patients who had worn a splint was that the limb was much more useful after the splint had been discarded The splint was regarded by the majority as an evil necessary to obtain recovery Exception must be made in one limited category patients in whom bilateral abductor paralysis at the shoulder is combined with weakness of elbow flexion with the result that the forearm cannot be raised against gravity In such a patient the upper limbs lie by the side, and he cannot make the best use of any muscles that have remained active in the forearm and hand, because he cannot bring either hand up to waist level After a time he develops trick methods of placing the hand where he wishes it to lie, but, as a temporary expedient, an abduction splint angled at 45° rather than 90° will raise the elbow to a level from which weak elbow flexors can flex the joint This use for an abduction splint is especially indicated in infants or young children in whom muscle re-education mainly depends on spontaneous activity and play

We must emphasise that a splint for this purpose differs in principle and in design from that shown in fig 1 Its function is to act as a platform rather than as a rigid splint A "lively" splint of the Capener (1949) type to which the limb is not tied is the most appropriate, it is not intended that it should be worn at all times but only as required In older children or in adults with bilateral paralysis it is occasionally useful but it is rarely indicated in unilateral paralysis Almost all patients, however young, eventually learn to facilitate activity in the paralysed limb by putting it into a useful position with the opposite hand

Discussion

The deleterious effects of over stretching of paralysed muscles was recognised by Lovett (1915) Many of the splints used in the treatment of the paralysis of poliomyelitis—e g, cock-up splints in paralysis of the wrist extensor muscles and apparatus for control of the paralysed foot—have been designed to prevent overstretching of muscles as well as to prevent deformity and aid function We do not deny this principle, indeed on several occasions one of us has witnessed late return of power in paralysed muscles following correction of deformity or after transplantation of powerful antagonist muscles

That the converse is true—i e, that relaxation of a muscle is necessary for its recovery—has never been demonstrated The recovery of the triceps suræ in poliomyelitis and in injuries to the sciatic nerve (Seddon 1949) in spite of the application of toe raising springs, the recovery of hamstring muscles, although the knee is splinted in extension, and numerous other examples suggest that relaxation is not essential for muscle recovery

Studies of the physiology of isolated muscle (Evans and Hill 1914, Doi 1921) show that an optimal initial tension is necessary for the development of maximal contraction in muscle In the body reflex mechanisms operating through muscle spindles and other proprioceptors enhance this action Provided that the principles of the prevention of deformity do not conflict with it, a mid-position of a joint that leads to moderate tension in the muscles controlling it is likely to encourage recovery

At the shoulder-joint all parts of the deltoid muscle are under optimal tension when the upper arm lies in the habitual position by the side of the body, the position of maximal stretch for the middle fibres of the muscle is with the upper arm fully adducted across the chest, and for the anterior and posterior fibres is with the upper arm abducted and extended or flexed respectively The position of the upper arm by the side therefore seems to be the ideal one for recovery of the deltoid muscle, and our results support this view

That the laxity of the shoulder-joint increases in proportion to the degree of paralysis in the scapulo humeral musculature is only to be expected, since one of the main actions of these muscles is to retain the humeral head in apposition with the glenoid cavity When the shoulder is abducted, the shape of the articular surface of the head of the humerus is such that all except the superior fibres of the capsule of the shoulder-joint are stretched, this may account for the increased joint laxity which we found in the splinted cases When the arm is by the side, only the superior fibres of the capsule are liable to be stretched by the weight of the limb, when, in a severe paralysis, this is likely to happen, a simple sling is adequate to minimise it

Provided that full passive mobility of the shoulder is present six weeks after the onset of the paralysis and is maintained by a single daily manipulation after this time, no contracture will develop, even though the arm lies by the side Before this time a position of abduction at the shoulder and the maintenance of as much mobility as is possible are essential Since the patient is usually confined to bed during most of this critical period, it is sufficient to support the limb in abduction on a pillow, and an abduction splint is inappropriate Only those patients who can become ambulant before a month require an abduction splint as a temporary measure to ensure that the adductor muscles of the shoulder do not shorten, and to guard against the development of œdema in the hand

There is no need to discuss here the inconvenience of splinting in abduction, the projecting encumbrance is a nuisance alike to the child and the adult and may be a positive danger to others in crowded places The position of the forearm and hand in an abduction splint is only useful for one purpose, that of feeding, since most manual activities are carried on at the level of the waist, splinting in 90° of abduction considerably diminishes the range of usefulness of the forearm and hand If, when the patient is confined to bed, he can feed himself better with the shoulder in abduction, an appropriate arrangement of vertical slings and springs produces the same effect as an abduction splint but allows much greater mobility without constraint to the chest

Conclusion —Except in the acute stage of poliomyelitis and in certain special circumstances in the convalescent stage, splinting in abduction is unnecessary and should be discontinued in the routine treatment of abductor paralysis at the shoulder

Summary

This study is based on 359 upper limbs in which some degree of abductor paralysis at the shoulder was present six weeks after the onset of acute poliomyelitis Records were made of the power of the deltoid and other muscles of the shoulder and upper arm, of the passive mobility of the shoulder joint, and of the function of the upper limb at this time and not less than eighteen months later The final state of cases in which an abduction splint had been used was compared with that in cases in which no splint had been used after six weeks from the onset of the poliomyelitis

The recovery of deltoid muscles paralysed (M R C grade 0) at the initial assessment was found to be diminished by splinting in abduction The recovery of paretic muscles (grades 1 and 2) appeared to be unaffected by splinting in abduction

The incidence of laxity of the shoulder-joint was shown to be related to the severity of the paralysis of the scapulo humeral muscles, this laxity was increased by splinting in abduction

Adduction contracture, if not already present, did not develop after six weeks in unsplinted shoulders that were passively mobilised daily In the acute stage of the poliomyelitis, on the other hand, immobilisation of the upper limb by the side, as happens when continuous respirator treatment is necessary, produced a more or less severe adduction contracture

Structural scoliosis was never found when the paralysis had affected the upper limb musculature alone, even where this paralysis was severe and unilateral Splinting in abduction to prevent scoliosis is therefore unnecessary

Occasionally a partially abducted position of the shoulder may allow better function of the remainder of the upper limb If so, a modified splint may be useful in bilateral abductor paralysis in young children

The principles underlying the use of abduction splints are discussed, it is concluded that, except in the acute stage of poliomyelitis and in special circumstances in the convalescent stage, splinting in abduction is unnecessary and sometimes harmful

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CHLORAMPHENICOL AND PENICILLIN IN THE TREATMENT OF LEPTOSPIROSIS AMONG BRITISH TROOPS IN MALAYA

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It is extremely difficult to assess reliably the value of any form of treatment in leptospirosis, because the severity, course, and complications of this disease vary greatly, even among patients infected by identical leptospiral serotypes There is still doubt about the value of antibiotics in leptospirosis, as is well shown by the conflicting opinions so far published.

Before the advent of antibiotics, the most widely used form of therapy was immune serum Inada et al (1916) were the first to try it in experimental infections in guineapigs, and later therapeutically in man Serum was effective in protecting guineapigs when given with an inoculation of *Leptospira icterohæmorrhagiæ* Walch Sorgdrager (1939) reviewed the results of serum treatment in cases examined serologically at the Institute of Tropical Hygiene, Amsterdam No definite evidence of its value was found, although there was a strong clinical impression that it was useful

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Most of the antibiotics now available have been examined for their effect on leptospirosis both in experimentally infected animals and in man At first sight the results of these experiments are encouraging

Previous Experience with Antibiotics

PENICILLIN

Experimental Observations

Alston and Broom (1944) and Chang (1946) found that penicillin inhibited the growth of *L icterohæmorrhagiæ* cultured in Fletcher's medium

Heilman and Herrell (1944) found that guineapigs artificially infected with *L icterohæmorrhagiæ* were protected by penicillin administered seventeen to twenty four hours after inoculation Alston and Broom (1944) agreed that penicillin administered eighteen hours after inoculation reduced the death-rate Augustine et al (1944) gave penicillin to guineapigs on the fourth day after inoculation, when jaundice was present, but observed no benefit They next gave the antibiotic thirty eight hours after inoculation There was no difference in the mortality-rate, but no animal became jaundiced, and life was prolonged Chang (1946) repeated these experiments, but gave penicillin on the third, fourth, fifth, and sixth days after inoculation Penicillin had a therapeutic effect if administered before the onset of jaundice, but once jaundice had appeared penicillin was useless This was similar to the findings of Larson and Griffiths (1945)

Throughout most of these experiments, difficulties arose over the possible toxic effects of penicillin on guineapigs It was noticed that some of the animals receiving penicillin died without evidence of leptospirosis or of any other disease Dunn and Thompson (1953) therefore tried the effect of penicillin on experimental infection in hamsters Treatment was started twenty four hours after inoculation, and it protected the animals against death But specimens of their livers and kidneys subinoculated into other hamsters produced leptospirosis, even when the inoculated animals were receiving sixteen times the amount of penicillin necessary to protect them against death

These experiments showed that penicillin must be given early if it is to be effective—probably within twenty-four hours after inoculation Even then, leptospiræ may be recovered from the liver during and after treatment (Chang 1946, Dunn and Thompson 1953) If these findings are applicable to man, treatment would have to anticipate the dissemination and multiplication of leptospiræ in the tissues, which normally takes place during the incubation period of four to twelve days In practice, treatment is seldom started before the fourth day of the disease—and often later

Clinical Observations

It is difficult, especially with a small number of cases, to decide whether an antibiotic has influenced the natural course of leptospirosis By the time the patient has been admitted to hospital, his illness diagnosed, and antibiotic treatment started, a natural improvement in his condition is usually starting

There have been many reports of the beneficial effects of penicillin in leptospirosis, based on a small number of treated cases (Bulmer 1945, Carragher 1945, Cross 1945, Baber and Stewart 1946, Niemi 1946, Moreau et al 1947, Patterson 1947, MacKay-Dick and Watts 1949, Dinaraj 1950, Lawson 1951, Suchett Kaye 1951)

Hutchinson et al (1946) reported a series of cases in Italy The illness was severe, and all patients were jaundiced 6 patients received penicillin in doses of 15,000 units three hourly, to a total of 600,000–660,000 units Hutchinson et al considered that penicillin had no significant effect on the disease, but it is difficult to draw any definite conclusions from this small series because treatment was started after the onset of jaundice, and the penicillin dosage was low by present day standards

Broom (1951) reviewed the results of penicillin therapy in 206 patients treated in several hospitals throughout Britain The mortality in this group did not differ significantly from that in 259 patients who were not given penicillin

Recently Doherty (1955) has recorded a larger series of cases treated with penicillin in dosages of 100,000–500,000 units three hourly Doherty concludes that penicillin in large doses significantly reduced the duration of fever Unfortunately this series was highly selected There were only 8 controls out of 111 cases, and the patients were treated at eight different hospitals, most of which used their own antibiotic regime Doherty also says that the time of temperature taking and the use of antipyretics varied from one hospital to another Finally, the observers were presumably aware of the type of treatment the patient was having This is important because the practitioners in the area were strongly in favour of penicillin therapy

CHLORAMPHENICOL AND OTHER ANTIBIOTICS

Experimental Observations

Chloramphenicol has given less encouraging results

Schlipkoter and Beckers (1951) showed that all the species they tested had considerable resistance, especially *L autumnalis* They anticipated that chloramphenicol would have no therapeutic action in man Dunn and Thompson (1953) found that in hamsters chloramphenicol gave no protection against death

Aureomycin and *oxytetracycline* have been found to be effective in vitro (Heilman 1948, Ormsbee 1953, Schlipkoter and Gram 1952) and in vivo provided they are given early (Schlipkoter and Beckers 1951)

Clinical Observations

Hall et al (1951) reported on 79 cases from an epidemic of leptospirosis in Puerto Rico

Antibiotic trials were made in sequence, one type of treatment finishing before another was started 12 patients who were not given antibiotics acted as controls, and the remainder received either *penicillin, streptomycin, aureomycin* (chlortetracycline), *oxytetracycline*, combined *streptomycin and aureomycin*, or *cortisone and aureomycin*

No significant effect on the course of fever, jaundice, renal involvement, neurological manifestations, and leptospiræmia was observed Because six different methods of treatment were employed, the number of patients in each group was small

Doherty (1955) drew no definite conclusion about the value of *chloramphenicol* from his series of cases

Several workers have reported that *aureomycin* and *oxytetracycline* are beneficial (Batchelor and Todd 1950,

TABLE I—CLASSIFICATION OF PATIENTS ACCORDING TO SEROTYPES

—	No of patients	Group A (controls)	Group B (penicillin)	Group C (chloramphenicol)
SEROTYPES				
L australis A	1		1	
L australis B	3		2	1
L bankinang	2			2
L canicola	8	3	3	2
L celledoni *	1			1
L grippotyphosa	3			3
L poi	1	1		
L pomona	1			1
L wolffi	1			1
SEROGROUPS				
Australis A	1			1
Autumnalis	3			3
Hebdomadis	17	4	8	5
Icterohæmorrhagiæ	5	1	1	3
Javanica	2	1		1
Pyrogenes	1	1		
Unidentified	33	20	6	7
Total	83	31	21	31

* A new serotype isolated in Australia by Smith et al (1954)

TABLE II—AVERAGE DAY OF ILLNESS ON WHICH PATIENTS WERE ADMITTED AND TREATMENT WAS STARTED

Treatment group	Admitted (day)	Treatment started (day)
A (controls)	4 0	4 0
B (penicillin)	3 4	4 7
C (chloramphenicol)	4 0	5 0

Brainerd et al 1949, Liebowitz and Schwartz 1951 Lurie 1949, Stagg and Liebowitz 1951, Whitehouse 1952) Nearly all these reports were based on a few cases, and are open to the same criticisms that apply to the reports on treatment with penicillin

Materials and Methods

Leptospirosis is quite common among British troops engaged in jungle operations in Malaya The mortality is very low, only 2 deaths were reported among 160 confirmed cases notified in 1954 1 of these 2 patients had malaria as well, and there was a certain amount of doubt about the diagnosis in the other (D G Lewis, personal communication) The disease is not severe, and of the present series only 4% became jaundiced and 5% had oliguria or anuria (oliguria is here defined as a urinary output of 10 oz or less in twenty-four hours)

In the present series the patients, all of whom were men, had been admitted to one of two military hospitals in Malaya Their ages ranged between 18 and 35 years, the average being 21 71 patients were British, 9 were Gurkhas, 2 were Malays, and 1 was Chinese The predominance of Europeans is not due to selection but reflects the lower incidence of leptospirosis among Asian troops

TABLE III—AVERAGE TIME FROM ONSET TO FREEDOM FROM SYMPTOMS AND SIGNS

Treatment group	Symptom free (days)	Sign free (days)	Apyrexial (days)	Symptom free and sign free (days)
A (controls)	9 4	9 9	9 0	10 8
B (penicillin)	8 2	9 5	7 6	9 7
C (chloramphenicol)	8 9	10 0	8 8	10 5

Paired specimens of serum were sent to Dr J C Broom, of the Wellcome Laboratories of Tropical Medicine, London, for agglutination tests In some cases blood was cultured in Fletcher s medium, and a few of the strains obtained were sent to Dr Broom for identification

It was possible to identify the serotype or serogroup in 50 out of 83 cases, either by agglutination or by culture In the remaining patients the agglutination tests were positive, but accurate identification of the serogroup was obscured by heterologous rises in titre

The patients were further subdivided into controls, and those receiving penicillin and chloramphenicol (table I)

The serotypes or serogroups among the controls were less easily identified In the few patients in whom jaundice or oliguria developed, no correlation with any particular serogroup was obtained

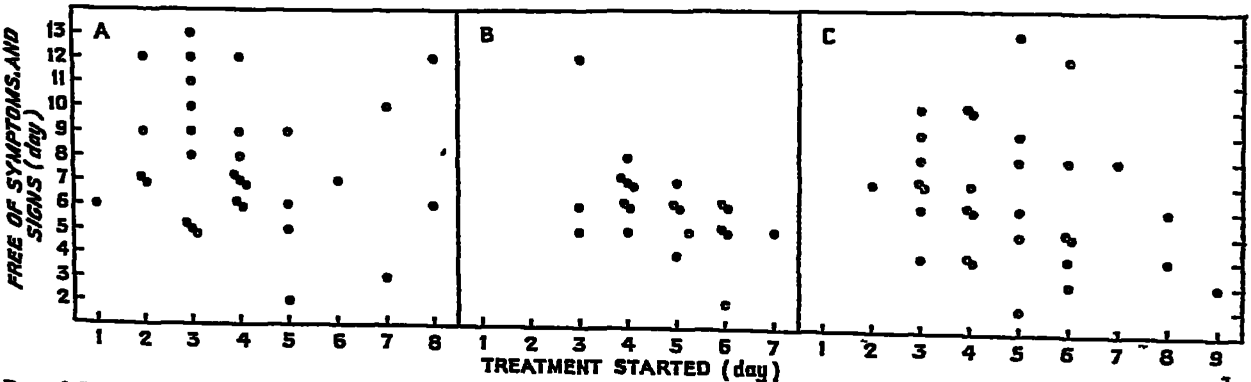
Patients were placed in rotation in one of three groups Patients in group A received no antibiotics and acted as controls Patients in group B were given penicillin 600,000 units six-hourly, and those in group C chloramphenicol 0 5 g six hourly Treatment was started as soon as the diagnosis was made Antibiotics were given for at least five days, and often beyond that until the patient had been afebrile and free of symptoms and signs for twenty-four hours The average duration of treatment in group B was six days, and in group C 6 2 days

TABLE IV—RESULTS CLASSIFIED ACCORDING TO WHETHER TREATMENT WAS STARTED ON OR BEFORE, OR AFTER, FOURTH DAY OF ILLNESS

Treatment group	Treatment started			
	On or before fourth day		On or after fifth day	
	No of patients	Av time from start of treatment till symptom-free and sign free (days)	No of patients	Av time from start of treatment till symptom-free and sign free (days)
A (controls)	22	8 2	9	6 7
B (penicillin)	10	6 9	11	5 0
C (chloramphenicol)	14	7 0	17	6 1

Symptoms and signs were recorded daily on a standard chart by one of two observers who were unaware of the group to which the patient had been allotted Subsequently, some cases were excluded because of an associated attack of malaria, or because the diagnosis was not confirmed This resulted in uneven numbers of patients appearing in each group, the numbers being group A (controls), 31, group B (penicillin), 21, and group C (chloramphenicol), 31 (total 83)

Table II shows the average day of illness when the patients were admitted, and the day on which treatment was started In the control group the day of admission was called the first day of treatment, which consisted in rest in bed, fluid replacement, and analgesics for pain This regime was also employed in groups B and C, but the day when antibiotics were first given was termed the day that treatment was started. There was a time-lag of approximately twenty-four hours in the start of treatment in groups B and C.



Days of illness on which treatment was started and patients became free of symptoms and signs in A controls, B patients treated with penicillin C, patients treated with chloramphenicol

Results

Table III shows the average time from onset of symptoms until the patients were symptom-free, sign-free, and apyrexial

There was no significant difference between the duration of illness in the three groups This is most convincingly shown in the last column of table III Symptoms and signs developing during a relapse are considered separately

The patients in each group are classified in table IV into those whose treatment was begun on or before the fourth day, and those whose treatment was begun on or after the fifth day Table IV shows that early treatment with antibiotics did not shorten the average length of the illness, in fact in all three groups the average number of days taken to become symptom-free and sign free was greater when treatment was started early This is confirmed by the accompanying figure, in which the day on which the patient became free of symptoms and signs after the start of treatment is plotted against the day on which treatment was started The wide scatter is not influenced by the antibiotics

"*After-peaks*" *of Pyrexia*

An "after peak" of pyrexia is here arbitrarily defined as any rise of temperature to 100°F or over, forty-eight or more hours after the patient first became apyrexial A few patients had transitory rises in temperature below 100°F unassociated with symptoms and signs, but these were regarded as insignificant

TABLE V—INCIDENCE OF JAUNDICE, OLIGURIA, AND ANURIA

Treatment group	No of patients with jaundice	No of patients with oliguria or anuria
A (controls)	2	2
B (penicillin)	Nil	1
C (chloramphenicol)	1	1

"After-peak" pyrexia occurred in only 14% of all the patients 6 were in group A (controls), 3 in group B (penicillin), and 3 in group C (chloramphenicol) The numbers are too small for any definite conclusions

Complications

Jaundice, and oliguria or anuria—Table V shows the incidence of these complications in each treatment group There was no significant difference between the three groups, but the numbers were too small for us to draw any definite conclusions from them

TABLE VI—BLOOD UREA LEVELS

Treatment group	Av day of illness blood urea first estimated	No of patients with blood urea estimated every third day	No of patients in whom blood urea rose after start of treatment
A (controls)	4 3	12	4
B (penicillin)	3 7	10	2
C (chloramphenicol)	3 3	11	4

Uræmia—In 33 patients admitted before the fifth day of their illness, the blood-urea level was estimated on admission and then every third day In 10 of these cases the level rose by 15 mg per 100 ml or more during treatment—the higher blood urea level always being above 40 mg per 100 ml The results are shown in table VI The numbers are small, but there is no significant difference between the distribution among the three groups.

Discussion

In this series no benefit was obtained from the administration of penicillin or chloramphenicol, and we suggest that these two antibiotics have no place in the treatment of leptospirosis in Malaya

This series included many mild cases, and complications were few. Because leptospirosis is common among troops in Malaya, the standard of diagnosis is high and few cases are missed, whereas in countries where the disease is rare it is mainly the more severe cases that are recognised This may partly account for the different descriptions of the severity of leptospirosis throughout the world In our series the serotypes were widely represented (table I), this suggests that if penicillin and chloramphenicol are of no value in the treatment of leptospirosis in Malaya, it is unlikely that they will prove useful elsewhere

Summary

A controlled trial of penicillin and chloramphenicol in the treatment of leptospirosis among British troops in Malaya is reported

Patients were placed in rotation in one of three groups One group of patients received no antibiotics and acted as control The second group received penicillin, and the third group received chloramphenicol

There were no significant differences between the three groups in the times taken to become symptom free and sign-free and apyrexial, or in the incidence of complications This was true even when treatment was started on or before the fourth day of the illness

Penicillin and chloramphenicol play no useful part in the treatment of uncomplicated leptospirosis in British troops in Malaya, and we suggest that these antibiotics are unlikely to be of value in the treatment of leptospirosis elsewhere

We thank Lieut General Sir Frederick Harris for permission to publish this paper, Colonel A P Trimble, consulting physician to the far eastern land forces, for his help throughout the trial, the sisters of the Q A R A N C for their coöperation in this work, and Dr J. C Broom for his help and advice

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DUODENAL BIOPSY

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THE method of gastric biopsy by blind suction through a gastric biopsy tube (Wood et al 1949) has been safely applied to many patients (Doig 1954, Palmer 1954, Joske et al 1955) but has not hitherto been extended to biopsy of the duodenum.

It was thought that a modified tube might be passed beyond the pylorus to sample duodenal or even jejunal mucosa, and that this technique might be of diagnostic value in such conditions as steatorrhœa, Crohn's disease, "duodenitis," and dyspepsia without positive radiographic findings.

The main modifications required were greater length and a shorter head embedded in a rounded metal shield. X-ray control was essential in guiding the course of the tube.

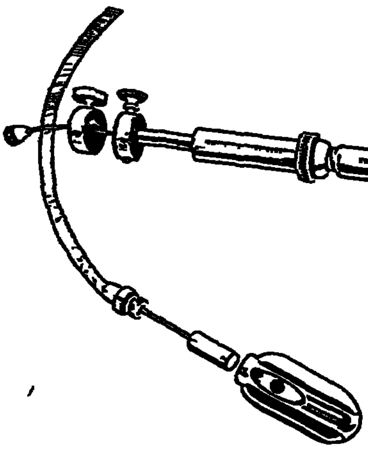


Fig 1—Tube 1: headpiece and tailpiece.

The histological findings of 12 successful duodenal biopsies are reviewed here.

Method and Patients Studied

The duodenal biopsy tube (fig 1) is a flexible tube, 128 cm long and 4·8 mm in diameter coated with plastic material to make it smooth and airtight. Its headpiece is a small tube 3·9 mm in external diameter, at whose centre is the circular biopsy aperture 3·1 mm in diameter. In this small tube the knife-cylinder is accommodated which is screwed to the wire running along the whole length of the instrument and ending in a small holder at the tailpiece. The small tube of the headpiece is embedded in a solid weighty elliptical nickel ball 12·3 mm in diameter to give smooth easy forward propulsion by gastric and duodenal peristalsis. The tailpiece contains the other end of the wire and the lateral exhaust-tube, to which a syringe or a pressure manometer can be attached to apply negative pressure.

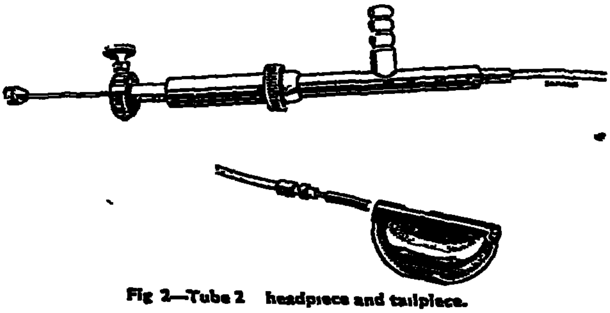


Fig 2—Tube 2: headpiece and tailpiece.

Fig 2 shows a second duodenal biopsy tube, which was used originally. It is as long as the first tube but only 2·7 mm in diameter. The headpiece is rather weightier and 14·2 mm in diameter. The biopsy aperture measures 2·3 mm in diameter and the small tube within the headpiece 3·1 mm in diameter. Both tubes have been used with about equal success.

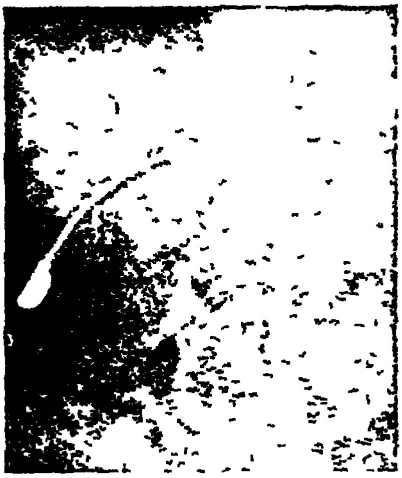


Fig 3—Headpiece of duodenal biopsy tube in first or second part of duodenum.

Samples were obtained from 12 patients with gastro-intestinal symptoms. In 7 the diagnosis was in doubt even after full radiographic and other studies. In the remaining 5, who had gastric ulcer (2), duodenal ulcer (2) and hiatus hernia (1), the instrument was used primarily for gastric biopsy; but, since there was no difficulty in passing the tube beyond the pylorus, duodenal biopsy was done as well. The procedure was carefully explained to the patients and permission obtained from all.

The fasting patient gargles with 2–3 ml of 1% amethocaine solution. The stomach need not be emptied beforehand, because gastric juice does not interfere with duodenal biopsy. With the patient lying relaxed on his left side with knees drawn up and head and trunk on the same level, the well-oiled tube is passed into the stomach. The tube is occasionally held up at the pharynx and the cardia; but this can easily be overcome by making the patient swallow and by exerting gentle pressure on the tube. When the stomach is reached, the head end of the tube is guided, under fluoroscopic control, by the palpating hands of the operator on the patient's abdomen. As soon as the required position in the duodenum is attained (figs 3 and 4) the biopsy is attempted. The wire is operated at the tailpiece to open the biopsy aperture, and a negative pressure of at least 25 inches Hg is applied. Then a sharp closing movement of the wire will secure the biopsy specimen within the knife-cylinder. If it is necessary to take samples from different levels, the position of the headpiece may be adjusted and the manœuvre repeated. Before the tube is withdrawn, its position is again checked fluoroscopically. After withdrawal the specimens are freed from the knife-cylinder and placed in 15% formol saline solution.

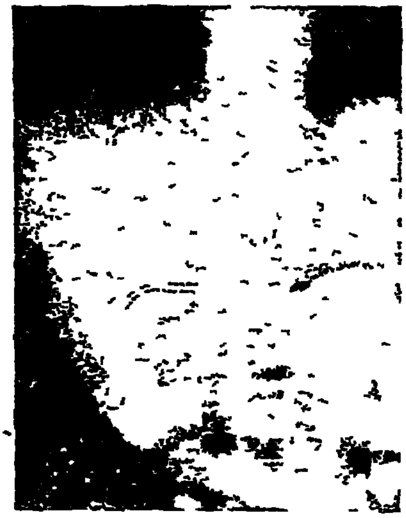


Fig 4—Headpiece of duodenal biopsy tube in second or third part of barium-filled duodenum.

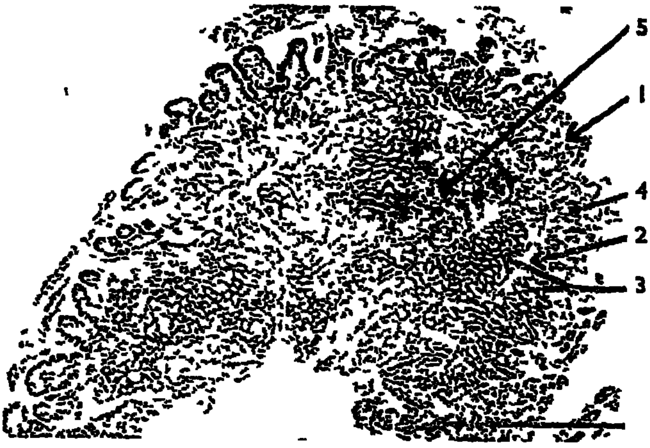


Fig 5—Type-1 biopsy specimen 1, villi, 2, muscularis mucosæ, 3, Brunner's glands, 4, crypts of Lieberkühn 5, hæmorrhage (Hæmatoxylin and eosin × 19)

or in formol calcium, and histological preparations are made The patient is given a light meal and closely observed for twenty-four hours No complications developed in the present 12 cases

Results

Duodenal biopsy was attempted in 19 cases and was successful in 12 of them Many of the earlier failures were due to inexperience and lack of practice The failures were due to inability either (*a*) to reach the duodenum or (*b*) to obtain specimens Inability to reach the duodenum was due to spasm at the pharynx, the cardia, or the pylorus Spasm at the first two sites was usually overcome when the patient relaxed, but spasm at the pylorus did not seem to be under voluntary control and caused failure in 2 patients Inability to obtain specimens when the duodenum was reached was responsible for 5 more failures and was probably due to earlier technical difficulties in the construction of the tubes

The size of the specimens was difficult to measure Usually several specimens were clumped together, and attempts to separate them before fixation may have broken them up The number of specimens obtained varied from 1 to 5 In size they compared well with those obtained by gastric biopsy The naked-eye appearances were those of small fleshy pinkish pieces of tissue held together by mucus The depth of the specimens varied according to their site, being deepest in the first part of the duodenum and becoming progressively less deep distally Of the 12 specimens 2 were not deep enough to warrant detailed histological description

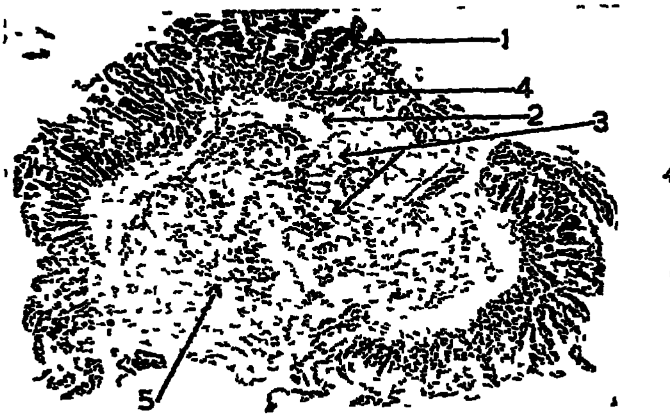
Histology

No correlation of the histological appearances of the duodenum with the clinical diagnosis has yet been attempted, nor does the number of biopsy specimens studied permit histopathological classification or comparison The over all histological appearances assumed three different patterns varying with the levels of duodenum from which the specimens were taken Some of the specimens showed typical Brunner's glands, whereas others showed the type of mucosa usually associated with the small intestine

Type 1—Of the 12 specimens 2 showed this histological pattern The site from which they were taken is shown in fig 3 The specimen shown in fig 5 comprises the full depth of mucosa and submucosa The villi are well marked though somewhat shorter and broader than those of type 2 (see below) Their surface epithelium contains columnar cells with goblet cells interspersed between them The stroma of the villi and lamina propria of the mucosal layer contains a moderate amount of lymphocytes, plasma cells, a few eosinophils, and an occasional polymorph The crypts of Lieberkühn and their glands lie in the mucosal layer and are continuous superficially with the surface epithelium and deeply with Brunner's glands They are composed of low columnar cells, Paneth cells, and argentaffin cells A thin layer of smooth muscle fibres, the muscularis mucosæ, separates the mucosa from the submucosa It is occasionally penetrated by a group of Brunner's glands, though most of these glands are found in the submucosa, which is rather deep containing numerous groups of Brunner's glands, characterised by their low columnar cells with clear cytoplasm and flat basal nuclei These groups of glands are separated by strands of fibrous tissue

Type 2—This type was seen in 3 specimens and differs from type 1 in possessing longer and narrower villi, denser cellular infiltration, and a rather thick layer of muscularis mucosæ In the specimen shown in fig 6 only a small group of Brunner's glands is evident at the centre, lying in the submucosa The type of cellular infiltration is similar to that described in type 1

Type 3—This type was seen in 5 specimens Fig 4 shows the site from which the specimen shown in fig 7 was taken, probably the third part of the duodenum Again, as in type 2, the villi are high and branching, and the muscularis mucosæ is rather thick and well developed Brunner's glands are not seen either above or below the muscularis mucosæ I have recently obtained several jejunal biopsy specimens from a patient who had previously undergone a Polya gastrectomy The histological appearances of these jejunal specimens resembled in every respect those seen in type 3 Possibly the lower part of the duodenum has the same histological pattern as the small intestine



ig 6—Type-2 biopsy specimen 1 villi 2 muscularis mucosæ 3, Brunner's glands in submucosa 4 crypts of Lieberkühn, 5 hæmorrhage (Hæmatoxylin and eosin × 23)

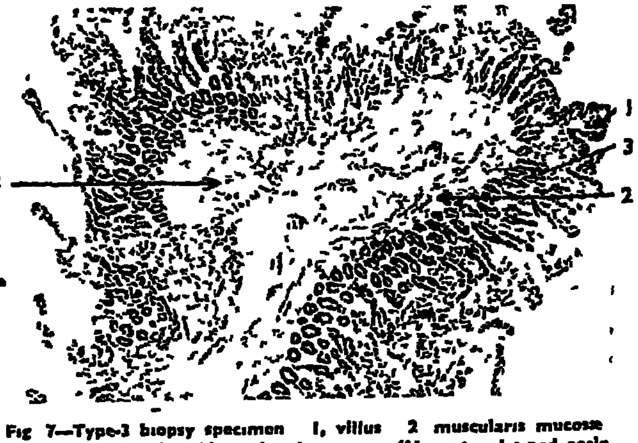


Fig 7—Type-3 biopsy specimen 1, villus 2 muscularis mucosæ 3, crypts of Lieberkühn 4 submucosa (Hæmatoxylin and eosin × 35)

Discussion

This technique has proved safe and satisfactory in obtaining duodenal specimens, but it has the disadvantage that the specimen is taken blindly and its exact position in the duodenum is uncertain If a little barium is given before the tube is passed, it may be possible to determine what part of the duodenum is being subjected to biopsy

As regards the construction of the two tubes, the advantage of tube 2 (fig 2) over tube 1 (fig 1) lies in possessing a larger and weightier headpiece on a narrower shaft The duodenum is reached with greater ease, and the long wire does not coil inside the narrow plastic tube The disadvantage lies in the smaller negative pressure obtained through this narrow tube Earlier failures to obtain specimens were attributed to this technical defect, so tube 1 was constructed with a greater diameter It was found that the wire tended to coil much more, but the size of the biopsy aperture and the improved suction were very satisfactory The range of movement of the knife cylinder to open and close the biopsy aperture is necessarily small and controlled at a point some distance away Moreover the tube, once in the desired position is not straight The curves of the tube vary from patient to patient, and there is no way of regulating the wire's movements beforehand It is therefore evident that a more certain way of knowing when the aperture is open is required Experience in handling the instrument has largely, if not entirely, overcome this difficulty

The risks attending duodenal biopsy are probably comparable to those attending gastric biopsy—namely, perforation of the pharynx, œsophagus, or stomach, and hæmorrhage, usually hæmatemesis Perforation has been reported in 1 of 589 cases (Coghill and Williams 1955), in none of 1226 cases (Joske et al 1955), and in none of 1000 cases (Doig 1954) Hæmatemesis is more common but rarely fatal it has been reported in 7 of 589 cases (Coghill and Williams 1955) and in 8 of 1000 cases (Doig 1954) No complications developed in my own series of 130 gastric biopsies, and in the present 19 attempts at duodenal biopsy

As already stated, 2 of the 12 successful duodenal biopsies did not yield enough tissue to warrant detailed histological analysis This is another difficulty peculiar to duodenal biopsy The gastric surface epithelium is smooth though thrown into rugæ, whereas the duodenum has large branching villi in continuous motion, with much debris and mucus overlying them Sometimes cellular debris and the tips of a few villi only are caught within the biopsy aperture Other specimens showed a satisfactory depth of mucosa, but the villi appeared "decapitated"

The three histological types described seem to represent different levels of duodenum Type 1 comes from the first and second parts of the duodenum and shows typical Brunner's glands Type 3 comes from the second and third parts of the duodenum and resembles intestinal mucosa A detailed study of the level at which one type of mucosa changes into the other is obviously necessary

Another point of interest for future studies arises from the part played by the duodenum, especially its lower end, in various diseases of the small intestine A jejunal biopsy specimen was obtained in 1 patient with a Polya gastrectomy Slight modification of the duodenal biopsy tube may enable us to reach the normally sited jejunum

Summary

A method of blind duodenal biopsy is described, and 12 biopsy specimens are discussed

The difficulties and the possible practical applications of the method are mentioned

The attendant risks are compared with those of gastric biopsy

No complications developed in 19 attempts at biopsy

My thanks are due to Dr Sheila Sherlock for stimulating and helpful criticism, the Genito Urinary Manufacturing Company, particularly Mr G Hawkins, for coöperation in constructing the duodenal biopsy tube, Miss E J Wernli for helpful assistance, Mr J G Griffin for the histological preparations, Mr F G Saunders for the drawings, and Miss R Klein for the photomicrographs

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THE HOSPITAL STAPHYLOCOCCUS

A COMPARISON OF NASAL AND FÆCAL CARRIER STATES

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The frequency with which staphylococcal disease is acquired in hospital causes increasing concern (*Lancet* 1955a) It is widely held that the nasal carrier is the main source of infection in outbreaks of such disease Is this the whole truth? We draw attention here to the fæcal carrier as a potential source of infection in staphylococcal disease and point out that such a carrier is commonly also a nasal carrier

Brodie et al. (1955) emphasised the value of serological typing of staphylococci in the study of outbreaks of staphylococcal disease This method of typing was adopted in the present study The search for fæcal carriers was based on isolations from rectal swabs Confirmation that the source of these strains was the fæces, and *not* the skin of the buttocks, was obtained by a series of comparative tests of the nose, skin, and fæces

The simultaneous search for nasal and fæcal carriers was made in two dysentery wards in which there was an outbreak of staphylococcal disease at the time of the survey

Results of Survey

CARRIER STATE IN THE WARDS

Table I compares the "snapshot" picture of the carrier status at the start of the survey with that of patients on admission to and after one week's residence in hospital This table includes the results for nasal and fæcal strains The following points are to be noted

(1) The general picture obtained by the single "snap shot" is little different from that obtained from the group of patients examined after one week's stay in hospital

TABLE I—COMPARATIVE ANALYSIS OF CARRIER STATES

—	56 ward patients at start of survey		127 patients on day of admission		74 ward patients after 1 week in hospital	
	Nasal swab	Rectal swab	Nasal swab	Rectal swab	Nasal swab	Rectal swab
Coagulase-positive	23 (*41%*)	21 (*38%*)	26 (*20%*)	22 (*17%*)	28 (*38%*)	28 (*38%*)
No serotype ac/	16 (*29%*)	16 (*29%*)	8 (*6%*)	6 (*5%*)	20 (*27%*)	26 (*35%*)
Other serotypes	7	5	18	16	8	2

TABLE II—ANALYSIS OF SIMULTANEOUS ISOLATION FROM NASAL AND RECTAL SWABS

Total no	No with same sero type	No both ac/-	Resistance patterns of ac/					No with different sero types
			No both POCST*	No both POCCST†	No nasal/POCST rectal/POCCST	No both POCCS‡	Others	
63	50	43	12	4	15	4	8	13

* POCST resistant to penicillin, oxytetracycline, chlortetracycline, streptomycin and tetracycline, sensitive to chloramphenicol and erythromycin

† POCCST = POCST, except resistant also to chloramphenicol

‡ POCCS = POCST, except sensitive to tetracycline

(2) On admission, 20% (26/127) of patients were nasal carriers, compared with 38% (28/74) after one week in hospital

(3) 17% (22/127) were fæcal carriers on admission, compared with 38% (28/74) after one week in hospital

(4) 6% (8/127) were carriers of serotype ac/- of nasal origin on admission, compared with 27% (20/74) after one week in hospital

(5) 5% (6/127) of patients were carriers of serotype ac/- of fæcal origin on admission, compared with 35% (26/74) after one week in hospital

(6) Residence in hospital resulted in a fall in the prevalence of carriage of all serotypes other than serotype ac/- This applied to both nasal and fæcal strains

The results obtained by antibiotic sensitivity testing of serotype ac/- confirmed the general experience that one week's residence in hospital was associated with a high frequency of infection with cross resistant strains But, whereas nasal strains were resistant to penicillin, oxytetracycline, chlortetracycline (aureomycin), streptomycin, and tetracycline, fæcal strains were resistant to these antibiotics and also to chloramphenicol All strains isolated from patients after one week in the ward were sensitive to erythromycin

SIMULTANEOUS CARRIAGE IN NOSE AND INTESTINE

Of 63 patients no fewer than 50 were nasal and fæcal carriers at the same time Of these 50, 43 were carrying serotype ac/- The resistance patterns of these strains differed considerably Some nasal and fæcal strains showed the same resistance patterns, while others exhibited different patterns Indeed, in one group of 15 patients the fæcal strains were resistant to chloramphenicol and 5 other antibiotics, whereas the nasal strains, although resistant to the 5 antibiotics, were sensitive to chloramphenicol (table II)

Discussion

Residence in hospital for one week resulted in an increase in the fæcal carrier-rate from 17 to 38% for coagulase positive staphylococci and from 5 to 35% for serotype ac/- staphylococci Hospital infection with serotype ac/- was in all cases an infection with antibiotic cross resistant strains A comparable rise in the nasal carrier rate also occurred over the same period

Oeding and Austarheim (1954), in a study of the intestinal conten[illegible] of routine necropsy material reported the frequent occu[illegible]ce of staphylococci in patients who had been treated w[illegible]th antibiotics The predominant serological type in th[illegible]s study was the enterotoxin producing group abc or a[illegible] which appears to be the same as our serotype ac/

The frequency with wh[illegible] intestinal infection with serotype ac/- staphylococci is [illegible]equired in hospital seems to have a twofold significance First it may explain pseudomembranous enterocolitis and diarrhœa starting during the first eight days after partial gastrectomy (*Lancet* 1955b) Secondly it underlines the need to reconsider our ideas about the sources of staphylococcal infection with particular reference not only to the nasal carrier but also to the fæcal carrier This change in outlook regarding the sources of infection must inevitably have repercussions on our ideas about the method of transfer of infection and the means of preventing cross infection

It seems reasonable to suppose that the "weight" of organisms released to the environment by the fæcal carrier greatly exceeds that of organisms released by the nasal carrier, and this would explain the ease with which staphylococci can be recovered from the hospital air and dust It also raises the question of the transfer of staphylococci by the fæcal oral route in the same way as that which is believed to operate in bacillary dysentery and infantile gastro enteritis

The tracing of sources of infection in staphylococcal outbreaks is possible only by typing The value of phage typing has been established at the academic level This is time consuming and specialised work The method of typing in this investigation has the merit of being within the scope of the clinical pathologist The only special requirement is the preparation and issue of standard antisera

Summary

Analysis of staphylococci by serological typing and sensitivity testing has shown that the staphylococcus carrier state of the general community (new admissions to hospital) differed from that of a hospital community

The general carrier-rate was doubled as a result of hospitalisation

Nasal carriers of serotype ac/- increased fourfold (from 6 to 27%), while fæcal carriers increased sevenfold (from 5 to 35%)

In hospital practice the fæcal carrier of staphylococci, especially serotype ac/-, seems to play a more important part in communicating staphylococcal disease than has been realised

We thank Prof W J Tulloch for encouragement, Dr W Jamieson for clinical facilities, Mr H Lawrence, A I M L T, for technical assistance, and the Medical Research Council for an expenses grant to one of us (T S) for a technician.

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MONILIASIS TREATED WITH PENTAMIDINE

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THE successful treatment of two cases of thrush œsophagitis with hydroxystilbamidine has been reported by Wolff et al (1955)

In vitro experiments (Stenderup 1955) have shown that even low concentrations of stilbamidine and pentamidine often prevent the growth of *Candida albicans* We have therefore tried pentamidine in the treatment of moniliasis and report here the results obtained in three cases All three patients had chronic malignant disorders, and it is well known that such patients are very susceptible to infection by *C albicans*

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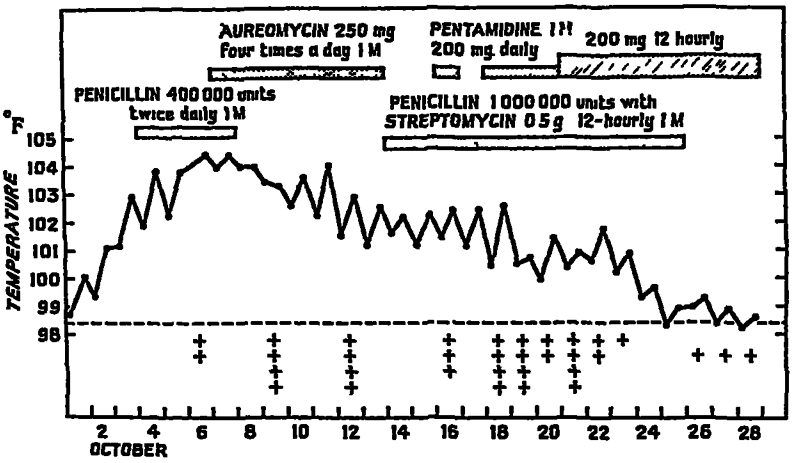
* Lady Tata Memorial scholars Aided by grants from the Anders Hasselbalch Anti Leukæmia Foundation and C P Schepler and Wife's Bequest, the Irma Foundation



Course and treatment in case 1 each + represents a colony of C albicans

Case-reports

Case 1—A man, aged 57, was admitted to hospital on Sept 14 1954, with chronic myeloid leukæmia On Oct 2 he became febrile and complained of pain in his left flank below the left costal margin on breathing He had no rigors, cough, or dyspnœa, but produced a little yellowish sputum Auscultation of his lungs revealed signs of pneumonia, and radiography showed a homogeneous opacity in the upper lobe of his right lung

Treatment and Course—Treatment with penicillin, aureomycin (chlortetracycline), and penicillin with streptomycin successively was unsuccessful (see figure), the patient became worse and cyanosis and dyspnœa developed Repeated bacteriological studies of the patient's sputum failed to reveal any pathogenic bacteria but showed increasing numbers of colonies of *C albicans* until they were present in almost a pure growth Therefore a course of intramuscular pentamidine 200 mg daily was started on Oct 16 By mistake no pentamidine was given next day, but from Oct 18 daily injections were given The response not being satisfactory after the first few days' treatment, the dose was increased to 200 mg twelve hourly on Oct 21 This led to rapid clinical improvement, and four days later the patient's temperature had returned to normal Daily mycological study of the sputum showed that the number of colonies of *C albicans* decreased with the fall in temperature (see figure) Pentamidine was given for the last time on Oct 28, and on Nov. 3 no fungi could be isolated from the sputum

In vitro studies of the patient's strain of *C albicans* showed that pentamidine in a concentration of 1/512 mg per ml of substrate partially inhibited growth, and 1 128 mg per ml of substrate completely suppressed macroscopic growth (for technique see Stenderup 1955)

Case 2—A man, aged 25, was admitted to hospital on May 27, 1955, with Hodgkin's disease of three years' duration During this period his condition had become progressively worse During his stay in hospital he complained of feeling as if he had a lump in his throat and of retrosternal pain in swallowing Inspection of the throat revealed a white membrane covering the pillars of the fauces and the posterior wall of the nasopharynx, from which *C albicans* was isolated Radiography of the œsophagus showed no abnormalities

Treatment and Course—The symptoms were thought to be due to monilial infection extending into the œsophagus, so treatment with intramuscular pentamidine 200 mg daily was started on July 9 Œsophagoscopy a few days later showed that the hypopharynx and the upper part of the œsophagus were covered with a dense white fungous membrane, and the underlying mucosa was red and œdematous and tended to bleed Since the mucosa seemed to be very friable, the œsophagoscope was introduced for a distance of only 20 cm Culture of a biopsy sample yielded a heavy pure growth of *C albicans* During pentamidine therapy the discomfort of the throat rapidly subsided, and after twelve days' treatment both the faucial coatings and discomfort had disappeared completely Pentamidine was therefore discontinued, and œsophagoscopy showed that the entire œsophagus was almost normal The mucosa was perhaps slightly swollen, and a few pinhead sized plaques persisted from which *C albicans* could still be isolated

Case 3—A man, aged 35, had had Hodgkin's disease from the age of 8 years and had been given large doses of X rays to enlarged lymph nodes of the head and neck After a course of irradiation in 1953 he complained of dryness and burning pain in his mouth His oral, lingual, and pharyngeal mucosa became atrophic, with a tendency to the formation of crusts, purulent secretion, and hæmorrhages These changes persisted and caused him great discomfort, and he was admitted to hospital on Sept 9, 1955

On admission he was critically ill, very weak, and anæmic He complained of the aforesaid symptoms in his mouth and throat and of white coatings in his mouth, which had lasted a couple of months and caused him considerable discomfort He had difficulty in swallowing and thought he had lost weight

Examination revealed that his entire oral mucosa, his tongue, the pillars of his fauces, and his pharyngeal wall were completely covered with a thick yellowish membrane, and his breath was offensive Œsophagoscopy showed that this membrane was present all over the œsophageal mucosa right down to the cardia Culture of the membrane grew *C albicans*, *C pseudotropicalis*, and *C krusei* In vitro studies showed that pentamidine in a concentration of 1/512 mg per ml of substrate suppressed the growth of all three species

Treatment and Course—From Sept 8 intramuscular pentamidine 200 mg twelve hourly was given After a week's treatment only scattered plaques remained on the oral and pharyngeal mucosa Œsophagoscopy on Sept 15 showed that the œsophagus was still covered by a membrane, which, however, was less adherent, the underlying mucosa was red and inflamed and tended to bleed Pentamidine therapy was therefore continued The general condition of the patient deteriorated, and the symptoms due to the state of the mucosa did not subside, even though the monilial infection decreased On the morning of Sept 21 the patient was found unconscious in bed, and he died a few hours later

Necropsy revealed extensive granulomatous change in the spleen, liver, and lymph nodes, probably due to atypical Hodgkin's disease No membranes on the hypopharynx and œsophagus were visible to the naked eye The œsophageal mucosa was red and atrophic, and microscopy revealed chronic œsophagitis Scattered fragments of mycelium and candida spores were still present

The objective improvement of the moniliasis, despite the deterioration of the general health and the poor condition of the oral and pharyngeal mucosa, seems remarkable and must be ascribed to the treatment with pentamidine

Discussion

In view of the good results obtained with pentamidine in these cases and with hydroxystilbamidine in the cases of thrush œsophagitis reported by Wolff et al (1955) the diamidines must be assumed to be useful in the treatment of moniliasis

The effects were not obtained in the present cases so quickly as in those treated by Wolff et al This may be due to the fact that these workers administered the drug intravenously Hydroxystilbamidine may also exert a greater effect than pentamidine does on *C albicans*, but it is scarcely possible to be definite about this, because different strains of *C albicans* may differ in sensitivity even to the same diamidine

Summary

Three cases of moniliasis were successfully treated with pentamidine

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THE EFFECT OF 3:5:3′-TRIBROMO-DL-THYRONINE IN MYXŒDEMA

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It has been shown (Mussett and Pitt-Rivers 1954) that DL-tribromothyronine possesses considerable activity in preventing thiouracil-induced goitre in rats. In these experiments it was found to be nearly half as active as DL-thyroxine, while DL-tetrabromothyronine only had about 1/200 of the activity of thyroxine. Tetrabromothyronine has previously been shown to have some thyroxine-like activity in man (Lerman and Harington 1949). It is possible, however, in view of the 100-fold difference in the goitre-preventing activity of tribromothyronine and tetrabromothyronine, that the response in human myxœdema obtained by Lerman and Harington may have been, in part, due to contamination of the tetrabromo compound with tribromothyronine. In the present study the tribromothyronine used was demonstrated to be chromatographically free from the tetrabromo compound.

This study was not undertaken in anticipation of any therapeutic advantage of tribromothyronine over other thyroxine analogues but because the demonstration of high thyroxine-like activity of non-iodine-containing analogues of thyroxine in man must cause a reorientation of fundamental views of thyroid physiology.

Two myxœdematous patients have now been treated with tribromothyronine.

Case-reports

Case 1.—A man, aged 68, was first seen as an outpatient on Dec. 17, 1954. He complained of swelling of the hands and feet and of "big bladders" around the eyes for three weeks. He admitted to excessive lethargy, rising weight, constipation, coldness and pins and needles in the legs, "thickness" of the voice, and increasing deafness for a few months. The history was amplified by his wife, who stated that for two years, since giving up his work as a butcher, he had become progressively more slow in all his activities. He had tended to fall asleep at the slightest opportunity and spent his day huddled over the fire.

Examination.—When admitted to the Royal Free Hospital on Dec. 30, his appearance was typical of myxœdema. His responses were slow but there was no suggestion of psychosis. His voice was very low pitched and rasping. His features were coarse, his skin thickened and dry. He had supraclavicular pads. His scalp hair was normal but his eyebrows were deficient. He had pitting œdema of the hands, feet, and ankles. His mucosæ were normal. No thyroid tissue was palpable. His pulse-rate was 64, pulse regular, blood-pressure 180/105 mm. Hg; there were no signs of congestive heart failure, and no abnormality was found on examination of the heart. The lungs, abdomen, and central nervous system were normal.

On clinical grounds a diagnosis of primary myxœdema was made.

Investigations

The basal metabolic rate (B.M.R.) was −34% (Aub Du Bois) and the blood-cholesterol level 300 mg. per 100 ml. The uptake of radioactive iodine was subnormal, only 9% of the dose being taken up in the neck at twenty-four hours. Radiography of the chest showed cardiac enlargement, with normal lung fields. Hæmoglobin 13·3 g. per 100 ml. (90%); no morphological abnormality of blood-cells; generalised hypoplasia in bone-marrow. Electrocardiography showed sinus rhythm, normal voltage, Q R S 0·13 sec., and left bundle-branch block.

Treatment and Progress

Treatment with tribromothyronine was begun on Jan. 13, 1955. In view of the patient's age and electrocardiographic evidence of degenerative heart disease very small doses (100 µg.) of intramuscular tribromothyronine were used initially and gradually increased to 1000 µg. This dosage was also indicated because the degree of thyroxine-like activity that tribromothyronine might prove to have in man was unknown.

Progress was judged clinically, by B.M.R., by blood-cholesterol levels, by weight changes, and by fluid balance. The dosage of tribromothyronine and other data are recorded in fig. 1.

Soon after the start of treatment the patient stated that he felt better and he became increasingly alert and active. His voice, by the end of the period of study, was normal, and hearing had improved. His B.M.R. had risen from −34% to 0%, his blood-cholesterol level had fallen from 300 mg. to 144 mg. per 100 ml., and his weight from 159½ lb. to 138 lb. There was a period from five to ten days after the start of treatment when his weight increased temporarily in association with increasing œdema of the legs.

Fig. 1 shows that about four weeks after the start of treatment the character of the fluid-balance chart alters. At that time, and for three weeks subsequently, the patient's fluid intake was equalled by his urinary output. Although dietary fluid and insensible fluid loss have not been included in the fluid balance, probably during this period he was in a negative fluid balance owing to a diuresis.

Treatment with tribromothyronine was discontinued on March 30 and he has since then been maintained on thyroid gr. 4 daily. During a further three months' observation he has remained clinically normal, his weight has been steady, and his B.M.R. has remained in the normal range.

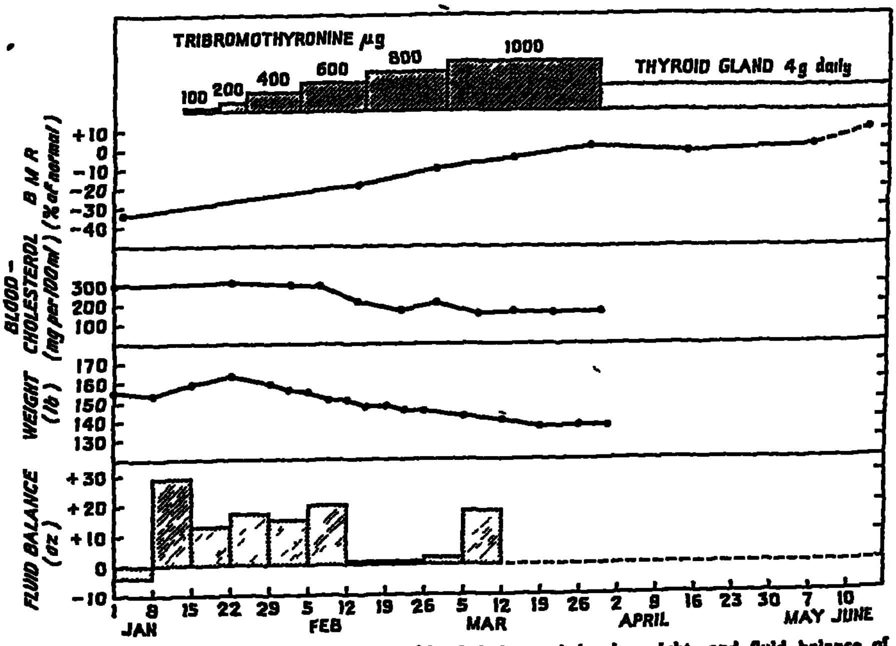

Fig. 1—Dosage of tribromothyronine, B.M.R., blood-cholesterol level, weight, and fluid balance of case 1. Intake and output of fluid are expressed as the average daily difference during each week of observation.

Case 2.—A man, aged 65, was admitted to the Hampstead General Hospital as an emergency on Jan. 16, 1955. On the

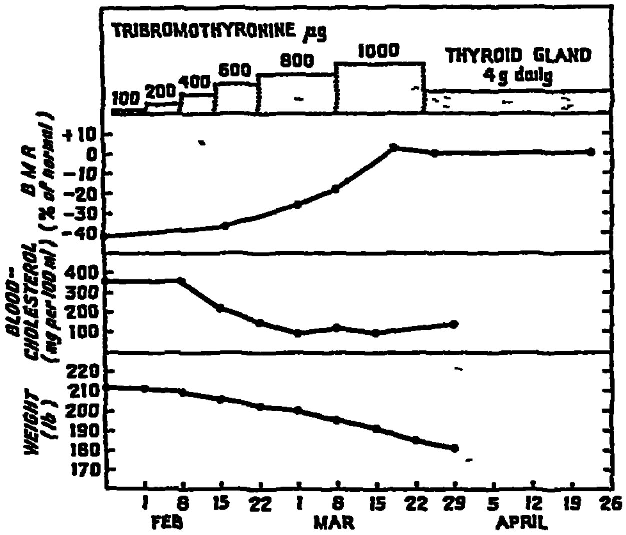

Fig 2—Dosage of tribromothyronine B.M R blood-cholesterol level and weight in case 2.

morning of admission he had suddenly become confused and lost consciousness for an hour. On admission he had dysphasia in association with mild pyramidal tract signs on the right side. He also appeared myxœdematous. At first it was impossible to obtain a history, but after a few days and with the help of his wife the following history was obtained. For some years he had been becoming increasingly lethargic both physically and mentally. He had gained much weight. His eyes had been puffy for a year, and his voice gruff for many years. He had recently felt the cold excessively.

Examination

His scalp hair was coarse and sparse and his eyebrows were thin. His voice was typically myxœdematous. He was deaf and had been so since middle life, but his deafness had increased in the last few years. There was no clinical evidence of anæmia. No thyroid tissue was palpable. The pulse rate was 66 and the blood-pressure 140/100 mm Hg. The apex beat could not be localised, the heart sounds were distant, but no other abnormality was detected. The chest and abdomen were normal. There was pitting œdema of the legs.

On clinical grounds a diagnosis of primary myxœdema was made.

Investigations

The B.M.R. was −40% (Aub Du Bois), and the blood-cholesterol level 356 mg per 100 ml. There was no uptake of radioactive iodine in the neck in twenty-four hours. Radiography of the chest showed moderate cardiac enlargement. Electrocardiography showed sinus bradycardia (54 per min.), low-voltage Q R S complexes, flattened P waves in all leads, and flattened or inverted T waves in all leads. Hb 87%, packed-cell volume 41 mm., generalised hypoplasia of bone marrow with no morphological abnormality.

Treatment and Progress

Treatment with intramuscular tribromothyronine 100 µg daily was begun on Jan 27 and the dose was gradually increased to 1000 µg daily.

Progress was assessed clinically, by B.M.R., by blood-cholesterol levels, and by weight changes (fig 2). There was a temporary increase in œdema for the two weeks following the start of the treatment. Under treatment with tribromothyronine this patient's B.M.R. rose from −41% (Aub-Du Bois) to −2%, his serum cholesterol level fell from 356 to about 100 mg per 100 ml, and his weight decreased from 212½ lb to 185 lb.

On March 24 treatment with tribromothyronine was stopped and the patient was given tab thyroid *B P* gr 4 daily. A month later the B.M.R. was still normal and his clinical state satisfactory. Further observations were impossible, because this patient died after a road accident.

Comment

From these results it is apparent that DL tribromothyronine in a dose of 1 mg daily can restore normal metabolism in myxœdema. In the two present cases normality was maintained, after treatment with tribromothyronine had been stopped, with thyroid gr 4 daily, but owing to the death of the second patient the follow-up was not long enough to establish that dosage as being the permanent requirement. If this dosage is indeed equivalent to 1 mg of tribromothyronine it appears that 1 mg of DL-tribromothyronine is equivalent to 0·4 mg of L thyroxine (the quantity contained in gr 4 of desiccated thyroid).

One may reasonably assume from previous published evidence that the D-isomer in DL-tribromothyronine is virtually inactive in human myxœdema. It therefore appears that tribromothyronine has only slightly less activity than thyroxine itself, since 1 mg of the DL-compound (containing 500 µg of the L isomer) had activity equivalent to gr 4 of desiccated thyroid.

Conclusions

Two patients with primary myxœdema were treated with DL-tribromothyronine.

Both patients responded fully to a daily dose of 1 mg. of this compound.

Tribromothyronine appears to have only slightly less thyroid-like activity than has thyroxine.

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SICKLE-CELL/HÆMOGLOBIN-D DISEASE

IN A MULATTO GIRL

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SICKLE-CELL anæmia is a well known congenital and familial hæmolytic anæmia, first described by Herrick (1910) in a West Indian Negro from Granada. For many years it was considered to be peculiar to Negroes but it occurs also among peoples in whom no negroid ancestry is apparent (Cooley and Lee 1929, Lehmann and Cutbush 1952, Choremis et al 1953).

It owes its name to the peculiar shape assumed by the erythrocytes under reduced oxygen tension, when the hæmoglobin inside the cells does not remain in solution (Perutz et al 1951) and the resultant "crystallisation" or "gelling" is responsible for the characteristic deformity.

The hæmoglobin inside the sickle cells differs from normal hæmoglobin both in its solubility under reduced oxygen tension (Singer and Singer 1953) and electrophoretically (Pauling et al 1949, Wells and Itano 1951). This abnormal hæmoglobin is called hæmoglobin S. The terminology used here for the various types of hæmoglobin is that recommended by the National Institutes of Health (1953).

Neel (1947, 1949, 1951) has shown that hæmoglobin S is inherited as a mendelian dominant, and he has postulated heterozygous and homozygous genes to explain symptomless sickle-cell trait and the true sickle cell anæmia. If an individual receives the hæmoglobin-S gene from one parent only (the heterozygous state), he

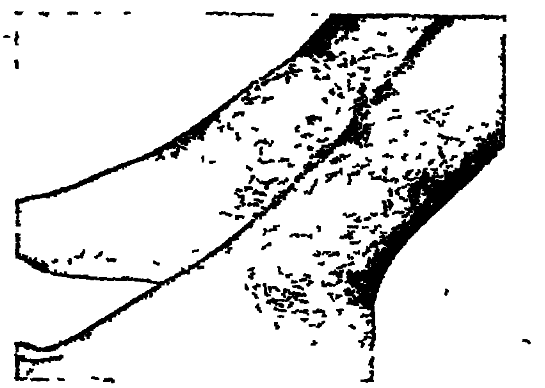


Fig. 1—Ulceration of patient's ankles.

will have the harmless sickle-cell trait, whereas if a hæmoglobin-S gene is received from each parent (the homozygous state), then the individual will suffer from sickle cell anæmia. Sickle cell trait is very much more common than sickle-cell anæmia and occurs in 5–40% of Negroes (Jelliffe et al. 1954).

Neel (1951) recognised that there were occasional exceptions to his hypothesis—for example, cases of sickle cell anæmia in which the erythrocytes of only one parent sickled. Further study of these exceptional cases has disclosed two other abnormal inherited hæmoglobins (C and D) and shown that the inheritance of hæmoglobin S from one parent and either hæmoglobin C (Itano and Neel 1950, Kaplan et al. 1951, 1953, Neel et al. 1953) or hæmoglobin D (Itano 1951, Dacie 1954) from the other produces a condition clinically very similar to sickle cell anæmia.

We report here a case of sickle cell/hæmoglobin-D disease.

Case-report

A single woman, aged 32, attended surgical outpatients with ulceration of her ankles (fig. 1). She was a mulatto with an English mother and was also said to have sickle cell anæmia.

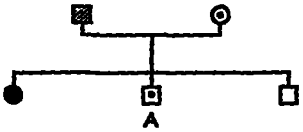
Examination of her blood showed anæmia (Hb 60% = 8·7 g. per 100 ml.). *Her erythrocytes sickled readily into the long filamentous forms typical of sickle cell anæmia (fig. 2).* Fresh wet marrow flecks showed mycelia-like filaments (fig. 3) similar to those described by Vandepitte and Louis (1953). The electrophoretic pattern of her hæmoglobin was indistinguishable from that seen in sickle cell anæmia.

Family History

Thus both clinically and hæmatologically the case appeared to be one of true sickle-cell anæmia in a girl of mixed African and English descent (Stewart and MacIver 1954), but her family history (fig. 4) was most unusual. Her deceased father was a West African Negro, so we assume that he was the source of the patient's hæmoglobin S gene. Her mother was English, and had no known foreign antecedents. Her blood-count was normal and her erythrocytes did not sickle. The patient's two brothers also had normal blood counts, and their erythrocytes did not sickle. The sickle test was made by three different methods—plain wet sealed, 2% sodium metabisulphite, and 2% sodium dithionite—and at least six preparations were made for each member of the family. Only in the patient was the sickle test positive.

Filter-paper electrophoresis of hæmoglobin solutions from all surviving members of the family was done with the vertical tank of Flynn and de Mayo (1951) and a barbitone buffer pH 8·6 at 220 V and 6 mA for 20 hours. The results are shown in fig. 5, including normal and abnormal controls run at the same time. It will be seen that the mother and the brother A have an abnormal band of hæmoglobin of reduced mobility compared with normal hæmoglobin. Density scanning of the strips indicates that about half of each type of hæmoglobin is present in the samples. The patient's hæmoglobin gave a single abnormal band of similar mobility to the abnormal hæmoglobin of her mother and her brother A. In the other brother a normal hæmoglobin pattern was found.

The patient's hæmoglobin was of the same electrophoretic mobility as hæmoglobin S. This can be interpreted as showing that her hæmoglobin is either of this type alone or mixed with hæmoglobin D, which is the only type so far known to be of the same electrophoretic mobility as hæmoglobin S. The electrophoretic pattern in the mother and brother A also shows a band in the S and D position, but their erythrocytes do not sickle.



A See text

● Patient: sickle test positive

▨ Not examined (dead)

◎ Sickle test negative: electrophoresis shows abnormal hæmoglobin

○ Sickle test negative: electrophoresis shows normal hæmoglobin

Fig. 4—Patient's family tree (see text).

Any erythrocytes containing 50% of hæmoglobin S will sickle readily by any of the methods which we used. Therefore this abnormal hæmoglobin must be hæmoglobin D.

We are indebted to Dr. J. C. White, of the Postgraduate Medical School of London, for the following report on the solubility of a hæmoglobin sample from the patient's mother:

“The solubility of the reduced hæmoglobin was determined in pH 6·7 phosphate buffer, ionic strength 4·75. In a system containing 10 g. per litre of protein, the solubility was 5·7 g. per litre. The hæmoglobin-D trait which I examined (Dacie 1954) gave a result of 6·0 g. per litre. These values are below the normal mean, though in the lower normal range, but are far higher than for sickle cell trait under the same conditions.

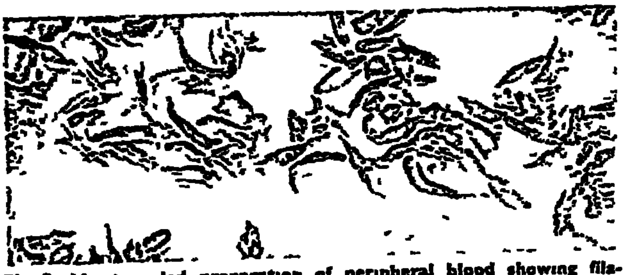


Fig. 2—Moist sealed preparation of peripheral blood showing filamentous sickling (×470).

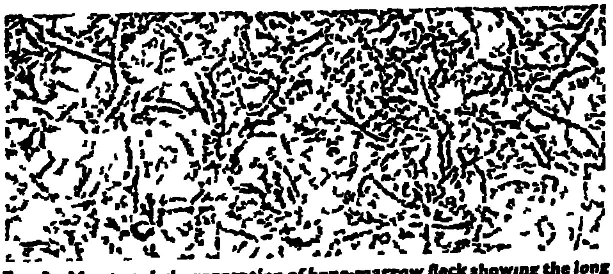


Fig. 3—Moist sealed preparation of bone-marrow fleck showing the long mycelia-like structures (×470).

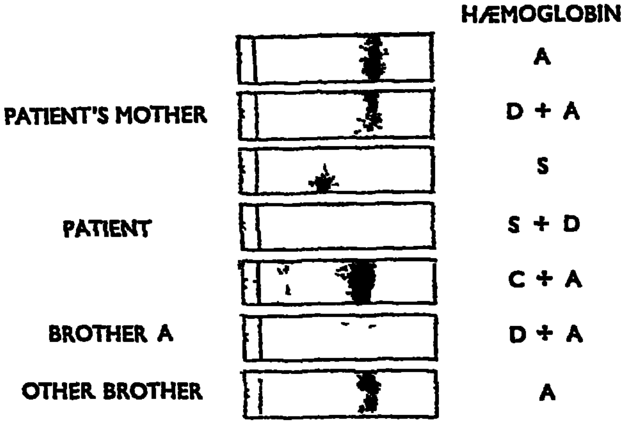


Fig 5—Filter-paper electrophoresis of different hæmoglobins run in parallel

(1–3 g per litre) Together with the electrophoretic result of a normal hæmoglobin fraction and a fraction with the mobility of hæmoglobin S this fully confirms that the patient's mother has hæmoglobin-D trait "

Discussion

Sickle-cell anæmia is usually due to a homozygous gene for hæmoglobin S—in other words, both parents of a patient with sickle cell anæmia usually possess this abnormal gene at least in the heterozygous state (Neel 1947, 1949, 1951) In the present case we must assume the inheritance of the gene for sickling from the father, both because he was a West African Negro and because the mother did not have hæmoglobin S Since there was no normal hæmoglobin (hæmoglobin A) in the patient's erythrocytes, the mother must have passed on the gene for the only abnormal hæmoglobin which she possessed—hæmoglobin D Therefore the hæmoglobin in the patient's erythrocytes must be a mixture of hæmoglobins S and D The electrophoretic pattern of her hæmoglobin is compatible with this hypothesis

We have previously discussed the criteria to be fulfilled before sickle cell anæmia can be definitely diagnosed (Stewart and MacIver 1954) The patient satisfied all these criteria both hæmatologically and clinically Subsequently she was readmitted in extremis, and necropsy revealed pyelonephritis The changes in the other organs were as described for sickle-cell anæmia (Wintrobe 1951) In particular the spleen (fig 6) was very shrunken and measured only $1^3/_4 \times {}^1/_4 \times {}^3/_4$ in

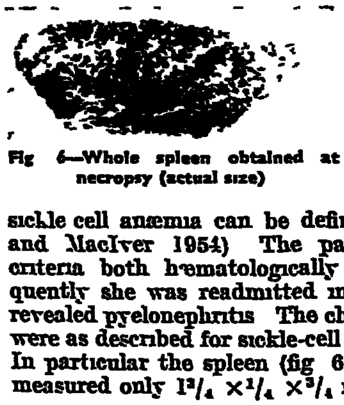


Fig 6—Whole spleen obtained at necropsy (actual size)

It is therefore evident that electrophoretic analysis of the hæmoglobin types present both in patients and their parents is necessary before a diagnosis of true sickle-cell anæmia can be made

Summary

A woman with sickle cell/hæmoglobin-D disease inherited the abnormal hæmoglobin D from her English mother The father, a West African Negro, was dead and is assumed to have supplied the gene for the hæmoglobin S One of the patient's brothers had also inherited the abnormal hæmoglobin D

This case emphasises the importance of investigating obscure hæmolytic anæmias for the presence of abnormal hæmoglobins

We wish to thank Prof A. Kekwick, under whose care the patient was admitted, for allowing us access to the case and for permission to publish, Miss H Silberman for the electrophoretic studies, and Dr P Harrison Hall for the post-mortem report

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Preliminary Communication

WILSON'S DISEASE

NEW ORAL THERAPY

In patients with hepatolenticular degeneration (H L D) there is an accumulation of excess copper in the tissues and an abnormally high excretion of copper in the urine The extensive literature on this subject has been reviewed and discussed by Cartwright et al [1] It has been shown by Cummings [2] and many subsequent workers that the excess copper in these patients can be mobilised by the parenteral administration of dimercaprol (BAL), intravenous 'Versene' and intravenous amino-acids are also effective,[1 3] and cortisone and high-protein diets have been found of value as adjuvant therapy [4] Dimercaprol has proved the most effective of these forms of treatment and if given over long periods causes distinct clinical improvement, particularly in patients with the more chronic forms of the disease [5] However, repeated injections of dimercaprol are extremely painful and are often associated with undesirable side-reactions, so not all patients can benefit from this form of treatment

The object of the present investigation has been to find a non-toxic compound that could be given by mouth and would promote the excretion of copper The activity of dimercaprol is due to the presence of two thiol groups in the molecule, these compete with the thiol groups in the tissues for the excess copper which is present, and the dimercaprol copper complex is then excreted in the urine Some earlier work [6] has suggested that penicillamine (β, β dimethyl-cysteine) is excreted in the urine after parenteral administration of penicillin Since this compound is excreted in the reduced (–SH) state after being formed in the body it appeared possible that it would also remain reduced when given by mouth and that the thiol group might prove active in the removal of copper

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So far two healthy people have each received a single dose, and two patients with H L D have received four and three trial doses, of penicillamine The copper excretion has been estimated and, in the patients, compared with that produced by a dose of dimercaprol containing an approximately equimolar amount of sulphur These preliminary tests suggest that dimethyl cysteine is as active as dimercaprol in promoting the removal of copper from the body Dimethyl cysteine hydrochloride was given as three daily doses each of 300 mg ; the drug was given about half an hour before meals in order to avoid its chelating with copper present in the diet In these short term experiments no toxic reactions were observed

A detailed report of this work is in course of preparation, and the possible use of this form of treatment for long term maintenance of patients with H L D is discussed with reference to possible chronic toxicity and precautions which should be taken in undertaking a long-term study Reference is also made to the treatment of other heavy metal poisonings with penicillamine

This work was done at the Thorndike Memorial Laboratory and the 2nd and 4th Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Massachusetts I am most grateful to Dr C S Davidson for his advice and encouragement, to Dr D Denny Brown for allowing me to study two of his patients, and to Dr Augustus Gibson, of Merck & Co, Rahway, N J, and to Prof John Sheehan, of the Massachusetts Institute of Technology, for supplies of penicillamine

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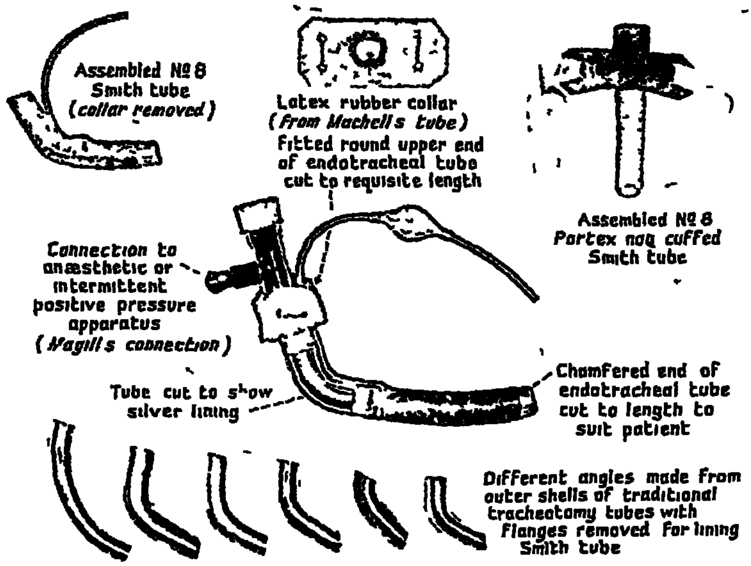
New Inventions

A TRACHEOTOMY TUBE FOR USE IN ACUTE POLIOMYELITIS

THE maintenance of a tracheotomy tube during emergencies may lead to many difficulties, especially before the tracheostomy tract has properly formed

Fixation —*The normal movements of patient and attach*ments with intermittent positive pressure inflation, routine posturing, and drainage may easily displace an ordinary cut down anæsthetic endotracheal tube which may cause surgical emphysema and traumatic pneumothorax If a long stemmed tube is used, a bronchus may become blocked, causing retention of carbon dioxide and respiratory embarrassment



Kinking —Complete occlusion of the lumen of a tracheotomy tube may be more obvious, but no more lethal, than partial occlusion, which may often be produced in anæsthetic tubes, even armoured tubes may close partially in the anteroposterior diameter This may be detected before use by trying to withdraw a suction catheter (which has previously just passed easily), if it is gripped when the tube is bent, the latter should be discarded

Tracheal Ulceration —In debilitated patients direct pressure of an inflated cuff may cause ischæmia *of the tracheal mucosa*, and a tube without a rigid angle may rub the posterior tracheal wall owing to its relative inflexibility

Angulated rubber tracheotomy tubes (Morrant Baker) may be the best of those tubes readily available for use with intermittent positive-pressure inflation, and, carefully selected to suit the patient, are unlikely to kink However, the short intratracheal portion of these tubes, especially in the smaller sizes, does not allow easy fixation of slip-on cuffs, which in any case are clumsy and unsuitable for prolonged use Moreover the fixation of connections to the flush external flange is difficult, especially when surgical dressings are present, as in the early postoperative stages Some rubber tubes are of inconstant diameter, having an irregular inner wall which prevents the easy passage of a suction catheter

In the Portsmouth Poliomyelitis Centre a tracheotomy tube has been improvised by several members of the staff jointly which appears to have none of the aforementioned disadvantages and many additional advantages None of us accepts full responsibility or claims any originality for this tube, so we call it the Smith tube after the first patient in whom it served as a reliable non-traumatic airway during many days of intermittent positive pressure inflation

The Smith tube is essentially a suitably selected and cut-down anæsthetic endotracheal tube into which is slid, to make a tight fit, a similarly selected silver lining, which is the outer shell of a standard silver tracheotomy tube from which the external flange has been removed In the accompanying illustration the wall has been cut away from a Smith tube to *show the lining* A latex rubber collar is attached

The advantages of the Smith tube are as follows

(1) The fixed curve and attached collar make fixation easy and reliable

(2) The tube *cannot* be *compressed* or occluded in any diameter

(3) A smooth and regular inner wall allows the passage of the largest possible suction catheter at all times

(4) The fixed curve ensures that there is no pressure on the posterior tracheal wall

(5) Variable intratracheal and extratracheal lengths can be selected (above and below angle) to suit the portion of trachea available above the carina, and to make easy connection with anæsthetic or intermittent positive pressure apparatus

(6) The Smith tube can be made of different sizes, lengths, shapes, and *lumina and cuffed or uncuffed from ready to hand* materials at low cost

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Reviews of Books

Biochemistry and the Central Nervous System

Henry McIlwain, PH D D SC, professor of biochemistry in the University of London at the Institute of Psychiatry
London J & A Churchill 1955 Pp 240 40*s*

TODAY emphasis in biochemical thought is on the nature of dynamic processes rather than on mere cataloguing of tissue constituents which was the preoccupation of earlier workers, and Professor McIlwain's book gives a striking illustration of this trend He discusses most of the important topics of current interest in cellular metabolism, and skilfully develops the basic ideas in relation to the special case of nervous tissue It is remarkable how much data he has assembled to demonstrate the actual behaviour of neural material without having to extrapolate from other organs Professor McIlwain's own work on the effect of electrical stimulation on the "in-vitro" metabolism of cerebral tissues receives due consideration, but is not overemphasised, and in this and other respects his presentation is extremely well balanced

After a brief historical introduction, there is a chapter on the study of cerebral metabolism in the intact animal, which summarises work on the oxygen and glucose consumption of the organ under various conditions, based on analyses of afferent and efferent blood Next comes a discussion of the chemical composition of the brain with particular reference to the constituents, such as creatine phosphate, whose concentration varies with cerebral activity The middle five chapters of the book are concerned with a straightforward account of intermediary metabolism The chapter on lipids reviews recent work on the fractionation of the cerebral lipids, and on turnover studies of these materials There follows a fascinating chapter on the changes in the make up of the brain through development before and after birth An account of chemical transmitters and the in vitro effects of depressant and excitatory drugs on brain metabolism leads to a final chapter on the speed of chemical changes in the brain, which includes some intriguing calculations made by the author from various published data on this subject

Written in a style that is unexciting but usually perfectly clear, the book will attract workers in neurology and psychiatry who want to keep up with the results of modern biochemical research, and biochemists and neurochemists will find that it gives a useful conspectus of familiar ideas

Blood Supply and Anatomy of the Upper Abdominal Organs

Nicholas A Michels, M A, D SC, professor of anatomy, Jefferson Medical College, Philadelphia Philadelphia J B Lippincott London Pitman Medical Publishing Co 1955 Pp 581 £8

THIS book is mainly concerned with the variations of the arterial supply to those organs which lie above the mesentery of the transverse colon

In part, it is a descriptive atlas of 165 figures, most of which illustrate these variations The essential features of the figures dealing with the gall bladder and liver are summarised in six plates Other figures show variations of the extra hepatic bile ducts, and the remainder illustrate the gross anatomy of the intrahepatic biliary, arterial, and venous systems

The atlas is preceded by a text which includes descriptions of the arterial variations, based on some 500 dissections by the author Accounts are also included of the blood supply of the œsophagus and the gut distal to the duodenum These are derived from the observations of others, but supplemented by Professor Michels's own experience There are discussions on collateral circulations in the upper abdomen and on the circulations within the liver and the spleen The text ranges widely over other material, and includes a chapter on the variations of the biliary system A vast composite chapter deals with the structural features, embryology, and anomalies of the upper abdominal organs Here the main emphasis is on the biliary apparatus, and the structure of the lower end of the common bile duct is dealt with in detail There are sections in this chapter on gall stones, on the comparative anatomy of the bile ducts, on the liver in relation to divination, and on the first cholecystectomy performed in America There is a bibliography of some 850 references, many more given in the text do not appear in it

The emphasis throughout is on the applied anatomy, and this is essentially a book intended for those who operate on the upper abdominal organs The terminology is clear, and the figures are admirably designed and executed, few surgeons could fail to learn something of value by looking through the atlas The text is in general clearly written and comprehensive though there are some repetitions and irrelevancies The general production is good, the price is frightening

Techniques in Blood Grouping

Ivor Dunsford, senior scientific officer, Regional Blood Transfusion centre, Sheffield, C Christopher Bowley, M B, M R C O G, director of the centre Edinburgh Oliver & Boyd 1955 Pp 250 21*s*

PRIMARILY a practical guide for use in the laboratory, this book concentrates on providing, in full detail, "a comprehensive set of techniques needed by those engaged in blood grouping work"

The first of the three sections explains briefly the theoretical and factual bases on which the practical schemes rest, and even in this section, the practical standpoint predominates For instance, in addition to dealing with the nature of immune iso antibodies and factors affecting blood group reactions, the authors have chapters on apparatus, causes of error, and the provision of antisera There is an interesting brief outline of basic and advanced courses for hospital laboratory workers

The second section gives really full details of 80 different techniques, beginning very properly with the cleaning of dirty glassware and ending with the identification of mixed antibodies In between every technique likely to be needed is thoroughly described the basic grouping techniques, the preparation of sera for diagnostic use, the differentiation of the sub groups of A (with a useful table), and more complex matters like rhesus genotyping Techniques for difficult situations—compatibility tests for children under 6 months, compatibility tests when time presses, and the investigation of cases of hæmolytic anæmia—are presented with commendable briefness The rare blood groups are all dealt with—but with a sense of proportion The rare blood groups also find a place in the third section which is a useful glossary

The book has a wire binding that enables it to lie flat wherever it is opened

This book will be welcomed with relief by all those who have to cope with the practical side of blood-transfusion work, but who have only the haziest ideas about the calculation of gene frequencies The price will enable every worker to have his own copy

Introduction to Hepatic Surgery

Henry Gans, M D, surgical resident, Cincinnati, Ohio New York Elsevier London Cleaver Hume 1955 Pp 265 70*s*

For his study of the anatomy of the Glissonian and the hepatic vein systems, Dr Gans cast the vessels in plastic material by injecting post-mortem specimens These casts have indicated a fairly constant lobe system within the liver which does not entirely correspond with the external appearances of the organ, some fine photographic reproductions illustrate this point, which is of importance to a surgeon contemplating partial hepatectomy Because of the anatomical detail and the technological style in which it is written, this book is more for reference than for reading Surgery is dealt with in general terms, physiology is not considered

Fractures of the Facial Skeleton

N L Rowe, M R C S, F D S R C S, and H C Killey, M R C S, F D S R C S, consultants in oral surgery, plastic and maxillofacial surgery unit, Rooksdown House, Basingstoke Edinburgh E & S Livingstone 1955 Pp 923 £6

THE two principal authors of this imposing textbook are primarily dental surgeons, and they have been assisted by two anæsthetists, four plastic surgeons, an ophthalmologist, and an oral surgeon This team has produced a splendid volume that covers virtually every aspect of maxillofacial injuries—a difficult and complex subject

Many clinical problems are fully explained and illustrated, including gunshot wounds, head injuries, secondary bone grafts, and soft tissue lacerations, and the technical matters discussed include the construction of metal cap splints and the various methods of interdental wiring There is an admirably terse chapter by Dr G J Romanes on ophthalmic injuries, though in face of this contribution it is a pity to find support elsewhere for the fallacy that loss of periorbital fat causes "an alteration of the pupillary level and a complaint of diplopia" Best of all, there is a fascinating chapter on the diagnosis and treatment of residual traumatic deformities by Sir Harold Gillies

An encyclopædic book is liable to lack balance, and some of this work's copiousness is due to material which might well be compressed or omitted The historical chapter runs to 50 pages, there is a long section on metallurgy and electrolytic phenomena, the chapter on radiography and radiology occupies 46 pages, and there are over 40 line drawings illustrating how to insert and tie skin sutures

Nevertheless, this book is clear, persuasive, and comprehensive, and it deserves to enjoy a special position in the maxillofacial literature of English-speaking countries

Medical Treatment of Mental Disease

The Toxic and Organic Basis of Psychiatry DANIEL J MCCARTHY, M D, LL D, consulting neurologist, Philadelphia General and Norristown State Hospitals, KENNETH M CORRIN, M D, neuropsychiatrist, Wilmington General Hospital Philadelphia J B Lippincott London Pitman Medical Publishing Co 1955 Pp 653 96s

LAUDABLY eager to remind family doctors and young psychiatrists that "there is much more to psychiatry than the purely psychological aspect," the authors go to the other extreme They assert, without evidence, that all, or almost all, mental disorder is a matter of disordered chemical and physiological processes

They leave aside not only the dynamic or psycho analytical psychopathology so prominent in most American textbooks of psychiatry, but also the findings of applied psychology, and they are evidently unaware of their own psychological assumptions There is certainly a need for a well informed American textbook that has not a strong psycho analytical bias, but this book does not supply the need

A Classification for Medical and Veterinary Libraries

2nd ed CYRIL C BARNARD, B A, F L A, F I L, librarian, London School of Hygiene and Tropical Medicine London H K Lewis 1955 Pp 279 £4 4s

THE late Sir John MacAlister once said "You can't classify a medical library without doing more harm than good", and many of those who have had to struggle with some of the schemes for keeping books in order would agree with him In a large library the choice of a classification is one of the librarian's biggest problems, and unfortunately some of the ingenious methods that have been devised are too complicated for everyday use Universal schemes suitable for all libraries have been widely adopted in medical libraries because they often form part of a bigger library and because they must provide for books on non-medical subjects Mr Barnard has adopted the method which starts with the books themselves and builds up a classification to fit them

First published in 1936, the Barnard classification was originally devised for the London School of Hygiene and Tropical Medicine No less than 8 of the 26 main divisions were allotted to bacteriology, parasitology, and medical zoology, classes which constitute less than a tenth of the stock of most medical libraries The specialties of medicine, which may comprise nearly half of the stock of a medical library, were all compressed into one main class Mr Barnard has now removed this bias by providing an alternative notation The new arrangement is very ingenious and should enable the scheme to be applied in libraries of almost any type

The main schedules of the classification have been thoroughly revised and brought up to date In common with all the major schemes, the Barnard classification provides for further expansion and definition by means of auxiliary schedules and tables

No classification has been (or is ever likely to be) devised which will meet the needs of both general and specialised medical libraries, large and small, but the Barnard classification is an heroic attempt to provide one It has already been adopted by more than thirty medical libraries, including those of the Royal College of Surgeons of England and the World Health Organisation

Maternal Emotions

NILES NEWTON, PH D, research associate in obstetrics, school of medicine, University of Pennsylvania New York Paul B Hoeber 1955 Pp 140 $3

THE researches described in this monograph were concerned with women's feelings toward menstruation, pregnancy, childbirth, breast-feeding, infant care, and other aspects of their femininity Dr Newton has had much experience as a psychologist, working in close association with her husband in the department of obstetrics and gynæcology of Jefferson Medical College, and she records work done over nine years Her own investigations have covered many of the subjects studied, but the references to other work are copious, though limited mainly to American sources

There is no doubt that Dr Newton is anxious to show how important maternal emotion is for both mothers and children She deplores the present progression of American women towards artificiality, and points to the evidence for the satisfaction to be gained from following Nature's methods She gives many useful facts on matters about which there has hitherto been endless argument based on untested assumptions One instance is her tested finding that if a breast fed baby takes his complementary feed (in American, "supplemental feed") from a spoon rather than a bottle, the length of the breast feeding period will be doubled

There are plenty of stimulating ideas for students of obstetrics, natural childbirth, or breast-feeding, and many challenges to pursue or review their work more closely For psychologists, there is a great deal of material in the various appendices setting out methods of approach to the patient

Radiographic Atlas of Skeletal Development of the Knee

S IDELL PYLE, PH D, NORMAND L HOERR, PH D, M D, department of anatomy, Western Reserve University School of Medicine, Cleveland, Ohio Springfield, Ill Charles C Thomas 1955 Pp 82 31s

THE work recorded in this book was undertaken to produce a standard of reference for the maturation of the knee-joint "for clinical use by a tested inspectional method"

The authors have analysed the various changes in the radiographs of knees during growth, and they reproduce 29 plates which they consider illustrate the normal development of the joint The general production of the book is excellent and the reproduction of the films adequate, but it is difficult to see where its practical value lies or who would find it useful apart from those interested in the minutiæ of skeletal development The changes from year to year in the growing knee seem too slight for confident differentiation, and they depend for their identification very much on the exact positioning of the joint, which may be surprisingly difficult There are easier ways of estimating skeletal age than this

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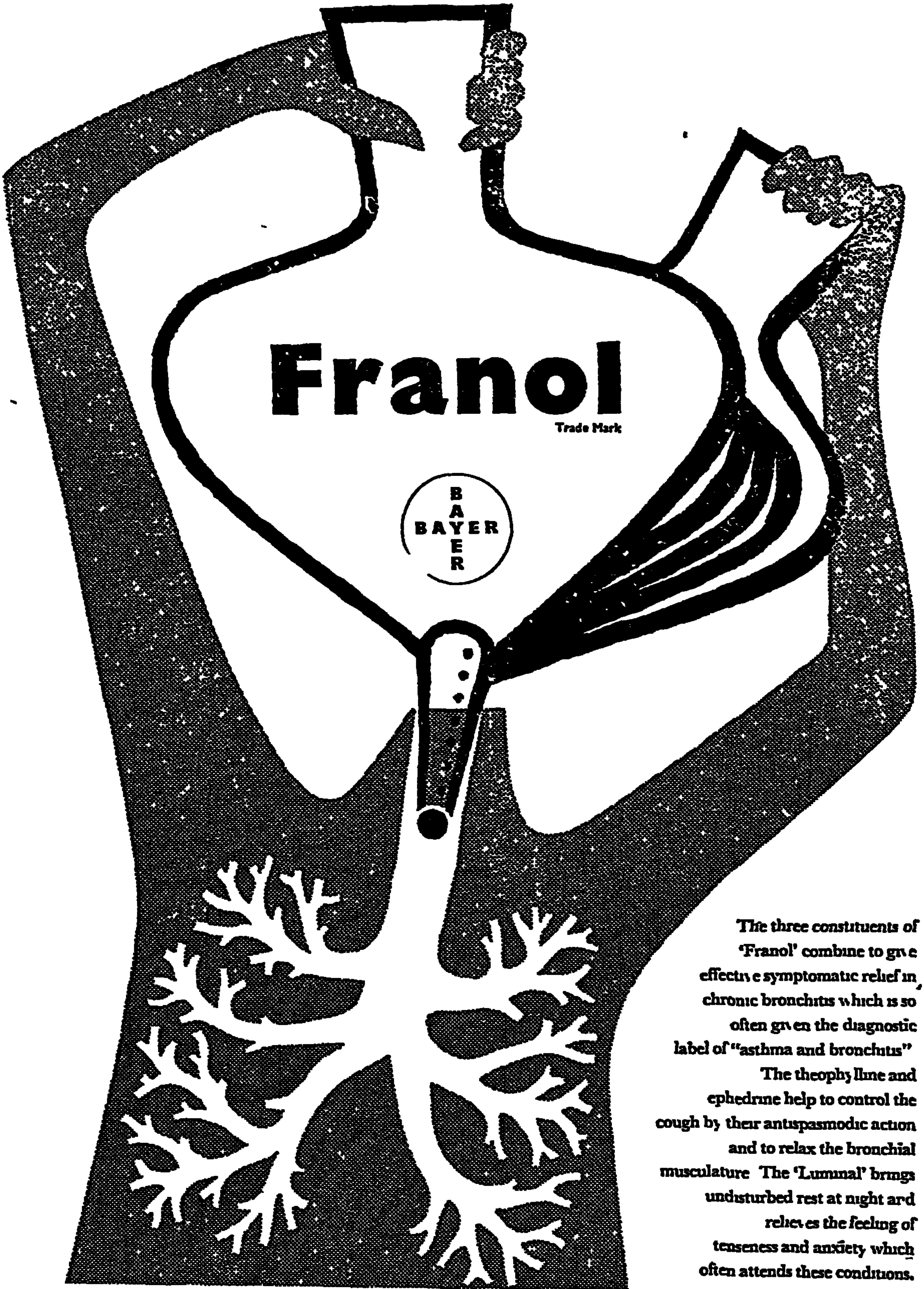
Textbook of Pharmacognosy (3rd ed London J & A Churchill 1955 Pp 578 42s)—Most drugs introduced in the past ten years have been synthetic, but among the new material now included in Professor Wallis's well known text book are sections on *Rauwolfia serpentina* and *Rauwolfia canescens*, the sources of reserpine, on *Ammi visnaga* from which khellin is obtained, and on bentonite which is used in ointment and cream bases For the rest, the third edition retains the lucid text and clear line drawings which have made the earlier editions deservedly popular with students and teachers alike



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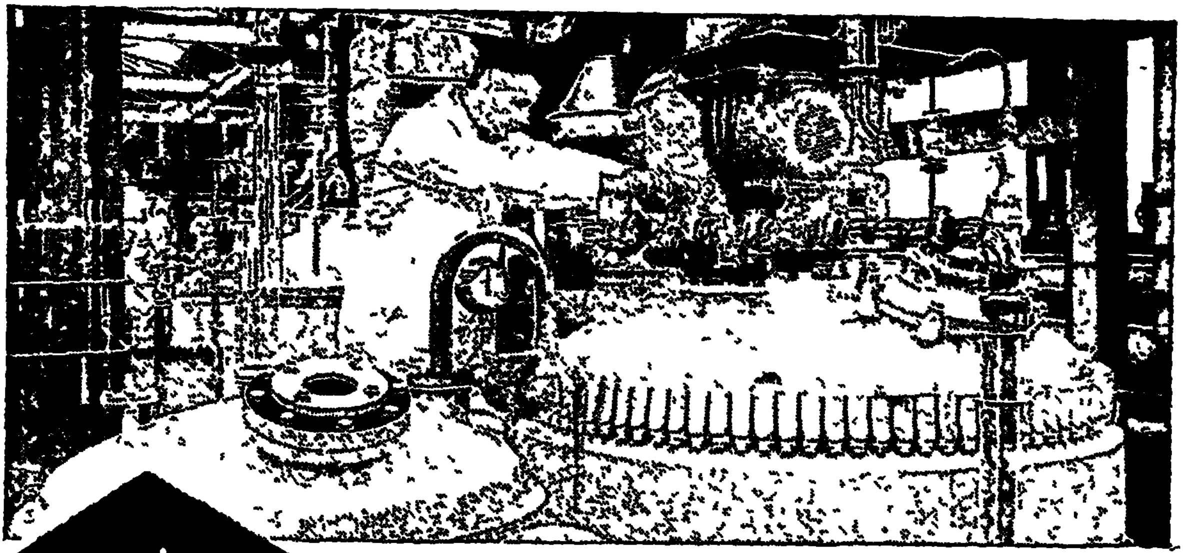

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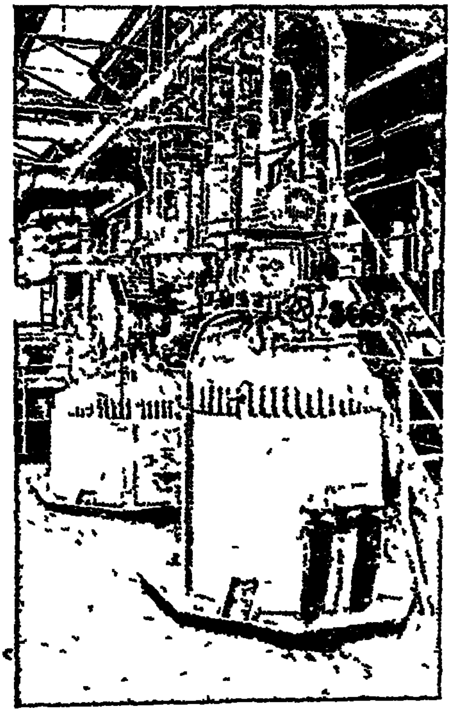

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THE LANCET

LONDON SATURDAY, JAN 7, 1956

The Strategy of Medical Research

MEDICAL research in the United States—its achievements and prospects—is reviewed in two fascinating volumes from the American Foundation[1] The second, in discussing the investigation of some of the major problems of the coming half-century, such as virus diseases, atheroma, hypertension, rheumatic disorders, and cancer, is lucid and readable, but the first volume may ultimately be more important, with its account of the activities of research institutes and the organisation of work within them Almost every facet of the complex that makes for medical advance is examined in a study which has been in process for fifteen years and may have as much influence on American medical research as FLEXNER's reports of forty years ago had on American medical education

In organising research the first need is to recognise the born investigator We have only to think of CHARLES SHERRINGTON, J S HALDANE, and their peers, to appreciate that sustained continuity of effort towards a single major objective characterises the work of really outstanding men They usually bring to this work a wide knowledge based on their academic quality, and some early diversity of research interest supplies a breadth of biological and technical experience before they settle down to the task which they make their own The great discoveries often come from observing the significance of some unexpected finding, which turns up in the pursuit of some apparently commonplace inquiry The chance observation of glycosuria in depancreatised dogs led to insulin, the accidental fogging of a photographic plate gave us X rays, and the initial discovery of penicillin was the result of chance acting on "the prepared mind" Hence the danger, to which WIGGERS[2] calls attention, of research "by proxy" in which technicians and junior assistants do the laboratory work In his own circle of acquaintance, WIGGERS says, at least three Nobel laureates did their own technical work with their own hands It is only the inspired investigator, with a feeling for finer detail, who is likely to perceive the potential interest of the unexpected laboratory finding GAUSS, when he was once asked how he had become the greatest contributor to mathematical thought, answered simply "By thinking about *it all the time*"

The growth of team-work, so necessary in the use of our increasingly complex technologies, brings its additional problems There are the difficulties of integrating into a medical team scientists who may not have had even a biological training and are apt to be baffled by the vagaries of living patients and their diseases Again, such may be the difficulties of resolving jealousies between members of the team, and of making use of the total brain-power of the group, that successful leadership is often as much an exercise in social and personal relationships as it is in science

The American writers make a strong plea for the promotion of fundamental as opposed to applied research—a plea the more necessary because problems of immediate importance are more likely to appeal to the laity, who in one way or another must foot the bill It is curious that in the United States, the wealthiest country in the world, medical schools seem to have financial troubles as great as or greater than our own At least half of them are said to have budget deficiencies, or to need large sums to keep up their standards, and yet there are immensely wealthy foundations in a position to spend money on a lavish scale (Perhaps it is not entirely fortuitous that, since these volumes were written, the Ford Foundation has announced its intention to make a grant of 500 million dollars to the American medical schools and associated institutions[3]) Sometimes, of course, the money given by the public can be used only in some specific direction, such as cancer, psychiatry and poliomyelitis, and the public does not necessarily give most generously to the most necessary purposes (A child with a crutch elicits more financial sympathy than a man with a hearing-aid, though deafness may be a much greater total national physical handicap) During years of intimate contact with investigators, research foundations become more sensitive to actual scientific possibilities, but unfortunately they do not pool their experience, and one after another they spend eight, ten, or more years in finding out the disparity between paper planning and actual needs Some of the bodies financing research are apt to think in terms of immediate practical return for money spent, but others, of which the Markle Foundation[3] gets special commendation, concentrate on helping promising men to enter the academic field

The pattern of research is influenced also through direction of government funds, State and Federal The richer States can afford to give their State universities greater freedom, but others insist to a greater or less extent on using the university as a "local service station" Thus in the dairy State of Wisconsin about two-thirds of the problems under study are connected in some way with the economic needs of the State an example is the *study of* enzymes concerned with the ripening of cheese To suggest that such applied research is not fruitful would be wrong it has led, for instance, to the understanding of sweet-clover disease of cattle which had caused bleeding and death of whole herds, and from this to the trial of dicoumarol as an anticoagulant in medicine Indeed, direct governmental interference in research has led to many excellent advances On the other hand, control by politicians has obvious dangers The recent outbreak of political nervousness in the U S A has apparently caused on occasion the abrupt withdrawal of research grants because of unspecified political suspicions, and the authors of this survey recognise that research and the freedom of speculation which go with it cannot flourish in such an atmosphere

America has immense resources, technical and intellectual as well as financial Research is done in university medical schools and allied institutes like the Massachusetts Institute of Technology, under various Foundations (some with their own independent institutes, like the Rockefeller), in self-supporting clinics like the Mayo, in the pharmaceutical and chemical industries, and under the ægis of scientific societies and voluntary health organisations In spite of unevenness and difficulties of integration, medical research proceeds in an immense productive flood In this country our resources are meagre in comparison Nevertheless perusal of this work should make us appreciate the value of our system by which grants to the universities and Medical Research Council are made through the Privy Council and are thus beyond any ill-informed or undesirable political pressures Also, while we should all welcome more money through private benefactors and research foundations, we may recognise that from such sources it may come with too many strings attached Money, as JOHN M RUSSELL[3] says, can sometimes do harm

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[1] Medical Research Mid Century Survey Vol i pp 797 Vol ii, pp 772 Published for the American *Foundation* by *Little* Brown & Co Boston and Toronto 1955 *Price $15 the set*

[2] Wiggers C J *Circulation Res* 1953 1, 475

[3] See *Lancet* 1955 ii, 1348

Hypertrophic Pulmonary Emphysema

THE essential features of hypertrophic pulmonary emphysema are loss of pulmonary elasticity and the disappearance of alveolar septa, but despite intensive investigation in recent years no decisive information about the precise causes has so far emerged Some hypotheses, such as deficient blood-supply to the elastic tissue of the lung and over-stretching of the lungs because of a barrel-shaped thorax, do not now seem worthy of consideration, and the long-cherished view that emphysema was especially common in glass-blowers and players of wind instruments was given its quietus by CHRISTIE[4] in 1939 The suggestion that an inherent defect of elastic tissue is responsible for emphysema[5] is hard to disprove, but any hypothesis should take into account the almost invariable association of hypertrophic emphysema with bronchial diseases such as chronic bronchitis or asthma Coughing and obstruction to air-flow have been put forward as relevant factors Coughing does not seem likely to produce loss of elasticity from overdistension of lung tissue, certainly in the expiratory phase, when the glottis is closed, the intrathoracic pressure rises abruptly as the lungs are squeezed by the thoracic and abdominal musculature, but the pressure on either side of the alveolar septa must be equal, except in the less supported apices, which may bulge outwards Again, during the deep inspiration which follows the expiratory phase, the lungs are no more distended than they are in the course of physical exercise regarded as beneficial Nevertheless, as CHRISTIE[6] has pointed out, it may be that the violent pressure changes to which the delicate alveoli are subjected during persistent coughing may lead eventually to loss of pulmonary elasticity, and in that event the lungs would increase in volume and the thoracic cavity would undergo the familiar enlargement to accommodate their increased bulk But it is difficult to produce satisfactory evidence in proof or disproof of this contention, because patients with persistent cough almost invariably have some bronchial affection producing increased resistance to air-flow, and many believe this is the important factor in the genesis of emphysema, as well as a consequence of it This resistance to air-flow is greater in expiration, and, as an attack of bronchial asthma clearly shows, air may be trapped in the lungs Even so, provided that air is distributed equally to the alveoli, the lung tissue will not be unduly stretched It is certain, however, that in conditions like chronic bronchitis and asthma the obstruction is greater in some bronchioles than others, and GORDON[7] suggested that during inspiration alveoli supplied by normal or less obstructed bronchioles would have to accommodate not only their normal quota of air but also an extra amount to compensate for that which had failed to pass through the more obstructed bronchioles Under these circumstances, although the total volume of air in the lungs would not be excessive, some of the alveoli would be grossly overdistended, and repetition of this process might lead to rupture and loss of elasticity This theory of compensatory overdistension is supported by the pathological finding that in emphysematous areas of lung the associated bronchioles as well as the alveoli are dilated,[6 8] and by the persuasive, if indirect, experimental evidence reported by MEAD et al,[9] to which we recently drew attention[10]

It is possible, however, that further work on the ætiology of hypertrophic emphysema may illustrate the complexity of the subject rather than indicate any simple solution this has certainly been the case in the matter of diagnosis FLETCHER[11] showed that physical examination is an unreliable guide, and KNOTT and CHRISTIE[12] demonstrated that radiological prediction may also be fallacious It is necessary, therefore, to have recourse to the techniques of applied respiratory physiology, but it is uncertain at present which are the best and most practical ones The test which has generally been regarded as most informative is the determination of the proportion of residual volume to total lung capacity, and a ratio of more than 35% is usually taken to indicate emphysema But it is known that higher figures may be reached in older people without emphysema, and the test is too laborious for routine clinical use A reduced vital capacity is generally recognised as of little value in the diagnosis of emphysema, yet, as DONALD[13] has pointed out, the ratio of residual volume to total lung capacity may not be much better, since the total lung capacity in many cases of emphysema is not appreciably increased, and is made up of vital capacity plus residual volume DONALD said that if he were forced to diagnose the presence or absence of emphysema on the results of a single test he would choose the maximum breathing capacity (M B C)—the amount of air the patient can move in and out of the chest in one minute—despite the difficulty of excluding false positives due to reversible bronchospasm It is interesting, therefore, that the M B C and the ratio of residual volume to total lung capacity are among the tests lately assessed by CURTIS et al[14] in the diagnosis of early emphysema They estimated the MBC in 328 patients with pulmonary disease (tuberculosis in most cases) for which pulmonary resection was later carried out Suitable specimens for study were obtained at operation in all but 3 of these cases, and emphysema was demonstrated in 150 The MBC was considered abnormal when the volume was 95% or less of the predicted value and when, in addition, elevation of the spirogram indicated trapping of air On these criteria, the MBC was abnormal in 92 (61%) of the 150 cases of proved emphysema, but it was also abnormal in 22 (12%) of the cases in which emphysema was not demonstrated In some patients with emphysema, the spirogram was raised, although there was no apparent reduction in the volume of the MBC, and this evidence of air trapping came to be considered the more significant factor The ratio of residual volume to total lung capacity was determined in 48 patients with proved emphysema, but in only 17 severely affected patients did it amount to more than 35% of the total lung capacity, and this test therefore failed as a useful indication of early emphysema The timed vital capacity (TVC), a test in which prolongation of expiration is indicated by measuring the proportion of the vital capacity which can be expired in a given time, was performed in 113 patients, 79 of whom had proved emphysema A two-second TVC of 90% or less was considered abnormal, and this was found in 71 (90%) of the 79 patients with emphysema and in 18 (53%) of the others A test devised by Comroe and Fowler[15] to detect uneven alveolar ventilation during a single breath of oxygen was used in 114 patients, of whom 70 had proved emphysema A rise of nitrogen in the expired breath to more than 2% was regarded as abnormal This test was abnormal in 59 (84%) of the patients with proved emphysema and in 20 (46%) of the others The most sensitive indication of emphysema was a combination of prolonged TVC, elevation of the spirogram to hyperinflation level during the MBC test (whether or not the MBC was apparently reduced), and a rising curve of alveolar nitrogen after a single breath of oxygen

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[4] Christie R V *Edinb med J* 1939, 46 463

[5] Villemin, J A *Arch gen Med* 1866, 118 385

[6] Christie R V *Diseases of the Chest* London, 1952, vol ii p 101

[7] Gordon I *Dis Chest* 1944 10 180

[8] Kountz, W B Alexander H L *Medicine, Baltimore*, 1934, 13 251

[9] Mead J, Lindgren, I Gaensler, E A *J clin Invest* 1955, 34 1005

[10] *Lancet* 1955 ii 810

[11] Fletcher C M *Proc R Soc Med* 1952 45 577

[12] Knott J M S, Christie R V *Lancet* 1951, i 881

[13] Donald K W *Brit med J* 1953, i 115

[14] Curtis J K Rasmussen H K, Mendenhall J T *Amer Rev Tuberc* 1955 72 569

These tests are, of course, by no means specific and their practical value will have to be further assessed, but they are all easy to perform, and the first two do not require expensive apparatus Any work which may help the clinician to gather some fruit from the physiologist's tree of knowledge is certainly welcome

Soil, Water, and Cancer

In 1947, Stocks[16] noticed a peculiar distribution of deaths from cancer in Greater London which he could not explain by differences in age groups, social conditions, or number of hours of sunshine This led him to observe that the four London boroughs supplied largely by well water had lower cancer mortalities than most of the boroughs supplied by river water Stocks and his colleagues are continuing their inquiry, into the possible relation between what might be called the geological conditions of habitation and cancer mortality, in the North Wales area They have demonstrated an association between an increased mortality from cancer of the stomach in Anglesey and residence on a particular soil group,[17 18] though this association was less definite for agricultural workers The soil in question, because of the equable distribution of moisture at all levels and at all seasons, has a continuous period of plant growth and biological activity, whereas soils not associated with an excessive cancer mortality are subject to late spring or summer drought due to shallowness or rapid drainage, or they have a long wet season because of poor drainage Earlier work[19] in North Wales and elsewhere suggested that the high organic content of cultivated soils was associated with increased cancer mortality

To overcome the great shortage of drinking-water in the Netherlands, schemes have been suggested for the introduction of river water as the main source of supply Tromp,[20] aware of Stocks's ideas, took note of these plans and decided to study the relation between the physicochemical properties of drinking-water and cancer mortality In Holland, the highest total cancer death-rate for all sites had been found amongst municipalities supplied by river water,[21] and where the water had a high SiO_2 and low manganese and natron content Further studies suggested that a high manganese content of the drinking-water is associated with lower cancer frequencies Recently, Tromp and Diehl[22] have extended their work to a more detailed study of the relation between soil and cancer mortality and especially cancer of the stomach The period studied was 1900–40 The average cancer mortality (all sites together) per decade for persons over 50 years of age was ascertained for the seven principal soil types in the Netherlands These soils range from the acid reclaimed and poorly drained peat soils, through sandy soils, to the more alkaline river-clay type The highest cancer death-rate was found in municipalities situated on peat and reclaimed peat soils and the lowest on river-clay soils Thereafter, for the period 1946–52, they studied the total numbers of deaths from cancer of the stomach in men over the age of 50 living in municipalities on the various soil types As in the case of cancer in all sites, it was found that there was a lower mortality from cancer of the stomach, at all ages, among people living on river-clay soils and a higher mortality among those on peat soils Moreover, the order of frequency in relation to soil was, with one exception, similar to that of cancers of all types

Tromp and Diehl conclude that the association between soil type and cancer mortality is a real one They feel that they have eliminated differences in sex and age grouping which might influence such a relationship They also considered the question of differences in type and character of the municipalities (for instance, rural, semi-rural, and urban) which might have affected the figures Regarding genetic and racial factors, they say that no obvious correlations have been found in the department of anthropogenetics of the Netherlands Institute of Preventive Medicine between soil units and racial groups Nevertheless, in view of the work[23][24] which has shown that cancer of the stomach is commoner among people of blood-group A and is particularly rare in those of group O, they suggest that a study of the blood-groups in the Netherlands municipalities would be relevant to this question They are not prepared to speculate about the causes of the observed correlation between soil and cancer, except to point out that traces of metals in soil, drinking-water, and food (which in the smaller municipalities is mostly locally grown) would be sufficient to disturb enzyme balance, and they seem to have made a start in searching for such trace elements The labour involved in the search will be prodigious

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[15] Comroe J H jun Fowler W S *Amer J Med* 1951, 10 408

[16] Stocks, P Regional and Local Differences in Cancer Death rates London, 1947 General Register Office, Studies on Medical and Population Subjects no 1

[17] Davies R I Wynne Griffith G *Brit J Cancer*, 1954 8 56

[18] Wynne Griffith, G Davies R I *Ibid* p 594

[19] Legon C D *Ibid* 1951 5, 175 *Brit med J* 1952 ii 700

[20] Tromp S W *Brit J Cancer* 1954 8, 584

[21] Diehl, J C Tromp S W Foundation for the Study of Psychophysics First Report on the Geographical and Geological Distribution of Carcinoma in the Netherlands Oegstgeest, Holland 1954

[22] Tromp S W, Diehl, J C *Brit J Cancer* 1935, 9 349

All these considerations bring us back to the old question of how firm can be the conclusions drawn from death-certificates The Dutch workers believe that registration of deaths in Holland is accurate, partly because the secrecy of death-certificates is assured and partly because the mortality data are collected by a very competent organisation, the Netherlands Central Bureau of Statistics They assert that, except in the largest cities the population does not migrate much and that doctors and hospitals do not vary in competence or facilities in different parts of the country We can agree with all these arguments, but there still must be many inaccuracies in death certification without post-mortem examination (and even with it) Despite the evidence of a fairly stable population, changes in habitation must be considerable during a long life and with easy means of transport Perhaps the strongest argument in favour of a soil cancer relationship is its demonstration in two communities as widely separated as Anglesey and Holland

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[23] Aird I Bentall H H *Brit med J* 1953 i 799
[24] Koster, K H Sindrup, E Seele, V *Lancet* 1955, ii, 52

Annotations

MYXOMATOSIS

SINCE October, 1953, man and the rabbit flea (*Spilopsyllus cuniculi*) have contrived to spread myxomatosis through the length and breadth of the land Pockets of countryside have escaped entirely, in other areas the pestilence has passed and the few survivors are beginning to re stock the warrens, but in most farming counties foxes make do with rats, field voles, and even vegetable matter, while buzzards lack the rabbit meat they need to produce the normal 2–3 eggs Some of these changes were discussed not long ago at a meeting of the Mammal Society of the British Isles[1], but we must recognise that the entry of myxoma virus has redrafted the ecological play, and we are watching only the opening scene

Fleas feed on the head and ears of rabbits, and in this country the rabbit flea is the most important vector of the virus Its range is short and it probably cannot spread the disease more than a few miles each month in Kincardineshire, for example, there were many infected rabbits only a few hundred yards—but on the far side of a stream—from a single focus deliberately introduced some months earlier In Australia myxomatosis takes wing on mosquitoes, but here only *Anopheles maculipennis atroparvus*, which may carry virus for six months, is a possible vector Nor can infection be readily induced by mechanical contact, or by contaminated grass or vegetables, and this, no doubt, largely accounts for the absence of the disease in backyard and animal-house The virus still maintains its extraordinary host specificity, and, apart from a few brown hares, rabbits are the only mammals known to have been naturally infected

Our wild rabbit has qualities that will almost certainly ensure its survival, but a virus resistant strain has not yet emerged, and, though immune rabbits have been bred, their progeny are normally susceptible On the other hand, attenuated field strains of virus are well known, particularly in Australia but also in France, and recently recovered immune rabbits have been picked up over an area of 50,000 acres in the Dukeries in Nottinghamshire This attenuated strain is said to kill only about half its victims, compared with the 99% mortality by the strain prevalent elsewhere So far this seems to be an isolated instance, but, should the attenuated strain spread or appear in other areas, both myxomatosis and hordes of rabbits may be permanently with us To avoid this and to increase food supplies, the Minister of Agriculture is pressing on with the designation of rabbit clearance areas in which occupiers of the land must destroy the rabbits or, if this is impossible, prevent them causing damage There is strong financial inducement to farmers to carry out the provisions of the 1954 Pests Act, for conservative estimates for England and Wales show that last year the grain yield in rabbit-free areas was raised by about two hundredweight an acre—equivalent to something over £10 million sterling These are immediate returns, but the eventual gains could be much more striking For those with only an eye for the countryside, ash and oak saplings are beginning to appear where they were scarcely seen before, gorse is shooting prodigiously, grasses are higher, and wild flowers such as cowslip and rock-rose, and even the rarer orchids, have bloomed unexpectedly

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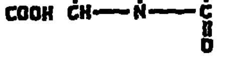
[1] See *Nature Lond* 1955, 176 1155

CHEMISTRY AND ACTION OF ANTIBIOTICS

THE structure of antibiotics and the way in which they work have lately been reviewed by Regna[1] and Umbreit[2] The term "antibiotic" has come to refer to any chemical substance produced by a micro organism which can inhibit the growth of, or otherwise destroy, other bacteria or micro-organisms By this definition, the first antibiotic was penicillin In the molecule of penicillin the side chain R can have various configurations such as benzyl, pentenyl, amyl, and so on The elucidation of the chemical structure of this molecule was finally achieved by a brilliant and painstaking crystallographic analysis of the molecule,[3] after organic chemists, both in Great Britain and in the United States, had been unable to decide between two possibilities Biosynthetic pathways[4] have been used to vary the group R, and other clinically useful preparations have been devised by salt formation with the free acid group of penicillin (the procaine, chloroprocaine, and ephenamine salts, for example) Penicillin seems to be adsorbed to and thereby deactivates a specific component of the cell wall of the bacterium[5] This inactivation appears to lead to a disturbance in the synthesis and metabolism of the nucleic acids,[6] and this causes, in turn, disturbances in



Penicillin

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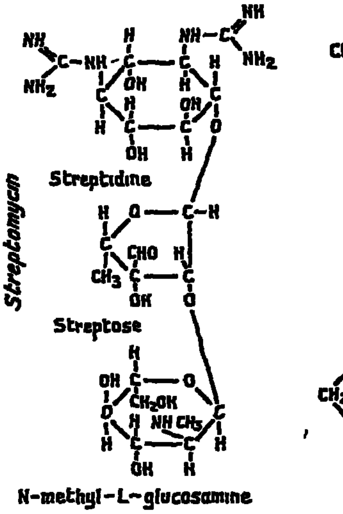
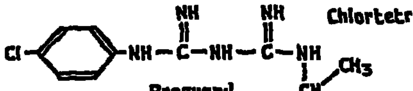
[1] Regna P P *Amer J Med* 1955 18 686
[2] Umbreit W W *Ibid* p 717
[3] Crowfoot D Bunn C W Rogers Low B W Turner Jones A *In* The Chemistry of Penicillin (edited by Clarke H T Johnson J R Robinson R) Princeton, 1949 p 310
[4] Behrens O K *Ibid* p 657
[5] Few A V Cooper P D Rowley, D *Nature Lond* 1952 169 283
[6] Gale, E F Symposium on Mode of Action of Antibiotics, 2nd Int Cong Biochem Paris 1952

amino acid incorporation and protein synthesis[7,8] But a more detailed understanding of the action of penicillin is still lacking

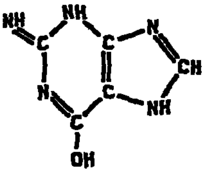
The combination of the unusual 4-membered lactam ring and a hitherto unknown α amino-acid in the penicillin molecule suggested that other antibiotics, as they were discovered, were likely to have structures differing unexpectedly from any of the known groups of natural products This feeling has been amply justified Streptomycin was shown[9] to contain 3 separate moieties (streptidine, streptose, and N methyl-L glucosamine) joined by glycoside linkages The guanidine residues in streptidine recall the active antimalarial drug proguanil ('Paludrine') and the biologically important guanine, which is contained in nucleic acids, streptose and the L glucosamine fragments had not previously been encountered from natural sources The cultures of *Streptomyces griseus* which produce streptomycin produce some closely related antibiotics (mannosido *streptomycin*,[10] *hydroxystreptomycin*[11]) and also actidione[12] which, although inactive against bacteria, is useful for its action against fungi



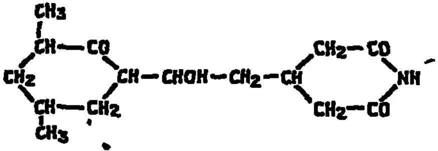
Streptomycin



Proguanil

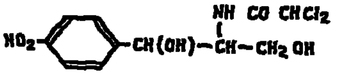


Guanine



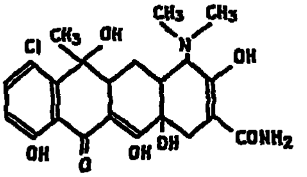
Actidione

In contrast to penicillin, *streptomycin* can be shown to react with a variety of cellular constituents It forms a complex with proteins and nucleic acids, with subsequent alteration in the surface charge on the *bacterium, and* it inhibits several enzyme systems[13] Of these, the oxalacetate pyruvate system appeared to be an important seat of action, and it was found that the formation of a hitherto unknown metabolite, 2 phospho 4 hydroxy-4 carboxyadipic acid,[14] from a dicarboxylic acid and pyruvate was inhibited by streptomycin at dilutions comparable to those required to inhibit growth

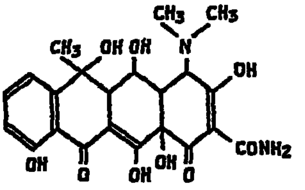


Chloramphenicol

Chloramphenicol has unusual chemical features[15] The molecule contains a nitrobenzene fragment and an amide derived from dichloroacetic acid Although both of these compounds had been known to generations of organic chemists, the isolation of chloramphenicol was the *first* indication that they could be natural products The stereochemical configuration of the side chain is related to D threose and is an absolute requirement for antibacterial activity Chloramphenicol is also unique among antibiotics used clinically in that it can be synthesised on a commercial scale[16] A clinically useful chemical derivative is obtained by esterification of the primary alcoholic group with palmitic acid[17] This ester is slowly hydrolysed in the duodenum, releasing the active principle and thereby providing long sustained therapeutic blood-levels Practically nothing is known about the mode of action of chloramphenicol, but interference with amino acid formation and metabolism is probably not the initial reaction



Chlortetracycline (aureomycin)

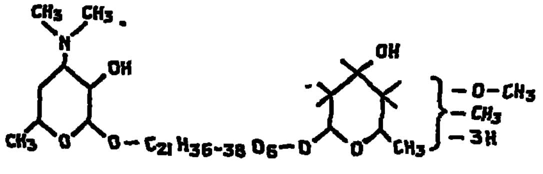


Oxytetracycline (terramycin)

The tetracycline antibiotics, to which chlortetracycline (aureomycin) and oxytetracycline (terramycin) belong,[18] all possess a nucleus of 4 partially hydrogenated 6-membered rings and are produced by species of streptomyces The mode of action of this group is unknown The members of another group, which includes the various tyrothricins gramicidin, and bacitracin, have structures with which the organic chemist is already familiar The family of polypeptide antibiotics which are usually cyclic in structure do, however, contain various amino acids in the D (or "unnatural") configuration For example, tyrocidine A is believed to be composed of the following amino-acids in a cyclic *configuration*[19]

┌—L-ornithine—L-leucine—D phenylalanine—L proline—
│ L phenylalanine—D-phenylalanine—L-tyrosine—L-valine
└————————————————————————————┘

It is interesting that oxytocin, the oxytocic principle of the posterior pituitary, is also a cyclic polypeptide[20] The structures of erythromycin and carbomycin, two of the newer antibiotics, are not known in full, but degradations have been reported,[21] suggesting a partial structure for erythromycin



Erythromycin

The question of how an antibiotic acts and the problems of bacterial resistance[22] are closely related It is probable that bacterial resistance does not necessarily arise as a result of the action of the drug, but that there

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[7] Gale E F *Bull Johns Hopk Hosp* 1948 83 119
[8] Hotchkiss, R D *Ann N Y Acad Sci* 1950 53, 13
[9] Brink N G Folkers K *Advanc Enzymol* 1950 10 145
[10] Fried J Stavely H E *J Amer chem Soc* 1947 69 1549
[11] Benedict R G, Stodola F H, Shotwell O L, Borud, A M, Lindenfelser L A *Science* 1950 112 77
[12] Whiffen, A J Bohonos N, Emerson, R L *J Bact* 1946 52, 610
[13] Umbreit, W W *Trans N Y Acad Sci* 1952, 15 8
[14] Umbreit W W *J Bact* 1953 66 74
[15] Rebstock M C Crooks H M, Controulis J Bartz, Q R *J Amer chem Soc* 1949 71 2458
[16] Olive, T R *Chem Engng* 1949 56 107
[17] Glazko, A J Edgerton W. H Dill W A Lenz, W R *Antibiotics* 1952 2 234
[18] Stephens, C R, Conover, L H Hochstein F A Regna, P P, Pilgrim, F J, Brunings K J Woodward, R B *J Amer chem Soc* 1952, 74 4976
[19] Paladini A, Craig L C *Ibid* 1954, 76 688
[20] du Vigneaud, V, Ressler C, Trippett, S *J biol Chem* 1953, 205, 949
[21] Flynn E H Sigal M V Wiley, P F Gerzon K *J Amer chem Soc* 1954 76 3121
[22] Bryson, V Demerec M *Amer J Med* 1955, 18, 723

are natural mutants which are able to develop and multiply under conditions fatal to the wild type This resistant strain can then be expected to develop mutants which are as well fitted for survival as the original strain

PREVENTION OF JUVENILE DELINQUENCY

So far most attempts to deal with juvenile delinquency have concentrated upon the established condition—correction rather than prevention Yet bad social and economic circumstances need equal attention, and we therefore welcome a report[1] recently published by the City of New York mayoral office which describes a concerted and planned approach, at municipal-authority level, to the prevention of delinquency These measures were based upon sound preliminary research into the backgrounds most likely to promote delinquent trends among young people in New York It was recognised, for example, that there is a need for more guidance and friendly supervision of certain adolescents in their recreational pursuits, and for the education of their parents in handling emotional problems within the family group The report therefore provides for more trained workers in the youth club movement and at community centres on certain housing estates The juvenile liaison department of the City Police Service is also to be augmented to provide more staff for informal contact with the youth in vulnerable districts In education, the report proposes the formation of a pool of senior school teachers, experienced in handling pre delinquent children, and they will circulate among schools in "difficult" localities Certain disabilities, such as backwardness in reading, are associated with delinquency in children of potentially normal intelligence, and the report therefore advocates wide extension of remedial coaching to counteract this tendency Under privileged senior school students, who might otherwise drift into unsavoury associations, are to be encouraged to complete their education, if necessary while working half-time in private industry at prevailing wages The programme for advising and guiding parents, through parent teacher associations, is to be extended by means of informal evening discussion-groups, led by experienced counsellors

These proposals do not depart radically from previously accepted principles No specific proposal is new, and indeed similar provisions, on a more limited scale perhaps, already exist in many places in this country What is noteworthy, however, is the degree of coordination the report advocates the formation of an independent planning committee, which will assess the results of the new drive, so that promising developments can be given further scope, and duplication of effort may be avoided It is in coordination that the report's lesson lies

The New York plan is an expensive one and it would be hard to get approval for spending so lavishly on a comparable scheme for London, for example But it should be possible, without ruinous cost, to do more in support of a vigorous coordinated policy of prevention in this country, and it is good to read in Dr J A Scott's report on the health of London in 1954 that steps are being taken to bring into effect the main recommendations of the L C C study group on preventive mental health in the maternity and child-welfare services[2] What is in fact needed is not so much new services as a re orientation of existing ones and their closer collaboration to avoid overlapping Sir Basil Henriques, in his Peter Le Neve Foster lecture to the Royal Society of Arts last April,[3] made substantially the same point, when he referred to the need for a composite child welfare office in every town and in every district of cities, to contain the headquarters of all statutory and voluntary bodies dealing with the welfare of children Sir Basil's concept of a Ministry of Juvenile Welfare, combining the children's departments of the Home Office, the Ministry of Education, the Ministry of Labour Youth Employment Council, and the Ministry of Health, is not perhaps so fanciful in the light of the New York report it might simply be a national extension of the coordination that New York is seeking on a municipal scale

HYDROCORTISONE FOR URETHRAL STRICTURE

In recent years improved treatment of urethritis has greatly reduced the incidence of inflammatory stricture of the urethra, and, by comparison, traumatic stricture, whether from injudicious instrumentation, long continued catheterisation, or other causes, has become more significant As urethral strictures, whatever their cause, are notoriously hard to treat, there is always a strong incentive to try any novel means of dealing with them In advocating local treatment with hydrocortisone, Bonner and his colleagues[1] in Boston base their method on the ability of hydrocortisone to diminish proliferation of fibroblasts in wounds and on its fibrolytic activity which they observed in established scar tissue They first dilated the stricture as far as possible without danger of rupture, and then an aqueous suspension of hydrocortisone was injected into the stricture at two points on its circumference Meatal strictures were injected directly with a small hypodermic needle, and those more deeply placed were located through an endoscope (under local or general anæsthesia) and injected with a special needle of suitable length The procedure had generally to be repeated once or twice later, according to the response 18 urethral or meatal strictures were dealt with successfully in this way

Compared with existing methods of treatment, the results recorded by Bonner et al are remarkable Much improvement undoubtedly followed the injections in several long standing and resistant strictures, but nearly half the patients in the series had recent meatal lesions which might have done well without hydrocortisone Moreover, cortisone treatment of other lesions of the urinary tract (such as chronic interstitial cystitis, Hunner's ulcer, and Peyronie's disease) has not borne out its early promise, and it would be premature to believe that hydrocortisone is a big advance in the treatment of urethral stricture

RISKS OF BOXING

Speaking to medical officers of the London Amateur Boxing Association on Dec 5, Dr Edwin Clarke said that the 6 deaths of amateur boxers since the war have all been from intracranial hæmorrhage, and the meeting recommended various precautions—that rubber floors should always be used for boxing shows, that a doctor should be allowed to assess the injuries of boys who have been stopped during a bout, that "all cases of prolonged unconsciousness or amnesia after a head injury should be sent immediately to hospital by ambulance", and that the medical officers should be provided with forms on which to notify the boxer's own doctor of any injuries received, so that treatment may be continuous The negative results of electro encephalography in 11 cases were held to show that "the policy of at least four weeks' rest from boxing after a severe head injury is paying dividends"

A few years ago, in reporting rules made by the New York State Athletic Committee,[2] which include the attendance of a doctor at the ringside who can if necessary advise the referee to stop the fight, we took the view

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[1] Perspectives on Delinquency Prevention By Henry Epstein, deputy mayor of New York Obtainable from the City of New York Office of the Mayor New York, 7 N Y Pp 66 $5 for 10 copies

[2] See *Lancet*, 1954 ii 1005

[3] *Ibid*, 1955, i 1016

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[1] Bonner, C D, Lyons, M K, Shields, D *New Engl J Med* 1955, 253 130

[2] *Lancet*, 1950, i 1006

that it is virtually impossible to detect a potential candidate for intracranial hæmorrhage, and we pointed out that though early signs and symptoms of traumatic encephalopathy ("punch drunkenness") may be discovered in veteran professionals, it is rare in amateur boxers Electro encephalography has been used to detect early brain damage,[3] but the results are by no means conclusive and there would be serious difficulties in enforcing this investigation as a routine in amateur boxing

Many people, while agreeing that professional boxers are liable to severe injuries, especially after they reach 30 years of age, maintain that amateur boxing is relatively safe, but Doggart,[4] who describes the eye injuries sustained by boxers, stands four-square against both forms of the sport "Medical supervision" he remarks, "cannot alter the anatomy of the human skull or lessen the delicacy of those organs which subserve our highest faculties," and he quotes the opinion of Carroll[5] that probably no head blow is taken with impunity and each knock out causes definite and irreparable damage He also deplores the effect of boxing on the spectators

HOSPITAL COSTING

As in previous years the Hospital Costing Returns for 1954–55[6] set out the costs for every hospital in the National Health Service in England and Wales under itemised headings The object of these analyses is to enable comparisons to be made between broadly comparable hospitals, in order "to promote economy, increased efficiency and improvements in methods of administration"

The classification of hospitals has been somewhat changed The term "general hospital" has now been replaced by "*acute hospital*", *and consequently a* class by class comparison of costs cannot be made as accurately as in earlier years This, however, is unimportant, for the whole structure of the analysis is riddled with inconsistencies, on account of which comparison between hospitals is virtually impossible—except perhaps in the column "average weekly cost of provisions per person fed," and in the column giving the final over-all figure The greatest source of difficulty is the variation in numbers of outpatients, which are allowed for at an arbitrary cost The ratio of casualty to true outpatient attendances must, however, vary considerably between different districts, and the actual cost per attendance must vary greatly with the type of service given The outpatient cost is allowed for in the final cost column per inpatient bed, but not among the individual items of running costs Until the cost of outpatients and casualties is excluded from the main hospital inpatient analysis these costing tables will remain too full of fallacies for any serious comparisons to be made

In practice, these annual publications are not significantly aiding economy, but they are proving of some indirect value to patients When a difference between two comparable hospitals is studied, there is invariably a good reason for the discrepancy, and usually the difference reveals a need for greater expenditure in the less costly hospital, rather than for reduction in the more *costly one Hospitals* by and large still have a remarkable amount of old-fashioned and extravagant equipment, particularly for heating Again, some hospitals have reduced maintenance to dangerously low levels The general public is perhaps more keenly aware than hospital staff themselves that there is a greater concentration of dangerous organisms in hospitals than anywhere else in the community The low hygienic level still prevalent in some hospitals owing to economy in maintenance constitutes a real danger and is paid for by recurring outbreaks of cross-infection or food-poisoning sometimes with loss of life

It is surprising that indices of comparison, such as "cost per patient treated" and "average length of stay," are omitted, but these figures are available to the regional boards It is very doubtful whether any sufficient purpose is served by publication of these annual tables in their present form They will never bring about true long-term economy What is needed is an over-all figure, together with a few tables free from gross fallacies Each year some aspect of hospital activity could be studied by a true costing system and the lessons published as a guide to policy

LYSINE DEFICIENCY

LYSINE is one of the amino acids essential for man—that is, it cannot be synthesised in the body and if it is not supplied in the diet symptoms of lysine deprivation *occur Osborne and Mendel*[1] *showed* that animals remained alive when gliadin provided all the dietary protein, but they grew only when lysine was added to the diet Deficiency of lysine has also been shown to cause anæmia in animals[2] In humans Albanese and Holt[3] found that experimentally induced lysine deficiency caused negative nitrogen balance, which was reversed as soon as lysine was added to the diet The only woman in their inquiry menstruated during the period of lysine deprivation, and she noted a complete absence of the swelling of the breasts, headaches, and weight-gain which usually preceded her periods This observation is interesting in view of the influence of lysine deficient diets in suppressing the œstrus cycle in animals[4] Albanese et al[5] showed that people on a lysine deficient diet had a greatly increased urinary excretion of non-ketonic organic acids Restoration of lysine to the diet promptly reduced the excretion of these acids to normal During the period of high organic-acid excretion they all complained of nausea, vertigo, and hypersensitivity to metallic sounds

In the body lysine seems to be remarkably inert Thus Schoenheimer and Rittenberg[6] found that lysine was the only amino acid which failed to take up N^{15} when they fed rats with isotope tagged ammonia and various amino acids When *l* lysine tagged with deuterium and N^{15} was given to rats, the lysine of the tissues contained the isotopes in the same proportion as that in which they had been given, although N^{15} from administered lysine was found in other amino-acids But the lysine which was incorporated into the tissue proteins had undergone no chemical change Although lysine can donate amino groups, its main function is in the formation of proteins It is not surprising therefore that Albanese et al[7] have now recorded that lysine added to milk mixtures given to infants had a remarkable effect on weight and nitrogen balance

Currently fashionable fresh or dried milk mixtures were given to 15 children from one to twenty-seven months old After a control balance period, lysine was added to the diet in the form of 100 mg of *l*-lysine HCl per kg body-weight per day *A control series of 9 children* aged two to eighteen months received no lysine supplement During the period of added lysine, 5 of the children on supplemented diets gained in weight and went into positive nitrogen balance, 6 had no spectacular weight gains but went into positive nitrogen balance, and in all these 11 the blood proteins increased The other 4 children in this group, whose growth rate was already above average, showed no response to added lysine Albanese and his colleagues conclude that lysine-fortification will improve the nutritional value of many infant foods, including cow's milk, but that this is only effective with children who are not deriving adequate nourishment from their food They also suggest that whereas the lysine-tryptophane ratio in the diet of young adults necessary for growth is from 2 0 to 3 2,[8 9] the needs of an infant can only be met by a ratio of 6 0 If they are right, it seems that human breast-milk with a lysine-tryptophane ratio of 3 8[10] may be insufficient to meet the growth requirements of infants—and there is no evidence that that is so A more recent report[12] by Albanese et al confirms their earlier findings and suggests a simplified scheme of dosage for feeding lysine to infants

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[3] *Ibid* 1953 i, 283 1955 i 1114

[4] Doggart, J H *Arch Ophthal*, N Y 1955 54, 161

[5] Carroll, E J *Amer J med Sci* 1936 191, 706

[6] National Health Service Hospital Costing Returns year ended March 31 1955 H M Stationery Office Pp 127 17*s* 6*d*

[1] Osborne T B Mendel L B *J biol Chem* 1914 17 325

[2] Hogan A G Powell E L Guerrant R E *Ibid* 1941 137 41

[3] Albanese A A Holt L E Brumback J E Hayes M Kajdi C Wangerin, D M *Proc. Soc exp Biol* N Y 1941 48 728

[4] Benedict, F B Finn M D *Amer J Physiol.* 1928 86, 59

[5] Albanese A A, Holt, L E Frankston J E Kajdi, C N, Brumback J E Wangerin, D M *Proc Soc exp Biol*, N Y 1943, 52 209

[6] Schoenheimer, R Rittenberg D *Physiol Rev* 1940 20, 218

[7] Albanese A A Higgons R A. Hyde, G M. Orto L *Amer J clin Nutr* 1955, 3 121

ARTIFICIAL RESPIRATION IN CHILDREN

SOME 120 children under the age of five die in Great Britain each year from drowning, and mechanical suffocation in bed or cradle is given as the cause of death of an even larger number, but this diagnosis is almost certainly wrong in many cases Nevertheless, some of these lives might well be saved if parents were better able to deal with the emergency by applying manual artificial respiration at the earliest possible moment The time spent in summoning help may make the difference between success and failure of artificial respiration Moreover, the aspiration of large amounts of water, especially fresh water, causes profound circulatory changes, hæmodilution, hæmolysis, and ventricular fibrillation[13] These changes develop rapidly and may be the most potent factor in death from drowning, and one of the main reasons why action must be swift

A method of artificial respiration for reviving children must be effective, simple, easy to teach, and not fatiguing to use These requirements have been considered by Rickard,[14] who concludes that there is as yet no satisfactory method for children under two, but for the older ones the now standard Holger Nielsen[15] method is suitable He has therefore proposed a new method for children under two which he has called the "Rickard prone tilting visceral shift method" This is an ingenious use of the rocking principle,[16] which Eve devised when treating a two year old child with diaphragmatic paralysis[16 17] The rocking method is also recommended in children in Garland's excellent handbook[18] In Rickard's method the prone child is laid length-wise along the operator's right forearm with the child's face cupped in the operator's right hand The right middle finger is inserted in the child's mouth, holding the tongue forward, allowing drainage of secretions, and maintaining the airway The patient is steadied by the operator's left hand and is then rocked rhythmically by alternate flexion and extension of the right elbow Rocking begins with a downward tilt of 45°, which produces expiration and expels the aspirate It is continued through an arc of 90° at a rate of eight to twelve times a minute Only experience can show whether this method is effective, but there is no reason to believe otherwise The excellent ventilation achieved with both the Eve and Nielsen methods was demonstrated on curarised anæsthetised adult volunteers,[19] but that experiment should not be performed with the Rickard method If, as seems likely, the method proves to be a valuable one, it should be made widely known

PARALYSIS TREATED BY MUSCLE TRANSFER

THE transfer of a single muscle attachment has been widely used in the treatment of permanently paralysed limbs, but apart from the pectoralis transplant described by Clark,[20] complete muscle transfer has not been recorded Schottstaedt et al[21] may therefore have opened a new field of orthopædic treatment Few muscles, of course, can be completely transposed, and unless the distance to be moved is small, a long and mobile neurovascular pedicle is essential Either the pectoralis major or the latissimus dorsi can be used in this way to provide flexion of the elbow, the insertion of each is transferred to the coracoid process and the origin to the radius The latissimus dorsi can also be used to unite coracoid to olecranon to produce elbow extension The restoration of neck flexion by transposition of the pectoralis major to replace a paralysed sternomastoid, and the use of an intact sternomastoid to replace a paralysed masseter, are each ingenious examples of the art of muscle transposition

Views on the value of tendon transplantation in poliomyelitis are changing, and it is clear that many procedures do little lasting good When complete muscle transposition is performed the strength of contraction may not be great, but further experience of the optimum fibre length for effective action may improve these results Although many patients with severe paralysis may be unable to afford the loss of a large muscle mass, others may find it of great value to have the independence of action which transposition brings

NEW YEAR HONOURS

OF the four new medical knights who work in these islands, Dr Greig Anderson, of Aberdeen, receives his promotion in the Royal Victorian Order by reason of his position as physician to Her Majesty's Household in Scotland, but his knighthood could as fittingly recognise his position among his colleagues and his services to old people Mr Mercer, who in 1948 became the first professor of orthopædic surgery at Edinburgh, was chosen by his fellows in the Royal College of Surgeons of Edinburgh to be their president in this memorable year of the 450th anniversary of its origin Mr Victor Negus, whose name has long been known wherever laryngologists or King's College Hospital men forgather, is a surgeon who has never ceased to be a biologist and has thereby learned much and taught much Professor Zuckerman, of Birmingham, simultaneously anatomist, physiologist, educationist, and much else besides, has combined a fruitful academic career with forms of national service including the study of ballistics in war and the direction of scientific policy in peace Overseas, Sir Arthur de Silva consulting surgeon in Colombo, becomes K C M G, Dr Paul Boffa is knighted for public services in Malta, and Dr S L A Manuwa, descendant of rulers and now chief medical adviser to the federal government of Nigeria, adds the honour of knighthood to the many others he has gained since the day in 1926 when he graduated at Edinburgh In congratulating these and many other doctors whose names appear on p 40 we must also express the pleasure that many will feel at the knighthood conferred on Mr George North, LL D, who as Registrar General has shown himself so helpful a collaborator in the work of our profession

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8 Bricker M, Mitchell, H H Kinsman G M *J Nutr* 1945 30 269
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Special Articles

THE EPIDEMIOLOGY OF LUNG CANCER IN NEW ZEALAND

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New Zealand is insular and remote. It was discovered and occupied by Polynesians about a thousand years ago. In the fourteenth century there was a major Maori invasion, and from then until the coming of Captain Cook in the late eighteenth century New Zealand had practically no contact with the rest of the world. This means that Europeans did not settle in the country until the mid-nineteenth century, and that when they did so they came (as they have continued to come) predominantly from Great Britain. Consequently persons, other than those of Maori extraction, born in New Zealand are predominantly of British descent.

Immigration has generally been continuous, and there exists in New Zealand today a numerous group of immigrants from Great Britain who can act as natural controls, being essentially of the same stock and now living under similar conditions and differing only in the fact that they have spent part of their lives in Great Britain before coming to New Zealand. Moreover, it is possible to divide these immigrants into groups according to their age on entry and hence according to the degree of exposure to another environment before coming to New Zealand. If this different environment which they experienced during the earlier years of life had an effect on the risk of contracting cancer it should be reflected in differences in mortality between those born in New Zealand and those born in Great Britain and between those in the immigrant group who came to New Zealand after a substantial period of residence in Great Britain and those who came at an earlier age.

Method

This study was made on deaths from cancer of various sites in immigrants from the United Kingdom and in the New Zealand-born non-Maori population in 1949–53. The population at risk was taken as the Census Population of 1951. It was confined to those aged 35 or more.

Expected deaths were calculated on the basis of these figures and the significance of differences between the expected and observed deaths was assessed in terms of χ^2.

TABLE I—EFFECT OF "URBANISATION" ON DEATH-RATES FOR CANCER OF VARIOUS SITES

Areas arranged according to degree of urbanisation	All sites except lung			Stomach			Large intestine			Rectum		
	No. of deaths observed	No. of deaths expected	Degree diff.	No. of deaths observed	No. of deaths expected	Degree diff.	No. of deaths observed	No. of deaths expected	Degree diff.	No. of deaths observed	No. of deaths expected	Degree diff.
Total	7646			1353			1000			451		
Auckland Urban Area	1413	1363.9		223	238.1		169	180.4		81	80.1	
Wellington Urban Area	795	739.3	–	127	125.1		111	97.4	–	40	42.9	
Christchurch Urban Area	902	827.1	–	150	144.5		118	109.2		52	48.4	
Dunedin Urban Area	542	506.9	–	88	89.0		73	68.2		37	29.8	+ +
Other Urban, N.I.	815	811.0		150	143.0		92	107.0	–	58	47.7	+ +
Other Urban, S.I.	364	373.8		73	66.2	–	54	49.5		16	21.1	– –
Remainder N.I.	1559	1732.2	– –	296	309.7		211	221.6		89	102.6	–
Remainder S.I.	1273	1292.0		246	237.4		172	166.7		78	77.4	

	Lung			Tongue, mouth, and pharynx			Larynx			Female breast		
Total	632			136			79			874		
Auckland Urban Area	143	106.7	– – –	35	24	– + –	17	16		155	163.3	
Wellington Urban Area	69	59.5	–	6	15		6	9		114	92.1	+ +
Christchurch Urban Area	72	64.8	–	12	15		5	7		109	99.3	
Dunedin Urban Area	43	37.1	–	9	9		7	5		52	61.2	–
Other Urban, N.I.	67	64.0		15	14		9	8		103	84.9	
Other Urban, S.I.	25	29.0	–	4	6		3	4		50	43.7	+
Remainder N.I.	113	157.2	–	28	32	–	12	18		154	186.0	–
Remainder S.I.	100	113.7	– –	27	21	+ –	20	12		137	133.5	

	Cervix uteri			Prostate gland			Skin		
	No. of deaths observed	No. of deaths expected	Degree diff.	No. of deaths observed	No. of deaths expected	Degree diff.	No. of deaths observed	No. of deaths expected	Degree diff.
Total	268			408			79		
Auckland Urban Area	64	49.6	– –	72	68.9		11	13.8	
Wellington Urban Area	31	28.5		42	33.2	– +	2	7.0	
Christchurch Urban Area	35	30.5	–	57	41.3	– – –	10	8.1	
Dunedin Urban Area	16	18.3		32	25.7	– –	6	5.2	
Other Urban, N.I.	31	29.0		36	42.7	–	4	8.4	
Other Urban, S.I.	9	13.2		17	19.5		5	3.8	
Remainder N.I.	53	58.1		77	98.3	– –	23	18.4	
Remainder S.I.	29	40.8	– –	75	78.4		18	14.3	

Degree of Difference Column

The percentage difference between the expected and observed numbers of deaths is represented by the following equation

$$\frac{\text{Observed no. of deaths} - \text{Expected no. of deaths}}{\text{Expected no. of deaths}} \times 100$$

Where (a) expected number of deaths is less than 20
or (b) percentage difference is less than (i) 5% for "all sites except lung" } the column is left blank
(ii) 10% for other sites
Where percentage difference is (i) 5% but less than 10% for "all sites except lung"
(ii) 10% but less than 20% for other sites—it is noted by – or +
Where percentage difference is (i) 10% but less than 15% for all sites except lung
(ii) 20% but less than 30% for other sites—it is noted by – – or + +
Where percentage difference is 30% or more it is noted by + + + –

Immigrants tend to settle more often in towns than in the country, in the larger towns than in the smaller, and in the North Island more often than in the South Island. It has been reported from other parts of the world (Stocks 1947, Spiegelman 1952) that the incidence of certain forms of cancer is higher in some regions than others in accordance with the degree of urbanisation. The data were therefore used in the first place to assess whether any similar differences existed in New Zealand. For this purpose the following areas were chosen: the major urban areas of Auckland, Wellington, Christchurch, and Dunedin, with populations near to, or greater than, 100,000; aggregates of other urban areas in the North and in the South Islands with populations of 20,000 or more; and the remaining areas in each of the two principal islands. Comparisons between towns and localities were based solely on deaths in those of New Zealand birth, and were, of course, allocated to the usual place of residence of the deceased.

The following sites were considered at first, as well as deaths from cancer of all sites: stomach, large intestine, rectum, lung and bronchus, breast, cervix uteri, prostate, and skin (other than malignant melanoma). Important unequivocal differences were found, however, in lung and bronchus only. It was therefore decided to take out figures for other parts of the respiratory tract. Accordingly larynx was added; and tongue, mouth, and pharynx were taken together.

Comparison was based on the actual and expected deaths for each of the sites chosen in the age-groups 35–, 45–, 55–, 65–, and 75+, the expected deaths being calculated in each locality on the basis of the rates for the New Zealand-born population as a whole; the figures for the separate age groups were then added together.

The only site that showed consistent differences in mortality in the areas considered was lung and bronchus, where a significant increase with urbanisation was shown in both males and females (table I).

Though a consistent or significant urban bias is not seen in the separate sites other than lung, there is such a bias for all other sites taken together. It is smaller than in the case of lung but, in view of the numbers involved, may be considered significant.

Accordingly, in assessing differences between those who were born in New Zealand and those who were born in the United Kingdom, the expected deaths were calculated for each area and then added together to allow for differences in the geographical distribution of the immigrant population compared with the indigenous population, though such differences in practice were found to have a negligible effect on mortality for any site other than bronchiogenic cancer.

TABLE II—OBSERVED AND EXPECTED MORTALITY FOR CANCER OF CERTAIN SITES ACCORDING TO WHETHER BORN IN NEW ZEALAND OR BORN IN THE UNITED KINGDOM

Site of cancer	Where born	Observed no of deaths	Expected no of deaths	Significance of difference between observed and expected*
All (less lung)	N Z	7646	7628.4	
	U K	3005	3022.6	N S
Stomach	N Z	1353	1342.6	
	U K	573	583.4	N S
Large intestine	N Z	1000	1015.4	
	U K	426	410.6	N S
Rectum	N Z	451	448.7	
	U K	182	184.3	N S
Lung	N Z	632	721.8	
	U K	369	279.2	p < 0.001
Tongue mouth and pharynx	N Z	136	138.1	
	U K	61	58.9	N S
Larynx	N Z	79	80.5	
	U K	36	34.5	N S
Female breast	N Z	874	876.8	
	U K	281	278.2	N S
Cervix uteri	N Z	268	271.1	
	U K	92	78.9	N S
Prostate gland	N Z	405	427.4	
	U K	252	232.6	N S
Skin	N Z	79	76.5	
	U K	34	36.5	N S

* Based on χ^2

TABLE III—OBSERVED AND EXPECTED MORTALITY FOR CANCER OF CERTAIN SITES IN IMMIGRANTS ACCORDING TO WHETHER THEY ENTERED NEW ZEALAND BEFORE OR AFTER THEIR THIRTIETH BIRTHDAY

Site	Age on immigration (yr)	Observed no of deaths	Expected no of deaths	Significance of difference between observed and expected*
All (less lung)	Under 30	1730	1787.4	
	30 +	1251	1193.6	0.05 > p > 0.02
Stomach	Under 30	319	334.3	
	30 +	244	228.7	N S
Large intestine	Under 30	239	244.8	
	30 +	179	173.2	N S
Rectum	Under 30	106	103.1	
	30 +	68	70.9	N S
Lung	Under 30	187	231.8	
	30 +	168	123.2	p < 0.001
Tongue mouth and pharynx	Under 30	28	36.0	
	30 +	30	22.0	p = 0.05
Larynx	Under 30	16	18.0	
	30 +	12	10.0	N S
Female breast	Under 30	157	165.5	
	30 +	120	111.5	N S
Cervix uteri	Under 30	44	47.4	
	30 +	34	30.6	N S
Prostate gland	*Under 30*	*143*	*145.0*	
	30 +	98	96.0	N S
Skin	Under 30	19	16.9	
	30 +	10	12.1	N S

* Based on χ

Findings

The numbers of deaths of New Zealand born persons and of immigrants from the United Kingdom, and the expected deaths of the two groups on the assumption that there is no difference in the incidence between them, are given in table II.

The assumption holds good for all forms of cancer except that of lung and bronchus. In the latter site the immigrant group has a much higher incidence of bronchiogenic cancer than would be expected on the basis of equity, suggesting that for this site, and this site alone, the immigrant has an increased susceptibility.

The United Kingdom-born were next divided into two groups according to the age at entry into New Zealand, those under 30 at the time of entry being placed in one group and those aged 30 or more being placed in the other group. There was a small residue of persons whose age on immigration had not been stated.

The observed deaths and the deaths expected on the hypothesis that age at time of entry to New Zealand has no effect on the risk of dying are shown in table III.

There is nothing to conflict with this hypothesis in any site except again lung. For all cancer, other than of lung and bronchus, taken together there is a suggestion that the incidence is higher in those who were over 30 on immigration; the difference, about 5% above the expected value, is of doubtful significance. It is not of the same order as the 46% seen in the case of the lung. Possibly the difference is partly due to exclusion of a few persons whose age at entry was not stated. Such persons numbered 14 in the case of lung and bronchus, and 76 for all other cancer; the number of immigrants from the United Kingdom whose age at entry was not stated at the time of the census in 1951 was 1723.

Lest it might be thought that a similar consideration can explain the difference in the case of cancer of the lung, all 14 persons whose age on entry was unstated were allocated to those who were under 30 at the time of immigration, and the 1723 of the population whose age at entry was likewise unknown were allocated to those who were 30 or over when they came into the country. This minimises the difference between the two groups, but it is unlikely that the persons concerned would be distributed in this extreme manner. Nevertheless the difference is still found to be significant, the observed and expected values now become as follows

Age at entry	*Actual deaths*	*Expected deaths*	*Significance of difference*
Under 30	201	229 2	0 01 > p > 0 001
30 or more	168	139 8	

Discussion

Immigrants to New Zealand from the United Kingdom have a higher incidence of lung cancer than New Zealand-born persons of the same stock The difference is greater in those who were aged 30 or more when they came to New Zealand This increased incidence is unlikely to be an artefact, for it is not seen in any other of the principal sites for cancer Moreover, it is the same for women as for men and is consistent at all ages over 35 and for all the principal parts of the country

The chances of dying of cancer of the lung are 30% higher for all United Kingdom immigrants, but for those who were 30 years of age or more on entering New Zealand the risk is 75% higher This is in agreement with the differences in the death-rates from cancer of the lung in the two countries (see table IV)

There has been a continued increase in New Zealand in the numbers of male deaths at all ages certified as due to lung cancer, but the incidence has always been substantially below that in England and Wales The peak of incidence in England and Wales is in the age group 55–64 during the two earlier periods, whereas in New Zealand it has always been in the group a decade older

Owing, at least so far as New Zealand is concerned, to the small numbers involved at the extremes of the age-distribution shown, deaths from lung cancer in females are subject to much random fluctuation There appears, however, to be little if any increase in those below the age of 45, but there is a steady increase thereafter The New Zealand figures roughly parallel the English figures, but, as in the male, the death-rates are well below those in England and Wales

The conclusion follows that immigrants from Great Britain to New Zealand are affected by their former environment and that this effect is related to the length of exposure in that environment It shows itself in an increase in lung cancer but not in cancer of any other site

Differences in habits of tobacco smoking are unlikely to contribute to this picture Consumption of tobacco in the two countries for the first half of this century is shown in table V

The environmental factors concerned are unlikely too to be of a personal kind related to the way of life of the immigrant, for this would make it difficult to explain the differences between the younger and the older immigrants

The evidence points to the factors being associated with urbanisation, as has been suggested in other studies (Kennaway and Kennaway 1951, Stocks 1952) It shows too that they may exert their carcinogenic effect a long time after the person has been removed from them, and this is in keeping with what is known of the mode of action of the carcinogens isolated from the atmosphere of industrial cities (Leiter et al 1942, Waller 1952)

TABLE IV—AVERAGE YEARLY DEATH RATE PER MILLION PERSONS FROM CANCER OF THE LUNG 1932–53 IN NEW ZEALAND COMPARED WITH ENGLAND AND WALES

Period	Country	Age-group (yr)				
		35–44	45–54	55–64	65–74	75 or more
			Males			
1932–36	N Z	13	87	158	204	62
1937–41	N Z	33	108	235	283	213
1940–41	England and Wales	126	424	802	715	448
1942–46	N Z	46	168	466	635	326
	England and Wales	132	466	1072	1032	527
1947–51	N Z	43	287	734	1014	735
	England and Wales	166	781	1682	1857	1073
1952–53	N Z	61	305	1027	1456	1110
	England and Wales	175	858	2171	2650	1688
			Females			
1932–36	N Z	14	37	65	95	48
1937–41	N Z	8	18	60	121	76
1940–41	England and Wales	26	75	151	220	212
1942–46	N Z	19	30	81	111	198
	England and Wales	34	83	165	247	225
1947–51	N Z	13	37	93	156	240
	England and Wales	39	102	211	337	320
1952–53	N Z	15	67	132	185	178
	England and Wales	40	109	245	354	422

TABLE V—YEARLY CONSUMPTION OF TOBACCO (LB) PER HEAD

Year	New Zealand	United Kingdom
1900	2 3	1 95
1910	2 69	2 22
1920	3 59	2 99
1930	3 28	3 31
1940	3 87	3 97
1950	5 36	4 22

Source Government Statistician, New Zealand
High Commissioner for United Kingdom in New Zealand

I record my thanks to Dr F Bielschowski, director of cancer research, Otago University, for his invaluable advice and friendly encouragement, and to Dr J Cairney, director-general of health, New Zealand, for permission to publish

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VITAMINS OF THE B COMPLEX

THE nutrition panel of the food group of the Society of Chemical Industry held on Dec 14 the second meeting of a series concerned with Nutritional Requirements and Food Fortification[1] Vitamins of the B Group were dealt with under nutritional requirements, dietary supplies, and food fortification

Dr H M SINCLAIR discussed nutritional requirements He said that the B M A figures covered requirements for the average person but individual requirements were affected by race, age, sex, and the other components of the diet The type of carbohydrate affected the requirements of thiamine by influencing the intestinal flora In addition the state of health might affect the absorption (for example, in pernicious anæmia, or by losses through vomiting and diarrhœa) and the use (for example, in fever and hyperthyroidism)

Thiamine was required for the oxidation of carbohydrate at the level of 0 4 mg per 1000 calories The requirements were increased considerably in old age, the reason for this was unknown The requirements of *riboflavine* were affected by alterations in the amount of fat and protein in the diet, probably because of change in the intestinal flora Although there was no evidence that the requirements were linked to calorie expenditure the B M A 's recommendations suggested 0 6 mg per 1000 calories On the other hand the U S National Research Council linked the riboflavine requirements with the protein intake, but Dr Sinclair pointed out that there was no clear reason for doing so Nicotinic acid was required for the oxidation of fat and carbohydrate, and the recommended intake was 4 mg per 1000 calories The requirements were influenced by the level and type of protein in the diet since tryptophan could be converted into nicotinic acid Carcinoid tumours produced large amounts of serotonin from tryptophan, and pellagra developed in some patients because of this loss of tryptophan Nothing was known of the requirements of vitamin B_6, but deficiencies did occur and diets were probably marginal Peripheral neuritis had been observed in tuberculous patients treated with isoniazid, due to combination of this drug with pyridoxine, and possibly many other drugs could behave similarly

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[1] See *Lancet* 1955, ii, 1184

Miss A M COPPING dealt with dietary supplies The average intakes of thiamine, riboflavine, and nicotinic acid were a little above the recommended average intakes About a third of the thiamine and nicotinic acid were provided by bread and cereals, and 40% of the riboflavine by milk and cheese Since much of the B vitamins in wheat was contained in the outer endosperm and germ, the B vitamin content of flour increased with the extraction rate Other members of the vitamin-B complex, including B_6, B_{12}, biotin, and folic acid, were fairly widely distributed in foodstuffs and were likely to be in reasonable supply, although nothing precise was known as to the requirements

Thiamine was partly destroyed by heat, especially in alkaline solution, and the Ministry of Food tables allowed 15% for the loss of this vitamin Riboflavine was relatively stable to cooking, but was destroyed by light, and milk exposed to light lost a considerable amount

Mr J B M COPPOCK, PH D, discussed food fortification The present white loaf, which appeared to be preferred by the public, was fortified with thiamine and nicotinic acid to the level of these vitamins found in flour of 80% extraction In the United States levels of enrichment were about three times those enforced in this country, and included the addition of riboflavine, Dr Coppock suggested that British practice was restoration rather than enrichment

The enrichment of rice with thiamine was carried out by soaking rice grains in a solution of the vitamin and adding 1% of this master mix to the main bulk of the rice The alternative was to spray the rice with a solution of the vitamin protected by a film coating which resisted washing

Dr Coppock pointed out that serious losses of vitamin B_1 occurred during the washing and cooking of rice, amounting to 20–90%, and there was, on the average, a 20% loss on baking bread Recent work had shown that this loss occurred with patent and whole-meal flour and was independent of prior treatment with bromate or chlorine dioxide The losses seemed to depend solely on the temperature reached, thus, in the case of toast, losses were greater with thinner slices The loss of thiamine in bread, cake, and biscuits was related to the internal temperature reached during baking Dr Coppock pointed out that the thiamine content of bread, after allowing for baking losses, was little more than adequate for the calories contained in that bread and did not provide any excess for the rest of the diet The fall in bread consumption suggested the need for an upward trend in fortification

In the discussion Dr SINCLAIR pointed out that the removal of nutrients and the restoration of only some of these nutrients was unsatisfactory For example, deficiencies of pyridoxine might arise, and pantothenic acid was essential to man, and the National loaf contained seventy times as much manganese as the 70% extraction loaf In reply to a question whether riboflavine should be added to the white loaf, Dr Sinclair said that the conference on the post war loaf had agreed not to add this since bread was not an important source of riboflavine, contributing only 12% of our intake He pointed out that in poor families with many children bread would be a more important source of riboflavine, and when asked his opinion he agreed that this vitamin should also be added to white bread

Mr A E BENDER, PH D, asked what levels of intake of vitamins were desirable to ensure not only that the average intake was above the required level but that the greater part of the population received more than this level Miss D F HOLLINGSWORTH replied that this question could not be answered since so little was known of the individual variation both of requirements and of intake She added that the intake of riboflavine did not include the losses in milk exposed to light

In reply to a question on the influence of different carbohydrates on the intestinal flora, Dr SINCLAIR said that there was experimental evidence that thiamine deficiency developed more readily with sucrose in the diet than with starch or glucose Volunteers on a diet deficient in vitamin B_1 had shown signs of deficiency when the carbohydrate was sucrose but not when it was dextro maltose This was apparently due to synthesis of the vitamin in the gut

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NEW YEAR HONOURS

THE list of honours published on Jan 2 contains the names of the following members of the medical profession

K C M G

SIR ARTHUR MARCELLUS DE SILVA, O B E, F R C S
Member, Public Service Commission, Ceylon, consulting surgeon, General Hospital, Colombo

K C V O

ALEXANDER GREIG ANDERSON, C V O, M D, LL D Aberd F R C P

Knights Bachelor

PAUL BOFFA, O B E, M D
For public services in Malta

SAMUEL LAYINKA AYODEJI MANUWA, C M G, O B E, M D, LL D Edin, F R C S E
Chief medical adviser, federal government, Nigeria

WALTER MERCER, M B Edin, hon F A C S
Professor of orthopædic surgery, University of Edinburgh, president of the Royal College of Surgeons of Edinburgh

VICTOR EWINGS NEGUS, M S Lond, hon D SC Manc, F R C S, hon F R C S E
Consulting surgeon, ear, nose, and throat department, King's College Hospital, London

SOLLY ZUCKERMAN, C B, B A Cape Town, M D Birm, D SC Lond, F R S
Deputy chairman, Advisory Council on Scientific Policy, Sands Cox professor of anatomy, University of Birmingham

C B (Military)

Major General FREDERICK CAVENDISH HILTON SERGEANT O B E, M B Lpool, Q H P

Surgeon Rear Admiral ROBERT CYRIL MAY, O B E, M C M R C S

Major General FRANCIS JOSEPH O'MEARA, M D Dubl, F R C P I, Q H P

C B (Civil)

EDWARD ROLAND ALWORTH MEREWETHER, C B E, M D Durh F R C P
Senior medical inspector of factories, Ministry of Labour and National Service

C M G

JAMES LESLIE MCLETCHIE, O B E, M B Glasg
Director of medical services, Eastern region, Nigeria

GEORGE DOUGLAS ROBB, M D, CH M N Z, F R C S, F R A C S
Consulting surgeon, Auckland, New Zealand

KOK CHEANG YEO, M D Hong Kong
Director of medical and health services, Hong Kong

C V O

STAFFORD ERIC SAINT, M R C S

C B E (Military)

Air Commodore GLEN ALBYN MARTIN KNIGHT, M B Melb, R A F

C B E (Civil)

JOSEPH EDWARD DEBONO, M D Malta, F R C P
Professor of medicine, University of Malta, for medical services in Malta

HUGH MONTAGU CAMERON MACAULAY, M D Lond
Senior administrative medical officer, North West Metropolitan Regional Hospital Board

CHARLES GEORGE MCDONALD, CH M Sydney, F R A C P
Consulting physician, Royal Prince Alfred Hospital, Sydney, New South Wales

CHARLES TITTERTON MAITLAND, M D Lond, F R C P
Principal medical officer, Ministry of Health
ROLAND NIGHTINGALE, M B Manc
President of the Association of Certifying Factory Surgeons factory doctor for Stockport district
LAWRENCE WILLIAM PLEWES, M D Toronto F R C S E
Consulting orthopædic surgeon, Luton and Dunstable Hospital
HENRY CAMPBELL WILKINSON M D
Lately director of health services, Bermuda
KATHARINE GEORGINA LLOYD WILLIAMS, M B Lond F F A R C S
Dean, Royal Free Hospital School of Medicine, London

O B E (Military)

Surgeon Commander HERBERT LEWIS BELCHER, M R C S, R N
Lieut -Colonel AUSTIN BERNARD DEMPSEY, F R C S, R A M C
Lieut Colonel TERENCE RICHARD JANSEN, M B E, E D, Ceylon Army Medical Corps
Lieut Colonel DOUGLAS DUNDAS MAITLAND, L R C P E, R A M C

O B E (Civil)

GERALD HENRY COORAY, M B E, M D Lond
Professor of pathology, University of Ceylon.
THOMAS DAVIES, B SC Lond and Wales, M R C S
Chairman, medical recruiting board Cardiff Ministry of Labour and National Service
KENNETH FRASER, M D Edin
County medical officer, Cumberland
RICHARD JOHN BURNSIDE HALL, M B N Z, F R C S E, F R A C S
Medical superintendent, Cook Hospital, Gisborne
WILLIAM CHARLES BURKE HARRISON, L R C P I
Director of medical services for Northern Rhodesia, Federation of Rhodesia and Nyasaland
JOHN SWINTON MEREDITH, M B Glasg
Medical specialist, Tanganyika
WILLIAM LEATHLEY NICHOLSON, M B Manc
Senior medical officer, Ministry of Pensions and National Insurance
WILLIAM MATHIAS QUIN, M B Edin, F R C S E
Lately senior surgical specialist, Sierra Leone
CHARLES MCCONAGHY ROSS, M B
Senior leprosy officer, Northern region, Nigeria
IAN NORMAN SAMUEL, M R C S
For political and public services in Battersea
HAROLD GRIFFIN VASE, M R C S
Chairman, Royal Air Force Benevolent Fund Committee in Jamaica

M B E (Military)

Captain HAMISH COATES NEALE, R N Z A M C

M B E (Civil)

ROBERT ASHLEIGH GLEGG, M D Edin
Hon secretary, East Sussex County Housing Association for the Aged
HARRY HAIGH, M B Camb
For medical services, Eastern region Nigeria
GLADYS CHEE ING HU
For medical services in Singapore
CENYDD RICHARDS JONES, M B Wales
Amerindian medical officer, British Guiana
EMERIC LOSONCZI, M D Naples
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OWOLABI ANIFOSHE OMOLOLU, M B Edin
School medical officer, Lagos Federation of Nigeria
GEORGE EDWARD RANAWAKE, M R C S
Secretary, Hospital Lotteries Board, Ceylon
JAN ZYGMUNT SLOMINSKI, M B Polish Sch Med, Edin
District medical officer, Carriacou, Windward Islands
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Senior medical officer (clinical), Federation of Nigeria
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For public services in Kandy, Ceylon

The Widdicombe File

XXX THE MEDICAL CURRICULUM

DEAR WILL,

You ask me to write to your young nephew and to give him some idea of what he will have to expect during his studies if he should take up medicine Nothing would give me greater pleasure—but only if I had as interesting an account to give him as you generously but quite wrongly assume that I must have For the truth is that his curriculum will be surprisingly similar to that from which you yourself emerged with distinction 25 years ago Because the curriculum is still very much what it was there's only one thing that I'd like to tell him, and it's this work well enough to pass but do not overwork to gain distinction

Defenders of the curriculum sometimes argue that those who criticise it are merely saying that there are many disappointing students—many who are lazy or too poor in intelligence or general education to get much good from any course of study But I refute that with three pieces of personal evidence

First, our students' medical society—bless it—has been sending its members to departments, for elementary demonstrations and discussions, as much as one and two years before they reach the subject in question in the normal course of their studies Over and over again I have heard my colleagues say what I have myself observed—namely, that the students show far more keenness and are far more observant and able to discuss things well at these early informal demonstrations than when, one or two years later, they come to the subject as a class They are steadily losing interest

My second bit of evidence is that I have taken on as assistants a number of men whose undergraduate records were far from good, although none of them was rank bad Some have remained only moderate performers, but more of them have suddenly come to life, confessed to a first awakening of interest in their books, and shown that—freed from our teaching and *examination* programme—they had it in them all the time to be really keen students of medicine

Thirdly, what effect has the curriculum on those who bend themselves the most willingly to its demands and manage to stay the course to the end? Three of our year, you will remember with modest pride, attained the eminence of graduating with distinction

Pringle, the first of us in the order of the prize-lists, went straight off to be house surgeon to the professor —Honest John—and was so disillusioned by that good man's ignorance that he pledged himself to the physiology department as soon as his year in hospital was up Unfortunately he had worked so hard and so *consistently* as a student that he was, unknown to himself, dangerously sensitised to professors and textbooks—with the result that he left physiology in 3 months to take a job in an obscure provincial hospital, from which he has not moved to this day He is now a *full time* consultant physician and is known locally as a sound chap with a surprising range of knowledge But he never publishes anything, he does no research, and he makes too little use of his brilliant gifts for analysis of really hard problems and for logical exposition His *undergraduate* devotion to the curriculum killed his fire and arrested his intellect You may say that making himself a distinguished student cost him his academic soul

I need not dwell on my own story, for you know it in full But I should remind you that for 8 years after graduation I went from one thing to another, mighty uncertain what I wanted to do and finding nothing that I was keen to work at with real devotion At that stage my experimental probing took me back to a post in our old school, but I should pretty certainly have left that also if I hadn't been given leave of absence to join the Army at the outbreak of war Six years in different parts of the world and in an extraordinary variety of situations seemed to neutralise most of the harm which I suffered from being a *diligent student* *After the war I returned* to my hospital and academic duties with real zest for the work, and my life would now be a thing of unclouded happiness if only I could adjust my expenditure to the hard fact that my net income is less than half of my gross earnings *But seriously I should estimate that it* required 8 years of restless seeking and a war to rescue me from the harm that was done to me from taking the curriculum seriously

You yourself, to all appearances, suffered least of the *three of us from your medical studies* For you laughed off your academic distinctions as an outrageous fluke and went straight into general practice in your own village I think that you came off best because in fact as a student you followed your own curriculum and indeed learned your *medicine in your long vacations* You dodged all the poor lecturers, although you went to practical classes and clinics , but I never saw you around the hospital in the holidays When I stayed with you in the summer of 1928 I remember that you then had two chief activities *outside your duties as a fast bowler for the village eleven* all unqualified, you took Dr Battersby's surgeries and made a great many of his visits on any day when he and his friend the village stationmaster concluded that the water and the wind were right for trout-fishing , and sitting in the study of the Rev William Smart, you composed thrilling sermons which that wise old gentleman was glad to deliver after he had purged them of their worst heresies By these vacation activities you gained for yourself two things that the curriculum could never have given you first, a real acquaintance with the whole problem with which the illness of one of its members confronts a family , and second, a taste for, and training in, the use of books and periodicals and the orderly expression of your thoughts

Modern developments, of course, have *probably* made it dangerous for you to let your nephew attend your patients until he is qualified and has joined a medical defence society They have probably also deprived you of a railway station and thus of a companion with enough control of his summer days to go fishing with the doctor And I should not be surprised if most parsons think it better to write their own sermons, because of the news value that now attaches to their pulpit indiscretions —as well as to their others, which have always been good for *two half columns and a photograph*

So your nephew may necessarily be thrown back on the curriculum, and it's just what it was before except that it now demands one year extra before graduation and two before *registration* *It allows less free time for personal* study, and has led to examinations that more searchingly probe a student's store of facts but less certainly ascertain whether he can safely be trusted with a patient's life

For years now the Faculty has been listening to pleas *for a few more hours for this, and for many more hours for* that Each teacher applying for more time has a good case who can deny a *plea based on the evident truth* that a great deal more is now known about nucleic acids, steroid hormones, chemotherapeutic agents, viruses, psychiatric disorders, anæsthetics, neurosurgery, isotopes, radiology, neoplasms, and all the rest ? If the teacher is a good fellow who seems likely to make a lively impact on the student, the Faculty gives him most of what he asks for , if he's a *fairly ordinary pedagogue* he is given a half or less , and if he seems a dull stick he's turned down flat or kicked around the subcommittees until his *plea is lost* So there is a certain rough justice and often approximate wisdom in what the Faculty does

But there's never *real wisdom* *For we never—or very* seldom—cut anything out Worst of all, we never ask ourselves what we think we are doing Last week I went to the Faculty with a plea for a little more time to let me deal half decently *with the fundamentals of* antibiotics and viruses Conscious of, and feeling rather guilty about, what I was doing, I coupled my plea with the proposal that the Faculty members should meet informally—without anybody's requests specifically before them—so that *we could tell each other*, in five minutes each, what we were aiming at in our teaching and roughly what ground we each covered I thought that we might then be able to see my plea, and those of others, in perspective I hoped we might face it that we are now asking 7 years *of a boy's life after he leaves school* before we turn him into his 2 years as a National Service medical officer I hoped that we might recall that we once made quite good doctors in 5 years and even in 4 years Every one agreed in principle There was even a witty suggestion that we could *probably* devise a 3-year curriculum if we sent each professor out of the room in turn and left the others to decide how much time his subject required I said that I was seriously worried about merely adding to the students' burden by asking for extra teaching time even *for new topics of obvious importance*—but they gave it to me out of the " free time " My proposal for an informal meeting was turned down because, as the anatomist truly said, so radical an examination of the curriculum would certainly need more than one *meeting*

But surely we shall have to face it Much as I personally shrink from change, I believe that we must turn things upside down because I think that our curriculum is now a bad one I believe that students should be seeing at least a few *patients in their first year of study*, and hearing something about nucleic acids in their last , *I think that lecturers capable only of dictating notes* must be proscribed , *and I think that we should need* at the most 5 years of undergraduate study (including that *for the first* M B) and 1 postgraduate year as a resident in hospital before registration I believe that we must examine the case *for a basic minimum* of study *for all, with the rest of the curriculum set out as* elective courses with the subjects in sensible groupings *I think* that we must give the student greater incentives to study on his own and more chances to take fully responsible care of patients I'd like to see the General Medical Council decree a 20 year period of experiment on these lines, leaving schools *to work out their own solutions* Details of these experiments would, of course, be made known to the G M C , and the results could be assessed by visitors and perhaps by some form of national examination conducted anonymously and based upon methods of testing *separately knowledge of facts, capacity* for self expression, and ability to deal with clinical problems as presented by the cases of actual patients

We have had enough deliberation about better medical education Our discussions have led us from fairly unsatisfactory to bad Are we to leave it to our American colleagues to make the only modern experiments in medical education ? *Let us agree the objects of our* own experiment and for goodness sake let us get on with them, each school making in all probability some *horrid* mistakes and some real discoveries

If we enter such a phase of experiment I'll write an enthusiastic letter to your nephew But if we rumble on as at present I'll only caution him *that he must* weigh the examinations carefully to ensure that he does not suffer from exposing himself innocently to our gross over instruction which certainly leads to progressive and visible dis education Unless we are ordered to mend our ways—for we seem *incapable of doing it* ourselves—he must do all that he can to side step the results of our excessive earnestness and *defective imagination*

Yours,
James Davey

Public Health

REPORT ON ATMOSPHERIC POLLUTION

THERE is no doubt that this country's air has been increasingly polluted during the past fifteen years by grit and dust there is less certainty about the increase in pollution by smoke and oxides of sulphur and the recent report[1] of the Department of Scientific and Industrial Research contains some contrary evidence in that it records a small decrease in pollution by smoke and sulphur oxides The report summarises the results of over a million measurements made during the past ten years—measurements made by local authorities and other organisations cooperating with the department's fuel research station The number of these "measuring" authorities has lately shown a welcome increase from 80 to 220, and the number of measuring instruments in regular use has risen from about 200 to nearly 2000 The department deserves much praise for accomplishing the heavy task of analysing and collating this mass of measurements

The amount of pollution of town air may be as much as forty times that in rural areas, and at times of smog the average level of pollution by smoke and sulphur may reach ten times the normal for the time of the year There may be some increase in air pollution in country districts which goes undetected, for the huge power-stations which now consume much of the nation's coal throw out by forced draught through their high chimneys oxides of sulphur and not a little dust, to be windblown perhaps for many miles The majority of measuring instruments are at present in congested towns, and there is a need for more measurements in rural areas In addition more daily-recording instruments are required so that important basic knowledge may be gained and serious smogs studied in detail

Many of the instruments already in use are designed to investigate particular local sources of pollution such as steel, chemical, and cement works, electricity-generating stations gas and coke works, various industrial boiler installations, railway-engine sheds, and colliery spoilbanks It is good to read in the report of greater coöperation from industrial undertakings responsible for the emission of pollutants an increasing number of industries are recognising their contribution to air pollution and some are taking the public more and more into their confidence

Measurements of air pollution are also of value to central and local authorities in their various building and development schemes Knowledge of the present levels of pollution is a help in planning for smoke abatement, and it will be of interest, when the "smoke control areas" envisaged in the Clean Air Bill come into operation to assess the progress made towards safer air It would be particularly useful to select one or more towns and make them entirely smokeless, thus providing a valuable means of studying the effects on health of a decisive reduction of air pollution

An important result of the London smog of 1952 was the establishment of the committee on air pollution under the chairmanship of Sir Hugh Beaver and the Department of Scientific and Industrial Research gave the committee valuable help Among the important recommendations of the Beaver Committee was the extension of research into the many problems of air pollution and health This would mean a considerable expansion of the research staff engaged in studying the relationships between various pollutants and the incidence of disease Already some special surveys on the influence of air pollution on bronchitis, lung cancer, and other respiratory diseases are being assisted by the department

Over five million tons of sulphur dioxide are discharged into the air of Great Britain each year, and this subject will need intensive examination. By each of our large electricity-generating stations as much as a million tons of coal may be burned each year Another problem in which the department has helped and can help further is that of the tens of thousands of hand-fired boilers still used in industry—boilers which are not equipped to burn raw coal efficiently without producing excessive smoke The special smoke-eliminator door developed by the fuel research station is inexpensive and simple to operate, it makes coal "work harder" by using it more efficiently, and it greatly reduces smoke

Among other work described in this important report, there is that relating to the removal of oxides of sulphur from flue gas, the production of coke that will give a satisfactory fire even on an old-fashioned fire grate, research on domestic heating, and the testing of equipment, one of the objects of which is the more widespread use of stoves and grates that will allow a satisfactory smokeless fire with ordinary coke

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[1] The Investigation of Atmospheric Pollution a Report on Observations in the 10 years ended March 1954 Department of Scientific and Industrial Research. H.M. Stationery Office 7s 6d

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London's Health in 1954

In his report[1] for 1954 Dr J A. Scott, county medical officer of health for London, refers to the increase in notifications of dysentery The figure of 4268 notifications in the year was the highest ever recorded The epidemic was already under way when the year began and came to its peak in April The heaviest incidence was among children of preschool age, but there was a slightly increased proportion of cases among school-children compared with the previous year Food-borne outbreaks of dysentery are at present very uncommon, and there is no evidence that the heavy incidence of recent years is due to food infection An investigation of cases in 1952-53 showed that children under 15 were more likely to give rise to secondary spread, and more susceptible to secondary spread than those over 15 Nearly half the cases notified had a clinical illness which was confirmed bacteriologically; less than a tenth were symptomless carriers, and two-thirds were in outbreaks of 2 or more associated cases A clear association was shown between the severity of the primary case and the resulting spread Where the infection was widespread, "sulphonamide appeared to present few advantages"

The *birth rate* was 15 2 per 1000 population compared with 15 3 in 1953 and 1952, 15 6 in 1951, 15 7 in 1950, and 13 4 in 1938 The birth rate, though well in excess of the pre war and early war years, seems to have stabilised at a little below the average of the last 21 years Since 1948 the stillbirth rate has remained relatively stable, and in 1954 there were 19 8 stillbirths per 1000 total births

Since 1951 there has been a steady decline in the *death-rate* to the lowest figure ever recorded in London—10 7 per 1000 population in 1954 Heart-disease accounted for nearly one third of the mortality and although the death-rate from cancer showed a slight decrease from 2 34 per 1000 in 1953 to 2 31 per 1000 in 1954, it remained the second leading cause of death (a detailed examination of the course of lung cancer in London over the last 25 years appears as an appendix to the report)

The *infant-mortality rate* continued to decline and reached the lowest recorded figure of 20 7 per 1000 live births, compared with 23 9 per 1000 live births in 1953 Of these, 15 1 occurred in the first four weeks of life, which was also a record low figure and compared with 17 8 for England and Wales

The total number of women *who died as a result of pregnancy or childbirth* (including post-abortion deaths) was 34, compared with 37 in 1953, 50 in 1952, and 42 in 1951

The number of cases of *diphtheria* continues to decline, and in 1954 there were only 4 confirmed notifications and no deaths There was a smaller incidence of *whooping-cough* than for some years past and there were only 4 deaths from this disease The notifications of *scarlet fever* were the lowest recorded since 1941 and there were no deaths The fatality-rate for *measles* has declined considerably in recent years, and from the 7445 cases notified in London only 2 deaths resulted

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[1] London County Council Report of the County Medical Officer of Health and Principal School Medical Officer, 1954 Pp 231 2s 6d

The report includes a detailed account and statistical data relating to recent trends in the mortality and morbidity of tuberculosis in London. About a century ago nearly one-fifth of all deaths in Londoners was due to tuberculosis, in 1950 the proportion had fallen to a thirtieth and in 1954 to a fiftieth. 77% of the deaths in 1954 from all forms of tuberculosis occurred among persons aged over 45 years, and the majority (79%) of these deaths were in men.

The routine vaccination by B C G of tuberculin-negative 13-year-old school children was inaugurated during the year. About 25% of parents withheld their consent to vaccination. Of the children whose parents consented to vaccination, only 15% of those not in contact with a known case of tuberculosis were found to be positive reactors.

There was a slight though welcome improvement in the "immunity state" of London children under 5: the number of primary immunisations against diphtheria increased from 36,004 in 1953 to 47,621 in 1954. At the end of 1954 it was estimated that 55% of children under 5 had at some time been immunised against diphtheria. In spite of the fact that no special publicity was given to whooping-cough immunisation, the demand for it continued to grow and during the past four years it had increased fourfold. The number of children vaccinated against smallpox in their first year of life has almost doubled since 1949, and during 1954 about a half of all children under 1 were vaccinated.

Safeguarding Agricultural Workers

Based on some of the recommendations made in 1949 by the Gowers Committee on health, welfare, and safety in non-industrial employment, the Agriculture (Safety, Health and Welfare Provisions) Bill[1] now before Parliament enables the Agricultural Ministers to make protective regulations.

These may deal, among other things, with the safeguarding of workers from dangerous parts of machines, with the training or supervision of young persons when working with prescribed machines, and with the protection of workers from the risk of falls and strains. The maximum loads which workers may lift under different circumstances may be specified. The Bill also provides for notices to be served requiring the provision of sanitary and washing facilities, and the Ministers may make regulations for the provision of movable sanitary facilities where workers are employed by a contractor or other person who is not the occupier of the land. In addition the Bill provides that children under 13 years of age may be prohibited from riding on or driving prescribed vehicles, machinery, or implements used in agriculture. (Local authorities are at present empowered to make by-laws concerning the conditions in which children, after their 13th birthdays and until they leave school, may assist in any trade or occupation.) All agricultural units are to have a first-aid box whose contents will be laid down by regulations. Regulations may require the notification and keeping of records of accidents and certain diseases connected with agricultural work. The Bill also makes certain rules concerning inquests on deaths which may have been caused by agricultural operations.

Colouring in Food

A supplementary report,[2] presented to the Food Standards Committee by their preservatives subcommittee, on the use of colouring matters in foods was published on Dec 21. In an earlier report,[3] published in January, 1955, the main recommendation was that the Public Health (Preservatives, &c, in Food) Regulations, 1925–1953, should be amended so as to permit the use in foods of specified colours only. The present position under these regulations is that, with a few specified exceptions, the addition of colouring matters to articles of food is permitted. The supplementary report reviews the representations which the subcommittee have received from trade and other interests. It sets out in greater detail than in the earlier report the subcommittee's views on the declaration of the presence in foods of added colour, and it recommends a slightly modified list of permitted colours. In other respects it reaffirms the earlier recommendations.

In the list of permitted colours, the report recommends the inclusion of two additional colours of natural origin, titanium dioxide and ultramarine, and there seems, it says, no objection to the continued use in foods of the other organic colours of natural origin customarily used in foods. In view of the need for certain coal-tar colours a revised list of synthetic colours recommended for inclusion in the permitted list is given in an appendix.

The earlier report recommended that in general the presence in foods of added colour should be declared to the purchaser, but it was recognised that exceptions might be necessary. In the supplementary report recommendations are made as to the form the declaration should take, the sales in respect of which declaration should apply, and the foods which need not be required to bear a declaration of added colour.

Before deciding, in consultation with other Ministers concerned, what action should be taken on its recommendations, the Minister of Agriculture, Fisheries and Food will consider any further representations from interested parties.

Representations already made to the subcommittee need not be repeated, but new representations should be sent to the Assistant Secretary, Food Standards and Hygiene Division, Ministry of Agriculture, Fisheries and Food, Great Westminster House, Horseferry Road, London, S W 1, to arrive not later than Jan 31.

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[1] Agriculture (Safety, Health and Welfare Provisions) Act, 1955. H M Stationery Office 1955. Pp 14. 1s.

[2] Food Standards Committee. Supplementary Report on *Colouring Matters*. H M Stationery Office. Pp 15. 9d.

[3] See *Lancet* 1955, i, 146.

Medicine and the Law

Right to Case-records

To whom do case-records belong—to the patient or to the doctor or hospital authority? The point arose recently when a woman was charged before a Metropolitan magistrate with stealing documents, said to be her own case-papers, from St Mary's Hospital, Paddington.[1]

The prosecution solicitor said that the defendant came for treatment at the hospital and took the papers from a table in an office while a doctor was being called. She took them home, and they were found there by the police. The hospital authorities, said the solicitor, were in an embarrassing position because the papers covered a long and difficult case in which civil proceedings had been threatened on several occasions. They wanted to establish that a patient had no right to confidential papers of this character.

For the defence, it was submitted that a hospital patient had the same right to his or her papers as a solicitor's client; the removal of the papers could not be larceny. The defendant had thought that she needed them in order to get treatment and because she wanted the information they contained.

The magistrate said that no one was going to hold in that court that a patient had a right to his or her records. *Prima facie* the documents must be the property of the hospital; until the matter was disposed of they should be handed back to the hospital, leaving the accused to take such action as she would be advised to secure possession of them. The magistrate suggested that the prosecution should withdraw the charge and he would direct that the papers should be returned to the hospital to be kept in safe custody until the ownership was decided by legal proceedings. This course was adopted.

The position as between solicitor and client is stated thus in Halsbury's *Laws of England*:[2] "Documents coming into existence in the course of business transacted under a retainer, and either prepared for the benefit of the client or received by the solicitor as agent for the client, belong to the client; but documents prepared by the solicitor for his own protection or benefit, and letters written by the client to the solicitor, belong to the solicitor."

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[1] *Times*, Dec 14, 1955; *West London Observer*, Dec 16, 1955.

[2] 2nd ed, vol 31, p 102.

In England Now

A Running Commentary by Peripatetic Correspondents

Bridge is an Easy Game is the title of the book which Iain Macleod published in 1952 Its theme is the ACOL system, which makes bidding easy for your partner and difficult for your opponent Many doctors are good bridge-players and the best doctors make conditions easy for their partners, give disease, which is the opponent, as difficult a chance as possible, use finesse where necessary, and respect conventions The best bridge-players reach their slams by agreeing on the suit, showing their strength with the minimum of bids, and then using cue-bidding or some convention like the 4–5 no trump or Blackwood convention Having arrived at the right contract bad or indifferent play can undo all the good of the bidding and lead to a post mortem which may be tedious but may help the player not to repeat his error

The best physician suspects a particular organ is at fault, or an infection is at work, investigates it appropriately and not with the full fury of every conceivable test and perhaps calls in his surgical partner for help If, by careful team-work, they decide that a person has an adenoma of the bronchus, or of the islets of Langerhans or a meningioma of the cord, or perhaps, with the help of the bacteriologist, decide that the patient has typhoid or psittacosis, their satisfaction is as great as the slam-bidder's But operation or treatment must be as precise as the play of the cards and the experienced operator or physician has yet to complete his task If operation fails, the post mortem may be revealing If the physician fails in his diagnosis, the patient may seek other advice and the second physician make the right diagnosis His chagrin is like that of the bridge-player who bid five hearts over four spades to save game or rubber and goes three down vulnerable, 800 points, only to find later four spades could easily be defeated Bridge may be an easy game for the real experts and medicine may also be easy at times, but let us never forget that basic principles have an overriding importance over investigations and that administration is an integral part of the profession's work And let us be thankful that for three years at the top of the administration we have had a player bold enough to study new methods, use finesse, and realise that the doctor-patient relation calls for real partnership In his new task his recent experience should help and so let us sincerely wish him the best of luck

* * *

Christmas week has been most confusing Sunday was recognisable—just church followed by over-eating, but then chaos set in Deutero-Sunday coincided with crypto-Monday, and was followed by pseudo-Monday Some found Wednesday normal while others confused it with iso-Monday On retro-Saturday sporadic cases of acute inversion of sleep rhythm heralded an explosive epidemic which raged throughout proto-Sunday and had died out again by midday on Sunday Monday of the New Year saw the normal calendar comfortably restored

* * *

On Christmas Eve there was a knock at the door and I heard a boy's clear voice asking permission to sing a carol I brought him into the lounge and said I would accompany his songs on the piano He was a genuine Christmas-card chorister with a skin of strawberry and milk and an expression of indestructible innocence He started with *Sleep Holy Babe* and sang with a clear reedy voice that would have brought tears to the angels Then he sang *Once in Royal David's City*, and finally the *Coventry Carol* I would have kept him singing all night, but knowing that he had only a little time in which to amass a fortune I asked my wife to bring in the mince-pies I poured him out a sweet sherry and searched in my pocket for half a crown I had to exercise some restraint not to give him five shillings After he had downed the pies and sherry he bent down and patted my golden Labrador on the head

"Hallo Su" he said

"How do you know my dog?"

"I know him quite well He chased me out of your "

"Don't tell me you are the wretched and degenerate youth who stole every apple from my *only* apple tree!"

The truth was too clear I turned helplessly to my wife "I have brought this shining youth into my house out of the cold of the night I have treated him like a princeling I have given him my finest vintage sherry and stuffed his pockets with silver only to learn that he is a monster of iniquity!"

The boy's head sank in an agony of remorse Slowly he opened his hand and offered me the half-crown back "No, my holy innocent—but before you go you will sing every verse of *The Lord at First had Adam made*—unaccompanied"

* * *

This week looks like marking the end of an epoch in our village They are going to fill up the hole in the road It has been there since three years last Christmas, something to do with one of those new-fangled sewage schemes that so disrupt the English way of life The steam-roller came clattering down the hill last Monday and is belching impatiently behind the vicarage Six barrels of tar and a load of granite chippings lie waiting on the village green—the green which has borne three cricket seasons and two and a half football seasons of the contractors' lunch-hour sport We feel just as the Britons did when the legions were packing up for Rome A tampon of tarmacadam will be a miserable placebo for the gap in our hearts

How different it was when the first lorry-load of men came to the village in 1952 and picked a spot outside the *Rose and Crown* It was thirsty work and only the landlord was pleased But Irish tongues and twinkling eyes, and the jingle of half-crowns on pay-night, softened the chill of the tap room The hay season was good the following year, the evenings warm and friendly By autumn time old George's battered taxi was rarely free of white ribbons and confetti Unfamiliar names crept into my midder bookings, Murphy and O'Brien, and even Pinzarelli A fine lot of christening parties we had, with a tot of the real proper peaty stuff for the doctor Too bad that one or two lucky lads got back across the sea, but we are a broad-minded lot in our village, quite used to our own English game of trial and error, so Mildred and Daphne were worked off on someone else, with a flying start for a dowry

We shall miss them all in lots of ways The odd hand scalded while making the nine o'clock tea The sciatica before the local races Mike O'Leary was shaping up nicely as a spin-bowler on Saturday afternoons Pinzarelli clipped the privet hedge around the surgery with the artistry of Michelangelo Poor simple Alf will soon be out of a job He used to twiddle the stop-and-go sign on the corner Nobody took much notice of it, of course, except the day he twiddled it too late and we had to jack the vicar's car out of the hole Mrs Ugglethorpe's paraffin sales will slump when the little red lights are snuffed out for the last time The *Rose and Crown* will seem cheerless

The hole might well have been there for another three years if the boss's son had not come back from his National Service He was a gangling pimply youth when he pegged out the claim, and he never really had a decent chance to get to know us before he was whisked away into uniform Now he has come back, bronzed and broadened, but contact with the wider world seems to have made him strangely intolerant of our hole Can you wonder that we are heavy-hearted?

* * *

I had called for some hair-oil, and found myself standing behind an anxious mother, I distinctly heard her ask for "Delinquent pastilles, please" The chemist looked mystified for a moment and then handed her a packet When she had gone, I could not resist asking him to resolve the mystery To my relief I found that the medicament required was Gee's linctus pastilles

* * *

News from the breakfast table

Jane (aged 13) "I am going to paint the dolls' house these holidays and sell it Then with the money I could buy at least two budgies"

Hugh (aged 9) "Do I get a share?"

Jane "No!"

Hugh "I don't think that's fair After all I helped to bring the dolls up"

Letters to the Editor

RECRUITMENT FOR THE OVERSEA MEDICAL SERVICE

SIR,—There is a certain amount of uneasiness about the future of what until recently was called the Colonial Medical Service. May I inflict on your readers some reflections of an amateur that have a bearing on the problem? *

The Present Situation

Although the Oversea Medical Service is still fairly healthy there is a shortage of doctors in certain territories, and in some places, such as Northern Nigeria, it is serious.

Owing to the progress of some dependencies towards home rule, and, ultimately, complete self-government, a career in Colonial medicine (as in other branches of the Colonial Service) is now robbed of some of its former security and of prospects of advancement for the competent man. It is doubtful whether the type of medical officer now being recruited is on the average quite as good as formerly. Not very long ago it was not unusual to find men who, although not perhaps shining lights academically, were energetic, independent, adventurous, and anxious to use their talents in places where they could make their weight felt. These men were the backbone of the service. Some recent recruits are able, but others would have had little chance of success in the United Kingdom in the fiercely competitive conditions that have prevailed since the war and seem likely to continue.

At the same time there is a surplus of good men in the United Kingdom. Some of them, especially those with a little knowledge of the opportunities for work in Colonial territories, would welcome a spell of duty overseas provided—and this is the crucial qualification—that they could be assured of a reasonable prospect of finding suitable employment at home if and when they decided to return.

Indigenous medical services are growing apace, and in a number of territories there are promising medical schools. Thus, so far as the British graduate is concerned, the service is steadily shrinking. It may therefore be asked what need there is to consider a problem that will solve itself within a generation or less. It is, however, clear that for a number of years to come British doctors should continue to help in building up medical services that are still defective and leavening those that have already achieved autonomy or will soon do so. It would be lamentable if the Oversea Medical Service, as we know it, disintegrated in haphazard fashion during the next ten years.

Recent information about resignations in West Africa is disquieting. That the service will contract is certain, but it is possible to make this an orderly involution rather than a rout. The introduction of the Oversea Service last year in place of the Colonial Service was a welcome step, but one cannot help wondering whether the remedy was too little and too late.

The Proposal

The Oversea Medical Service should be abolished. Each territory would continue to have its medical service which would be recruited locally or by secondment from a new Oversea Division of the National Health Service. In some cases the staff would be entirely autochthonous, in others the majority would continue for a time to be supplied by the United Kingdom.

The rates of pay in the Oversea Division of the National Health Service would be the same as in the existing health service plus whatever allowances were appropriate. Salaries would be paid by the National Health Service, the necessary funds being derived from contributions from the various territories supplemented as required by an allocation from the Colonial Development and Welfare Fund. The purpose of this allocation would be to ensure that in poor countries the rates of pay for overseas officers would be as good, or almost as good, as those in wealthier territories. Furthermore, it would be desirable to stabilise establishments so that they would no longer be subject to disconcerting fluctuations dependent on factors such as the prevailing price of coffee or sisal. Each territory would indicate to the Colonial Office, and, through it, to the Oversea Division of the National Health Service, what vacancies it wished to be filled from the United Kingdom. If a man chose to make his career in Colonial medicine he could apply for transfer to a local medical service, if he were prepared to take the risk, or for transfer (see below) to the permanent staff of the Oversea Division of the National Health Service.

The Difficulties

These are formidable and the list that follows is far from exhaustive, but no worth while administrative change can be made without a good deal of pain and suffering.

If one of the cardinal features of this scheme is that men may come and go between the United Kingdom and the oversea territories, then by far the biggest obstacle is the fact that the National Health Service is not unified so far as the appointment of medical officers is concerned. This important function has been wisely delegated to boards of governors of teaching hospitals and to regional hospital boards. The Ministry of Health as such can make no promise of reappointment to a man who is seconded for service overseas. This is the main reason why the regulations made to facilitate secondment proved unfruitful. The power of appointment is in the hands of the boards, many of which know little about the Colonial Service and care less.

An outstanding man whose pioneer work in a remote colony was fittingly recognised by Government returned to the United Kingdom at the conclusion of his three year contract. He was well known to his regional board and held in high esteem by his professional colleagues. All were aware of the duration of his term of service overseas. Yet on his return he was kept waiting for about nine months before he found employment, and it is possible that he might have been even worse off if pressure had not been put on the board from outside. This sort of thing is discouraging.

There are two possible solutions. The ideal but difficult one is that boards should agree to accept responsibility for filling vacancies in particular territories. The Hospital for Sick Children (Great Ormond Street) already undertakes to supply a registrar for the pædiatric service at Kampala, Uganda. However, the chances are that a single teaching hospital or regional board would find it impossible to supply the men with the necessary inclinations and qualifications for particular vacancies as they arose, or, even if the men were found, it might be impossible to guarantee appropriate vacancies for them on their return. Yet this system of adoption, as it might be called, has the merit of evoking personal interest and the pride of relationship. For that reason it may be better than the alternative and ought not, perhaps, to be lightly dismissed.

The alternative is that when the Oversea Division of the National Health Service is asked to supply medical officers for this or that territory it should notify *all* boards of governors and regional boards, these would submit to the Oversea Division the names of men who wished to be considered and for whom places would be available at the end of their term of service overseas An arrangement of this kind would be utterly valueless unless the boards, already overworked and often harassed, entered enthusiastically into this new and onerous responsibility They would need to learn something about the Colonies, but it is possible, and even likely, that if the ground were well prepared the boards would respond favourably And it happens that the Colonial Office can now command the services of a number of medical folk in this country with a good knowledge of Colonial medicine who would be willing to acquaint boards of governors and regional boards with the great significance of the new departure

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* The policy proposed is in line with that advocated in September, 1953, by a special correspondent to the *Times* and in letters contributed to that newspaper in October, 1955, by Sir Reginald Saloway, Mr Julian Snow, and Mr John Tilney.

Another serious objection to the scheme is that it tends to replace a regular army by one made of men serving on short term commissions Many of the hard-won benefits of unification of the service would be lost Yet it should be possible to maintain a corps d'elite of men who have decided to devote their lives to Colonial medicine and who could be transferred, as at present, to key posts in any territory as the need arose Within the Oversea Division there would be an enclave for such men, still paid by the United Kingdom Government, with regular grades of promotion, but with no guarantee (any more than at present) of their being appointed to posts at home on resignation or retirement

If the course outlined above were limited to medicine —and no more is suggested—it might be objected that the more or less uniform pattern of Colonial administration was being badly shaken The system described could not indeed be easily applied to other professional services because there is nothing in other professions wholly comparable with the National Health Service Here is the test of the value of these proposals If they are worth while, then administrative tidiness should not be taken too seriously And it may be pointed out that however neat the present pattern of central administration that in the territories themselves becomes increasingly kaleidoscopic, with the introduction of officers recruited locally, the direct appointment by Colonial governments of doctors from foreign countries, and the evolution of health departments responsible to elected ministers Even the semblance of uniformity is going, the loss of a little more would of itself do no harm

The Colonial Office would rightly feel reluctant to delegate responsibility for the selection of men for service overseas to another Government department which has little knowledge of Colonial affairs and is, indeed, still busy wrestling with the manifold problems presented by a huge and still young health service It should not be beyond human wit to devise machinery whereby the Secretary of State for the Colonies continued to exercise ultimate authority It would be of benefit to the Civil Servants in his department (as well as to those responsible for the National Health Service) if there were some broadening of selection committees Selection committees set up under the National Health Service, though still not ideal, are wider in composition and to that extent considerably better than in former times It is perhaps worth mentioning too that university bodies in the oversea territories seem well content to leave much of the selection of men, even for senior posts, to committees appointed by the Inter-University Council and sitting in London

I have said nothing about a possible relationship between general practice in the United Kingdom and the proposals I have outlined There are two reasons for this this letter is already too long, and it would be better for questions concerning the general practice aspect of the N H S to be discussed by someone well versed in the subject

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H J SEDDON

CYTOLOGICAL TESTS OF SEX

SIR,—I wish to plead for the utmost in caution and diplomacy in the use of such expressions as "female nuclei or male nuclei" and "genetic female or genetic male" when applying cytological tests of sex clinically Gonadal agenesis patients are feminine although their cells lack sex chromatin in the majority of cases Similarly a proportion of male pseudohermaphrodites are feminine, clinically and socially, although their body cells are of the male type A converse situation is encountered in some true hermaphrodites and in certain uncommon syndromes that are now being studied A well informed patient might be more disturbed than the circumstances warrant should he or she learn by a chance remark that the body cells are at variance with the obvious sexual anatomy Consequently, I would prefer to see used in the clinic such less committal expressions as "chromatin positive or chromatin negative"

The cytological tests of sex have important theoretical implications in the study of sex differentiation They also have a distinct diagnostic value in practice However, they should carry no weight beyond this, and I agree with Wilkins et al[1] who emphasise that the presence or absence of sex chromatin, in congenital errors of sex development, is a minor detail in the femaleness or maleness of the whole person It would be most regrettable if the advantages that accrue from having available a cytological test of sex were marred by placing an additional psychological burden on any patient who suffers from an abnormality in sex development

The recent applications of cytological tests of sex in clinical practice emphasise the necessity of fundamental cytological studies to establish what relation there is between the sex chromatin and the sex chromosomes The suggestion that the "female" sex chromatin is derived from heteropyknotic portions of two X chromosomes is only a plausible hypothesis that is based on indirect evidence[2] Should this hypothesis prove incorrect the cytological tests would retain their practical usefulness in differential diagnosis, but theoretical derivations might be greatly affected In particular, it is premature to equate female type nuclei with genetic femaleness or male-type nuclei with genetic maleness, as a generalisation in errors of sex development, for our present methods give no direct information concerning the genes that are concerned with sex determination and sex differentiation

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MURRAY L BARR

DISORDERS OF CONTEMPORARY SOCIETY

SIR,—Professor Pickering (Dec 3) refers to one factor which we, as a profession, could do something to control

It has been emphasised that the tyranny of the kings and princes has been replaced by that of the organised groups Today antagonisms grow up between groups as they once did between potentates

In war we are, as it were, thrown into a bag and shaken up together This gives many opportunities for understanding the other man's point of view and welds us together But when war ceases the opportunities thus presented are again taken away

In the field of industrial medicine this is painfully apparent, for those in one occupational group perceive dimly, if at all, their dependence on other groups Thus the factory workers distrust "the City" and those in the City condemn, all too easily, the factory man The fact that both are in the same production team is scarcely known and the two groups never really meet. Yet agencies exist that could facilitate such meetings by which, surely, mental health would be improved. Is not much sickness in industry of emotional origin and does not a lot stem from the antagonisms between groups?

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[1] Wilkins L, Grumbach, M M, Van Wyk, J J Shepard, T H, Papadatos C *Pediatrics* 1955, 16, 287

[2] Barr M L *In* Modern Trends in Obstetrics and Gynæcology Edited by Kenneth Bowes Second series London, 1955, chapter 7 p 123

The politicians seem to know little about the way in which the stresses mentioned arise and are aggravated. By grandiose planning they make things worse and expect, without reason, that an individual can easily attach his loyalty and affection to some immense organisation. Yet all civil and military experience shows how difficult this is. In health services they also make things worse by undue segregation of occupational groups in separate medical services. But we have often, when sick, one of the rare opportunities in a hospital or other institution to make unusual contacts which daily life denies us. At such times we can meet those in different walks of life.

Is it not then a mistaken policy to create special services for special groups, excluding others from these services? Does not this policy help to widen the rifts between one group and another?

I see no reason why those concerned with mental health should not take more positive steps to break down the antagonisms described. They need not talk politics to do this. As specialists in a field which baffles the layman we have a duty to help in this situation and, in doing so, to avoid jargon as Professor Pickering so rightly says.

Standardisation and uniformity, whatever politicians may say, are biologically impossible and the attempt to impose them can only be disastrous. Stimulation comes from diversity and from the same source should come a better understanding of our fellow men. Are we not members one of another?

Hitchin, Herts. G. C. PETHER.

ἐμοῦ θανάντος
EMOU THANANTOS

SIR,—According to the old Greek myth, the rebellious Prometheus stole the secret of fire from Heaven and was punished terribly by the eagle, servant of Zeus, but had to be acknowledged as the greatest benefactor of the human race. Modern men, successors of Prometheus, have discovered the secret of nuclear energy. Will they become destroyers of the world, or, by harnessing nuclear energy, will they become the greatest benefactors of mankind? Julian Huxley[1] likens their possible destructive activity to that of a cancer on the Earth.

This choice for good or evil reminds me of something that I wrote many years ago in a fanciful article on the Teleological Aspect of Cancer.[2] It was an imaginary conversation between two cells of a living human being. One cell was complaining of bad treatment, and said "he was determined to try the effect of undergoing a malignant neoplasic mutation." The other cell, arguing against such a step, said "that by undergoing such a mutation he would be destroying the body on which he lived." The answer was that "although he himself would doubtless be dead, his host would live long enough for the birth of hundreds of insurgent descendants,[3] especially in the metastases, and it would be his great great, great, grandchildren who would suffer and that one really could not be troubled by what would happen to them." Indeed there is an old Greek saying, quoted in the works of Euripides: "when I am dead (ἐμοῦ θανάντος) let the earth be dissolved in fire." This is what I call the *emou thanantos* way of looking at many an important subject.

Even now, one continually hears people saying: "Ah well, I don't want to waste my time thinking about that. I shall be dead long before. What will it really matter to me?" But civilised man should say: "The question *ought* to matter to us—whether the world will be destroyed by gangsters after our life or not." If civilised man does not concern himself with such things, can one expect the less civilised peoples in various parts of the world to bother themselves with such thoughts? And those peoples are rapidly gaining in world power and in numerical importance.

London, N.W.1. F. PARKES WEBER.

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[1] *News Chronicle*, Dec. 3, 1955.

[2] Weber, F. P. *Med. Pr.* 1932, 185, 271.

[3] The malignant neoplasic insurgent cells 'Stoop' (that is become less differentiated and more savage) in order to Conquer.

HYDROCORTISONE IN PAINFUL SHOULDER

SIR,—Dr. Cyriax (Dec. 31) fails to grasp the purport of my letter of Nov. 5: my aim was to point out that cervical spondylitis with nerve-root involvement is often associated with capsulo arthritis of the shoulder joint, and may be the fons et origo thereof; in such cases the lowered muscle tone and loss of support, which are demonstrable by electromyography, have resulted in undue strain being put upon the joint structures, which in time they come to resent.

Neither in the article to which he refers, nor in his *Textbook of Orthopædic Medicine*, do I find that Dr. Cyriax specifically refers to this clinical syndrome.

Sunderland. W. GRANT WAUGH.

ECLAMPSIA

SIR,—Dr. Schuurmans (Dec. 17) says that 17 years ago it was suggested that the high incidence of eclampsia in Australia might be due to the large quantity of meat consumed there. Surely Hamlin has disproved this fallacious view?

In Australia by means of a high protein diet he has caused eclampsia to disappear. On the other hand, as Hamlin has found that limiting the intake of carbohydrate prevents excessive gains of weight, and is followed by the disappearance of severe toxæmia and eclampsia, it is logical to conclude that heavy carbohydrate intake produces the dangerous and excessive gains of weight which are followed by toxæmia and eclampsia.

In any prolonged war eclampsia is apt to diminish or disappear. It happened in Germany in 1914–18. War leads to food shortage and rationing, and so prevents over-eating; reduced intake of food prevents any excessive gain of weight and so is followed by the disappearance of severe toxæmia and eclampsia; this in turn results in fewer toxæmia-produced stillbirths and premature births; and since, as I have shown (Nov. 5), toxæmia and eclampsia affect mothers who are producing boys more often than those who are producing girls, the babies whose lives are saved are more often boys than girls. By this means Nature is able, through producing a surplus of live male babies, to compensate for the male combatants who have died fighting in the war. Post-war male population increases are well known.

The disappearance of eclampsia in Holland during the late war was, I am confident, due, not to the quality of the food, but to its severely reduced quantity. With the end of the war, and an increase in the quantity of food, over-eating became possible and eclampsia reappeared.

The diet which is suggested by Dr. Schuurmans to prevent eclampsia is more likely to produce it, unless bread and potatoes are restricted.

In a region where the disease is fairly common, I have found that for each case of eclampsia there are about 20 cases of toxæmia severe enough to necessitate induction of labour. Using the frequency of this procedure as an index of severe toxæmia, it is possible to note the effect of diet on toxæmia, and indirectly on eclampsia. In the years 1947–51, without controlling weight, the frequency of inductions for toxæmia in my patients was 7.7% (52 out of 674, including 3 cases of eclampsia), while in 1952–55 it was 3.2% (23 out of 710, including 1 case of eclampsia). In the latter period, at first I attempted to control weight only with anorexigenic drugs, but later, owing to the results being inadequate, I also instructed patients to cut their bread and potato intake (i.e., those foods which Dr. Schuurmans is recommending), with improved results. Of the 23 patients who were "failures," 18 had had excessive weight gains (that is to say, my control of their weight was inadequate) while the other 5 patients consisted of 2 primiparæ who were initially hypertensive (essential hypertension) and 3 multiparæ with initial hypertension and histories of having had previous toxæmia (i e, patients who according to my theory had permanently retained a hostility to invading transplacental hormones) By the correct diet, eclampsia and severe toxæmia can nearly always be reduced in severity to little more than mild toxæmia "Many cases of mild toxæmia" that still occur probably include a considerable number of "aborted" severe toxæmias or eclampsias

Dr Schuurmans doubts my theory that mothers may react to the entry of fœtal hormones because, he says, these do not differ in any respect from those of the mother But this is not an established fact Steroid chemistry is complex enough in the adult, but it has never been studied, and could probably never be studied, properly in the fœtus Apart from the suspicion that the sex hormones of the fœtus are probably produced by the adrenal cortex, instead of by the ovary in the mother, it is quite impossible to prove the truth of Dr Schuurmans' incautious statement about the hormones of the unborn baby, though it may well be possible to disprove it

To predetermine the fœtal sex by biochemical means, it is essential for the fœtal sex hormones in the mother to differ from the maternal hormones, and for the presence or influence of the fœtal hormones to be detected I suggested in my article that it might be possible to predetermine sex before but not after, the onset of toxæmia, because entry of fœtal hormones into the mother would then be resisted This suggestion, if confirmed, should dispel Dr Schuurmans's doubts concerning the possibility of maternal reaction to fœtal hormones

Reading K D SALZMANN

EARLY DIAGNOSIS OF COMPRESSION OF THE SPINAL CORD

SIR,—I would like to congratulate Mr Rowbotham (Dec 10) on his efforts to encourage early diagnosis of neoplasms causing cord compression, and endorse his views on the disastrous results of late diagnosis Recently I have seen four such cases

One of these four patients had a ten month history and bilateral palsy of the fifth, sixth, seventh, and eighth cervical and first thoracic nerve roots, but no sensory changes He had been treated for cervical spondylosis At operation he had a pachymeningitis

The next patient had an eight month history and a bilateral palsy of the fifth, sixth, and seventh cervical nerve roots, with sensory changes, the plantar responses were flexor He also had been treated as a case of cervical spondylosis At operation a benign intramedullary tumour was removed, and he is doing well

The third patient had a four month history and a unilateral palsy of the seventh and eighth cervical and first thoracic nerve roots with sensory changes There were no radiographic changes in the cervical spine, and there was no evidence of a Pancoast tumour (which may cause this type of palsy), but further radiographic examination showed the seventh cervical vertebra collapsing and by this time a supraclavicular gland was palpable, which biopsy showed to be malignant

The fourth case was in a young adult who had a seven month history and a bilateral first sacral palsy, bladder symptoms, and sensory loss from the upper buttocks to the outer side of both feet, including the anal and perineal areas Operation disclosed a tumour of the cauda equina

Each of these cases had been diagnosed as a disc lesion

I would like to add six criteria which help towards early diagnosis of spinal tumours

1 A history of increasing and intractable segmental pain

2 Peripheral symptoms, starting distally and progressing proximally, in the upper limb

3 Sensory changes in more than one dermatome

4 Rapid increase in the palsy This is common with disc lesions, but then only one nerve root is affected If more than one nerve root is affected, then a spinal tumour should be suspected

5 Bilateral sensory or motor changes, especially if more than one segment is affected

6 The plantar response is unreliable, since the response may not be extensor until late in the course of the disease

London W 1 R BARBOR

INGUINAL HERNIORRHAPHY

SIR,—Mr Doran (Dec 24) argues that, since the conjoined tendon forms the lower border of an inelastic aponeurosis, the "primary fixed point" remains equidistant from the anterior superior iliac spines, and the distance of this point from umbilicus and pubic crest remains fixed, no "shutter action" of the conjoined tendon is possible While the clinical and experimental evidence adduced seems to support this hypothesis, the geometrical argument appears to be fallacious

In his fig 1 Mr Doran represents the "primary fixed point" as the point of intersection of the diagonals of a quadrilateral whose apices are the umbilicus, the anterior superior iliac spines, and the pubic crest Were this the case the argument would hold In fact, however, the geometrical representation of these points is an asymmetrical four sided pyramid, with the primary fixed point at the apex Theoretically this figure degenerates into a quadrilateral when all five points are co planar, and the apex of the pyramid becomes the point of intersection of the diagonals of the quadrilateral Even if this configuration were present in an individual it would only occur temporarily, since any change in intra abdominal tension would alter the position of the primary fixed point in the sagittal plane

Once it is appreciated that the correct representation of these points is a pyramid it may be seen from geometrical considerations that the primary fixed point is only "fixed" in the coronal plane In the sagittal plane it is able to occupy a wide range of positions without its relations to the other four points in the coronal plane being altered Normally the primary fixed point lies anteriorly to the three bony points and the umbilicus On increasing the intra abdominal pressure, as in coughing, it moves more anteriorly Bearing in mind that the tissues between the conjoined tendon and the primary fixed point are inelastic, if one accepts Mr Doran's hypothesis one would expect the conjoined tendon to become further separated from the inguinal ligament The experiments with radio opaque markers show that, in fact, the distance between the markers remains fixed

One is led to the inescapable conclusion that there must be some mechanism which prevents further separation, and that this mechanism can only be the shutter mechanism of the conjoined tendon I submit therefore that the argument against this action of the conjoined tendon is based on a too literal interpretation of the word "shutter" The fact that apposition to the inguinal ligament or, indeed, any movement does not take place is not a valid argument against its action in maintaining the integrity of the inguinal canal Failure of reparative operations based on this principle must be sought elsewhere

London W 11 J F ROBINSON

SIR,—Mr Doran, in his paper which was read to the Anatomical Society, understandably confined himself to anatomical facts

The value of his observations would be enhanced for surgeons if he would state what incidence of recurrent hernia, if any, was noted among the 12 cases in which the conjoined tendon and Poupart's ligament eventually parted company, and among the 25 cases in which these structures remained in apposition

The gratifying freedom from recurrence in my experience after operations similar to that performed in Mr Doran's series suggests that, even if the conjoined tendon and Poupart's ligament separate, they yet remain joined by a sheet of fibrous tissue strong enough to form an adequate posterior wall to the inguinal canal

When recurrence has followed suture of the conjoined tendon to Poupart's ligament after making a relaxing incision, this has usually been a direct hernia through the medial end of the posterior wall of the inguinal canal This has led me to pay particular attention to the placing of the most medial stitch exactly at the attachment of Poupart's ligament to the pubic spine

This "master stitch" by itself usually brings the conjoined tendon into close approximation with Poupart's ligament and minimises the strain on the more lateral sutures I use fine nylon for these and a stouter strand for the "master stitch" It would be of interest to know what suture material Mr Doran used in his cases

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CENTRAL SOCIETY FOR CLINICAL RESEARCH

SIR,—Your account[1] of this society's meeting includes an abstract of the paper on Renal Manifestations of Primary Aldosteronism which we presented with Dr Gordon Farrell This abstract contains an error

The patients were studied during hydropenia or 'Pitressin' infusion and osmotic diuresis In this situation they excreted slightly hypotonic urine The defect in net water reabsorption, measured as a negative $T^{c}_{H_2O}$, differed from that of diabetes insipidus in that it was not as extensive and was *not corrected* by pitressin Removal of the tumour resulted in at least partial recovery of the function of urine concentration The preoperative defect is apparently a manifestation of renal tubular potassium depletion

The aim of the paper was to indicate that hypertension with excretion of dilute alkaline urine should bring to the clinician's mind the suspicion of aldosteronism, and perhaps lead, from these simple indications, to the uncovering of further cases of this unusual and interesting condition

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A C CORCORAN
HARRIET P DUSTAN

ADRENAL HÆMORRHAGE

SIR,—I was interested by Dr Galpin's letter (Dec 17) The association of suprarenal hæmorrhage with an intracranial lesion has recently been commented on by Dr Buxton Hopkin (Nov 5) The presentation of his case as an exercise in the diagnosis of the "acute abdomen" prompts me to describe briefly a case I saw clinically and examined *post mortem*

A 43-year old man was admitted to Crumpsall Hospital on Dec 8, 1952, with left sided pleural effusion and underlying pulmonary collapse, which was confirmed radiographically Carcinoma of the bronchus was tentatively diagnosed The patient had had a chill four months previously, and a month later had complained of pain in the left side of the chest associated with breathlessness, slight cough, and weakness A week after admission the patient began to have severe constant pain in the epigastrium, penetrating through to the back, he did not vomit There was guarding but no tenderness and bowel sounds were absent His blood pressure was 140/80 mm Hg, having been 125/70 on admission A leaking perforation of a chronic duodenal ulcer was suspected in view of a history of ulcer pain, which had developed ten years previously after a fracture of the spine A policy of "wait-and see" was adopted Pain disappeared, bowel sounds became audible, and diarrhœa developed

Two days later, on Dec 17, the patient felt better, but suddenly his pulse rate rose to 128 per min, and his blood-pressure fell to 80/55, there were no signs of shock His blood pressure remained constant at this level, and he complained of weakness Addison's disease was suggested On Dec 30 the serum sodium level was 240 mg per 100 ml, and the serum chloride level 500 mg per 100 ml (as NaCl) The patient died quietly on Jan 4, his blood pressure never having risen above 80/60

Necropsy confirmed the presence of a carcinoma of the left main bronchus associated with bronchiectasis of the lung and chronic empyema The heart showed severe brown atrophy, and there was a chronic ulcer of the first part of the duodenum with no sign of perforation Both suprarenal glands had become shells of organised hæmorrhage, and it was impossible to say histologically whether there had been thrombosis or embolism Unlike the case recently reported by Mackenzie[1] no carcinoma was present in these glands

In many ways, both Dr Galpin's and my case are similar to the syndrome of "hæmorrhagic suprarenal infarction" reported by Keele and Keele[2] In their case there was repeated vomiting, severe persistent pain below the right costal margin with tenderness, and a remarkable absence of shock

I feel that if such a diagnosis is made during life noradrenaline by itself is insufficient, and full substitution therapy, and possibly chlorpromazine, are all worth giving, for otherwise the condition must be hopeless

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M LEVENE

ROSEOLA INFANTUM

SIR,—In your issue of Dec 3 Dr Letchner writes "Roseola infantum is a common infective disease, occurring nearly exclusively in the first 3 years of life, Complications are very rare, " I have observed in adults a very similar condition with occasional severe complications

In August and September, 1941, at No 12 General Hospital, Sarafand, Palestine, some fifty cases of what I termed (for want of a better name) "infectious roseola" occurred among the medical and nursing staff and patients Similar small outbreaks were noted in the surrounding district

Usually the onset was abrupt with frontal headache, pain on eye movement (a prominent feature in some cases), back ache, general muscular pains, and occasionally joint pains The fever was short lived and usually slight Three days was the usual duration, and 101°F the average highest temperature, though 104°F was recorded Anorexia and nausea, with coated tongue, were fairly common, and occasionally weakness of the legs, slight sore throat, and hyperalgesia of the skin occurred

The *rash* appeared on the 3rd to 8th day, but most commonly on the 4th or 5th day It lasted 5 to 7 days, and was of two types (1) a papulo erythematous, dusky, pink, discrete, morbilliform eruption, resembling measles, but not so blotchy, leading to no desquamation or subsequent staining, (2) less commonly, a much sparser and more discrete, pink, papular eruption The distribution of the two types was similar, affecting the following parts (in order of situation and density) (*a*) back, chest, upper arms, (*b*) forearms, abdomen, thighs, face and neck, legs, (*c*) hands and feet, palms, soft palate The eruption usually appeared a day or so after the temperature had become normal and was not accompanied by a secondary rise of fever There were no successive crops

The *glandular enlargement* appeared with the rash, though it was not seen in every case, and consisted of a generalised slight lymph gland enlargement without tenderness The epitrochlear glands were fairly commonly enlarged There was no splenic enlargement

The *blood picture*, in those cases that were examined, most usually included leucopenia (about 3000 white cells per c mm) with a relative lymphocytosis of 50%, in the first few days of the illness The great majority of cases cleared up completely and rapidly without sequelæ, although sometimes debility, anorexia, and nausea persisted for 10–14 days

The only serious complication was *encephalitis* and three cases of this, with a fourth possible one, were observed They were characterised by fever, headache, neck stiffness, positive Kernig's sign, mental change, and tremor, with no gross abnormalities in the cerebrospinal fluid (c s f) The fourth patient had fever, headache, and some mental confusion with no physical signs, and the c s f was not examined All recovered completely

I had the impression that *atypical cases* also occurred—e g, glandular enlargement without rash, a kind of prodromal

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[1] *Lancet* 1955, ii, 1120

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[1] Mackenzie D H *J Path Bact* 1955, 69 333
[2] Keele, D V, Keele, K D *Brit med J* 1942 ii 687

mottling without development of a true rash, or general symptoms without either rash or enlarged glands

The *Weil-Felix and Paul Bunnell reactions* were negative in all cases tested

From two cases in Tel Aviv, in which the practitioner concerned could obtain comparatively precise dates as to time of contact and removal therefrom, the *incubation period* appeared to be 4–5 days

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General Register Office
London, W C 2

A. MCKENZIE

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(1) The Ministry of Housing and Local Government have had for some time arrangements for "mutual aid" for water undertakings, though as far as I am aware no full survey of potential water-supplies has been made—at least not in this area

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For reservoirs, owing to the relatively short half life of some at least of the most dangerous fission products, storage would help, while, where there are filters, using an alum floc and the actual physical scraping of the sand *surface would* remove more It is highly unlikely that there would *be any* electricity for a number of days, so pumps for water and sewage would not be working unless Diesel operated

In such circumstances it is obvious it would be criminal to waste a drop, and this should be impressed on the Fire Service, which under present arrangements seems to imagine that unlimited quantities of water will be available *to put out* fires The answer is of course that houses would have *to be* dynamited for fire breaks and the rest left to burn

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With regard to (1) and (2) I would refer you also to the contamination of the Wabash River after the historic "Trinity" test, and also to a paper by Tsuzuki[1]

Penzance

W K DUNSCOMBE

NEEDLE BIOPSY OF THE KIDNEY

SIR,—We were delighted with the conservative attitude of your editorial of Dec 10 My colleagues and I have done over 400 renal biopsies in the past few years No patient has died as a result of the procedure, the patient has died as a result of the procedure, the morbidity has been slight, and in no patient was surgical exploration necessary None the less, we believe that, for the time being at least the procedure should be done in special centres and only by those who have been trained in this technique

We were interested in several points raised by you

> You state that "several patients have already had as many as four successive biopsies, giving detailed information of progressive renal disease which could not have been obtained by other means This is not, however, an adequate justification for a potentially dangerous operation, and biopsy should be used only when the information it gives will be of direct advantage to the patient, and not merely a rather academic addition to medical knowledge"

This is a most important statement, for it emphasises again that the clinical investigator must be first a clinician, whose chief consideration is the care of the patient[2] As we have shown, in selected cases, serial biopsy of the kidney has provided data which could not have been obtained in any other way and which was of great value in the care and management of our patients and their illnesses The serially taken biopsies have incidentally provided new knowledge of the natural history of diseases which, as John Ryle taught us many years ago on the wards of Guy's Hospital,[3] is not "merely a rather academic addition to medical knowledge"

> Later you state "that in patients with the nephrotic syndrome therapeutic trial [of cortisone or corticotrophin] would give the same information [as renal biopsy] with less disturbance to the patient"

Unfortunately this is not true Without histological information the response to cortisone or corticotrophin is always unpredictable, this is hardly surprising if we recognise that "nephrotic syndrome" is but a syndrome with many underlying pathological causes When the nephrotic patient is first seen the clinician is faced with the problems of how to treat him, for how long, and whether to treat a second time This decision can be made with far more confidence if the underlying pathology is known In our experience, no good has been achieved in patients with severe glomerular lesions who have been treated with corticotrophin or steroid hormones And in some cases at least it is our opinion that their clinical condition has deteriorated greatly as a result of treatment with these hormones As far as "*disturbance to the patient*" is concerned, our patients who have *needed a* bone marrow or hepatic biopsy as well as a renal biopsy have told us they have been least disturbed by the latter *procedure. It* has also come as a surprise to us to find *that* a number of our female patients were disturbed less by renal biopsy than by catheterisation of their bladders

> You end by saying "There are other interesting possibilities, but it seems unlikely that renal biopsy will achieve the importance that liver biopsy is now assuming Many

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1 Milian G Nouvelle pratique dermatologique Paris 1936, vol 2, p 803

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1 Tsuzuki, M *Münch med Wschr* Aug 5, 1955, 97
2 *Peabody F W Doctor* and *Patient* *Papers on the Relationship of the Physician to Men and Institutions* New York 1930
3 Ryle J A. The Natural History of Disease London, 1948

incision, this has usually been a direct hernia through the medial end of the posterior wall of the inguinal canal This has led me to pay particular attention to the placing of the *most* medial stitch exactly at the attachment of Poupart's ligament to the pubic spine

This "master stitch" by itself usually brings the conjoined tendon into close approximation with Poupart's ligament and minimises the strain on the more lateral sutures I use fine nylon for these and a stouter strand for the "master stitch" It would be of interest to know what suture material Mr Doran used in his cases

Edgware General Hospital FRANK FORTY

CENTRAL SOCIETY FOR CLINICAL RESEARCH

SIR,—Your account [1] of this society's meeting includes an abstract of the paper on Renal Manifestations of Primary Aldosteronism which we presented with Dr Gordon Farrell This abstract contains an error

The patients were studied during hydropenia or 'Pitressin' infusion and osmotic diuresis In this situation they excreted slightly hypotonic urine The defect in net water reabsorption, measured as a negative $T^{c}_{H_2O}$, differed from that of diabetes insipidus in that it was not as extensive and was *not corrected* by pitressin Removal of the tumour resulted in at least partial recovery of the function of urine concentration The preoperative defect is apparently a manifestation of renal tubular potassium depletion

The aim of the paper was to indicate that hypertension with excretion of dilute alkaline urine should bring to the clinician's mind the suspicion of aldosteronism, and perhaps lead, from these simple indications, to the uncovering of further cases of this unusual and interesting condition

Research Division
Cleveland Clinic Foundation,
Cleveland 6, Ohio, U S A

A C CORCORAN
HARRIET P DUSTAN

ADRENAL HÆMORRHAGE

SIR,—I was interested by Dr Galpin's letter (Dec 17) The association of suprarenal hæmorrhage with an intracranial lesion has recently been commented on by Dr Buxton Hopkin (Nov 5) The presentation of his case as an exercise in the diagnosis of the "acute abdomen" prompts me to describe briefly a case I saw clinically and examined post mortem

A 43 year old man was admitted to Crumpsall Hospital on Dec 8, 1952, with left sided pleural effusion and underlying pulmonary collapse, which was confirmed radiographically Carcinoma of the bronchus was tentatively diagnosed The patient had had a chill four months previously, and a month later had complained of pain in the left side of the chest associated with breathlessness, slight cough, and weakness A week after admission the patient began to have severe constant pain in the epigastrium, penetrating through to the back, he did not vomit There was guarding but no tenderness and bowel sounds were absent His blood pressure was 140/80 mm Hg, having been 125/70 on admission A leaking perforation of a chronic duodenal ulcer was suspected in view of a history of ulcer pain, which had developed ten years previously after a fracture of the spine A policy of "wait and see" was adopted Pain disappeared, bowel sounds became audible, and diarrhœa developed

Two days later, on Dec 17, the patient felt better, but suddenly his pulse rate rose to 128 per min , and his blood pressure fell to 80/55, there were no signs of shock His blood pressure remained constant at this level, and he complained of weakness Addison's disease was suggested On Dec 30 the serum sodium level was 240 mg per 100 ml , and the serum chloride level 500 mg per 100 ml (as NaCl) The patient died quietly on Jan 4, his blood pressure never having risen above 80/60

Necropsy confirmed the presence of a carcinoma of the left main bronchus associated with bronchiectasis of the lung and chronic empyema The heart showed severe brown atrophy, and there was a chronic ulcer of the first part of the duodenum with no sign of perforation Both suprarenal glands had become shells of organised hæmorrhage, and it was impossible to say histologically whether there had been thrombosis or embolism Unlike the case recently reported by Mackenzie [1] no carcinoma was present in these glands

In many ways, both Dr Galpin's and my case are similar to the syndrome of "hæmorrhagic suprarenal infarction" reported by Keele and Keele [2] In their case there was repeated vomiting, severe persistent pain below the right costal margin with tenderness, and a remarkable absence of shock

I feel that if such a diagnosis is made during life noradrenaline by itself is insufficient, and full substitution therapy, and possibly chlorpromazine, are all worth giving, for otherwise the condition must be hopeless

Pathology Laboratory,
Withington Hospital,
Manchester

M LEVENE

ROSEOLA INFANTUM

SIR,—In your issue of Dec 3 Dr Letchner writes "Roseola infantum is a common infective disease, occurring nearly exclusively in the first 3 years of life, Complications are very rare, " I have observed in adults a very similar condition with occasional severe complications

In August and September, 1941, at No 12 General Hospital, Sarafand, Palestine, some fifty cases of what I termed (*for want of a better name*) "infectious roseola" occurred among the medical and nursing staff and patients Similar small outbreaks were noted in the surrounding district

Usually the onset was abrupt with frontal headache, pain on eye movement (a prominent feature in some cases), backache, general muscular pains, and occasionally joint pains The fever was short-lived and usually slight Three days was the usual duration, and 101°F the average highest temperature, though 104°F was recorded Anorexia and nausea, with coated tongue, were fairly common, and occasionally weakness of the legs, slight sore throat, and hyperalgesia of the skin occurred

The *rash* appeared on the 3rd to 8th day, but most commonly on the 4th or 5th day It lasted 5 to 7 days, and was of two types (1) a papulo erythematous, dusky, pink, discrete, morbilliform eruption, resembling measles, but not so blotchy, leading to no desquamation or subsequent staining, (2) less commonly, a much sparser and more discrete, pink, papular eruption The distribution of the two types was similar, affecting the following parts (in order of situation and density) (*a*) back, chest, upper arms, (*b*) forearms, abdomen, thighs, face and neck, legs, (*c*) hands and feet, palms, soft palate The eruption usually appeared a day or so after the temperature had become normal and was not accompanied by a secondary rise of fever There were no successive crops

The *glandular enlargement* appeared with the rash, though it was not seen in every case, and consisted of a generalised slight lymph gland enlargement without tenderness The epitrochlear glands were fairly commonly enlarged There was no splenic enlargement

The *blood picture*, in those cases that were examined, most usually included leucopenia (about 3000 white cells per c mm) with a relative lymphocytosis of 50%, in the first few days of the illness The great majority of cases cleared up completely and rapidly without sequelæ, although sometimes debility, anorexia, and nausea persisted for 10–14 days

The only serious complication was *encephalitis* and three cases of this, with a fourth possible one, were observed They were characterised by fever, headache, neck stiffness, positive Kernig's sign, mental change, and tremor, with no gross abnormalities in the cerebrospinal fluid (C S F) The fourth patient had fever, headache, and some mental confusion with no physical signs, and the C S F was not examined All recovered completely

I had the impression that *atypical cases* also occurred—e g, glandular enlargement without rash, a kind of prodromal mottling without development of a true rash, or general symptoms without either rash or enlarged glands

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[1] *Lancet*, 1955, ii, 1120

[1] Mackenzie D H *J Path Bact* 1955, 69 333

[2] Keele, D V Keele, K D *Brit med J* 1942, ii, 687

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[1] Milian, G Nouvelle pratique dermatologique Paris 1936 vol 2 p 803

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[1] Tsuzuki M *Münch. med Wschr* Aug 5, 1955 97
[2] Peabody F W Doctor and Patient Papers on the Relationship of the Physician to Men and Institutions New York 1930
[3] Ryle J A The Natural History of Disease London, 1948

lives have been saved by liver biopsy in the differential diagnosis of prolonged jaundice, but accurate differential diagnosis of renal disease is rarely of such immediate and crucial importance "

We wonder whether this prognostication is based on personal and comparative experience in the use of needle biopsy in the care of patients suffering from either hepatic or renal disease

Our experience with hepatic biopsies goes back many years and is much more extensive than with renal biopsy To tell the truth, we are embarrassed to admit that we have saved lives with hepatic biopsies, but even this early in the game we will admit having cured some patients with renal disease as a result of biopsy of the kidney On the basis of our experience with both types of biopsies we suspect that biopsy of the kidney will be of greater potential value to patients with diseases involving the kidney than hepatic biopsy is to those with jaundice and other types of hepatic disorder As a matter of fact, we find less use today for hepatic biopsies than we did a few years ago This is to be expected because, *from hepatic biopsies*, we have learned so much of the natural history of the different diseases which produce cirrhosis or result in jaundice that we are now able to recognise them early and *clinically*

It is probable that few needle biopsies of the kidney will be necessary *twenty* years hence, *for by that time* clinical investigators will have sorted out, by renal biopsy, the early and *treatable* stages of the many diseases which produce the end stage kidney At present these are lumped together by physicians under the all inclusive "chronic glomerulonephritis"—the diagnosis of which is equivalent to a death sentence

Presbyterian Hospital
Chicago 12, Ill U S A

ROBERT M KARK

THE FORGOTTEN PATIENT

SIR,—The letter (Dec 24) from the president and secretary, Friends of Menston Hospital, states that the findings of a *Daily Express* investigation "cannot be dismissed so airily as Dr Duncan (Nov 12) would have us think" I can ignore the rebuke from Mr Carter and Mr Cripps, but not their inaccuracy My protest of Nov 12 neither included nor implied reference to any newspaper *investigation or articles*

Severalls Hospital,
Colchester, Essex

A G DUNCAN

CERVICAL VERTIGO

SIR,—*I was interested in last week's article by* Dr Ryan and Dr Cope

They describe five cases of vertigo associated with cervical abnormalities and attribute the vertigo in each case to interference with the tonic neck reflexes In describing each case they state that the aural findings were negative What does this mean? If every ear tested was clinically normal and gave normal audiometric and caloric results, they *should state this* If audiometry and caloric testing were not done their observations on the ætiology of the vertigo are valueless

Evidence is accumulating rapidly that labyrinthine vertigo is linked closely with the autonomic nerve-supply *to the* vessels supplying the inner ear It would appear that interference with the cervical sympathetic chain might well have caused the vertigo in all five cases by causing a temporary *alteration in the blood* supply to one or both inner ears

The conception of "cervical vertigo" put forward by Dr Ryan and Dr Cope merely increases the present confusion on this subject, and in laying stress on the cervical abnormalities present may tend to prevent proper otological investigation of these cases in future

Tyrone County Hospital
Omagh

T J WILMOT

STREPTOKINASE IN TREATMENT OF INFLAMMATION

SIR,—Professor Dubos, in his account of the *Micro* environment of Inflammation,[1] has reviewed a new field to which he himself has made many significant contributions

The œdema fluid in inflamed areas contains large amounts of fibrin The deposition of fibrin in the tissue fluids and the formation of thrombi in the arteries, capillaries, veins, and lymphatics help to wall off the area of infection by aiding in the formation of a *limiting* membrane This defence curtain has been correctly regarded as a beneficial structure, and its preservation, in order to inhibit the spread of infection, has been considered a basic surgical necessity

The advent of streptokinase has produced *a change* in thought about the barrier The chemical nature of the limiting membrane might be changed by administration of streptokinase, for this *will indirectly cause lysis* of fibrin through activation of plasminogen to plasmin, which is the active lytic agent Such a change *would* be beneficial, since the antibacterial drugs, being borne by the blood, cannot pass through the limiting membrane *from without any more than can pathogenic bacteria* from within The inefficiency of the antibacterial drugs in the treatment of abscesses, walled off cellulitis, and similar infections is well recognised

'Varidase,' which contains streptokinase and streptodornase, has been used as the source of streptokinase, since a pure preparation of streptokinase has not yet been made [2] (The streptodornase content can here be disregarded) Varidase was dissolved in physiological saline so that the final concentration of streptokinase was 10,000 units per ml The solution must be stored in a refrigerator, and a fresh solution was made daily 5000 units of streptokinase in 0 5 ml of physiological saline was injected intramuscularly, usually in the gluteal area, twice daily for a total of six doses or more if necessary One of the antibacterial drugs must be given, either orally or parenterally, when streptokinase is injected intramuscularly in the treatment of infection and/or œdema A spreading infection may result from dissolution of the membrane if protection against the contained bacteria is not provided

In 64 patients with abscess, cellulitis, empyema, epididymitis, hæmarthrosis, thrombosed hæmorrhoids, orchitis secondary to mumps, sinusitis thrombophlebitis and œdema, 45 excellent and 15 good results were obtained The 4 poor results were in a patient with paraplegia and extensive decubitus ulcers which were resistant to all forms of treatment in 2 patients with peripheral arteriosclerotic vascular disease with gangrene, and in a patient with thrombosed hæmorrhoids who did not receive sufficient treatment

Of patients who were benefited the redness and œdema started to decrease in a few after several hours, and in all receded considerably by the end of two days In the patients with granulating wounds, healing was hastened by reduction of the surrounding induration Delay in healing was not seen in any of the patients Pain and tenderness at the site of injection, noted in about 60% of the patients, disappeared about twenty four to forty eight hours after the injections were stopped The pain and tenderness were probably due to the streptokinase in varidase, since they were not encountered in patients given streptodornase alone A granuloma at the site of injection was not seen in any of the patients A rise in temperature attributable to the streptokinase was noted in about 10% of the patients A significant change in the total and differential white blood cell counts and in the prothrombin time was not *found*, fibrinolysis, determined by the whole blood technique, was not observed, hæmorrhage, hæmatomas, and petechiæ were not seen, and chills, cyanosis, or *allergic responses were* not noted Administration of anti histamine drugs was not necessary

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1 Dubos, R J *Lancet*, 1955 ii 1
2 Miller, J M Surmonte, J A Ginsberg M, Ablondi, I A *Maryland St med J* 1955, 4 188

To obtain good results from the intramuscular injection of streptokinase in the treatment of infection and œdema, the involved area must have an adequate circulation Because of the risk of hæmorrhage, streptokinase should not be given to patients with defects of the blood clotting mechanism

Veterans Administration Hospital
Fort Howard, Maryland, U S A
JOSEPH M MILLER

LIGNOCAINE

SIR,—Since lignocaine was introduced some six years ago there have been sporadic reports of toxic reactions, the latest being that by Mr Dutton in last week's issue

Recently, Lock and Greiss[1] have recorded a case of convulsions and death following the administration of 40 ml of 2% lignocaine ('Xylocaine') for pudendal block, which they regard as "a gross overdosage" Nevertheless, because of its many advantages over procaine, lignocaine is the agent of choice in obstetrical local anæsthesia, and it would be a pity if the occasional adverse report should deter obstetricians from employing this excellent drug

Having used lignocaine in many hundreds of cases over the past five years, I have sometimes noticed marked drowsiness during or soon after delivery, and at first welcomed this effect for its associated amnesia However, since observing an attack (fortunately transient) of pallor, twitching, and cyanosis after the injection of 60 ml of 1% lignocaine I have tended to use only the 0 5% solution, and like Mr Dutton I find 50 ml quite ample for pudendal block and perineal infiltration I should like to endorse Mr Dutton's plea for care in the use of this valuable agent, and for administration of the smallest effective amount in the lowest concentration possible

Pinner, Middlesex
J P O'DWYER

BLOOD-TRANSFUSION

SIR,—In your leading article last week you state "Hospitals that have no resident clinical pathologist should not undertake work in which transfusion is often needed" This suggestion is quite impracticable It is difficult enough, if not impossible, to maintain resident medical and surgical posts at their correct level in many non-teaching hospitals, let alone find resident clinical pathologists in the numbers which would be required

Blood-grouping and cross matching is a purely scientific technique which can be learned by any person with sufficient intelligence whether he has been trained in the art of medicine or not The classification of a case as a dangerous recipient depends almost entirely on information given by the clinicians on the request form A pathologist with duties at more than one hospital cannot possibly supervise individual tests, whether routine or emergency, and in practice the vast bulk of this work is done entirely by technicians Furthermore, experience shows that in reading difficult or doubtful agglutinations the opinion of the technician of a few years' experience is greatly superior to that of a doctor who has only been doing the job for a few months, indeed, such an opinion is frequently better than that of the pathologist in-charge who sees only occasional tests at irregular intervals

This is one aspect of the problem of the best use of man-power It must be pointed out that if technicians are not attracted to the hospitals because the salary-scales do not compare sufficiently favourably with those obtainable in other scientific appointments, the blood-transfusion service will be among the first to be the most seriously affected

Department of Pathology
Kingston General Hospital,
Hull
A J SHILLITOE

PULMONARY EMBOLISM

SIR,—In your leading article last week you cite the view that it is the first embolism that kills, and that the patient who survives has little to fear from later ones I am not clear whether this is intended to refer to postoperative cases only, of which it may be true, it is certainly sadly at variance with experience in medical, as opposed to surgical, practice I have recently reported,[1] in a different connection, three cases in which the warning emboli were misinterpreted as disease of heart or lungs, until a final one enabled the true sequence of events to be established by the pathologist at necropsy These are by no means unique, and an awareness of the possibility of premonitory non fatal embolism would, I am sure, save many lives It would be unfortunate if your words diminished our alertness in this respect

Although prophylactic division of veins may be, as you say, unjustified, the operation is, in my experience, the only effective therapeutic measure in those cases of recurrent pulmonary embolism from the legs that occur from time to time

London, W 1
P PETCH

PROTOPHRENIA

SIR,—In his attempt to demonstrate the rôle of emotional injury in the production of mental defect Dr Bourne (Dec 3) summarises observations on 154 severely defective children under 6 years of age who had been admitted to the Fountain Hospital during the previous two years It is surprising, however, to note *that*, whereas *138* of these children had an organic defect, only 16 belonged to the "residual" group classified by Tredgold as having the "simple variety of primary amentia," which in outpatients outweighs the organic defect For this unusually high proportion of "organic" cases there seem to be two reasons The first is that few parents of a normal-looking child below school age who can walk and can control his sphincter, will agree to have him certified as a mental defective and *sent to an institution* The second is that, with the existing shortage of institutional beds, normal-looking children without gross motor disability will not gain admission to hospital unless they show "socially intolerable" behaviour These two circumstances may *explain* why *(1) almost all Dr* Bourne's "residual" cases have feckless or otherwise unsuitable parents, and (2) these few "residual" cases show all "socially intolerable" behaviour disorders

Few would doubt that adverse environment tends to aggravate the clinical picture of mental defect by adding psychotic features to those of intellectual retardation They would even agree with Dr Bourne that psychotic traits of this kind are observed more often in children with normal appearances, for if a mentally defective child appears normal he is liable (and even more so) in the "good" home, to educational pressure, confronting him with incomprehensible and insoluble requests which would never be addressed to a defective-looking child It is to this educational pressure, in its manifold forms, that the handicapped child responds with growing withdrawal, sometimes terminating in complete autism

As Dr Creak (Dec 17) and Dr Dutton (Dec 17) indicate, however, cases of the "residual" kind may, after all, have organic disease, and I would go further and say that in fact *clinical* signs and symptoms of such disease can usually be *found in them* *During* the ten years I have worked on mental defect I have found such signs and symptoms in almost all the many hundreds of young imbecile children whom I have examined and observed They are to be found both in those presenting obvious symptoms of organic disease and in those presenting none Apart from disturbances in simple reflex patterns—such as deficient oculomotor response on visual stimulation, loss or weakness of the pupillary light reflex, inability of convergence, and absent startle reflex on sudden loud sounds—one finds a considerable number of functional disorders which, if they were seen in adults, every neurologist would regard as infallible symptoms of localised brain impairment I have elsewhere described in detail four different syndromes, which I have found singly or in combination in all children with intelligence quotients between 30 and 50,[1] and in most children in the moron range [2] These disabilities (visuo-somatic, auditory-somatic, visuo autonomic, and auditory-autonomic) probably originate in disintegration of exteroceptor (visual, auditory) impulses and either proprioceptor or interoceptor impulses Such disintegration may result from metabolic errors as well as from structural lesions, affecting visual or auditory pathways anywhere in their course If the pathological process is confined to these perceptual pathways, and if it is not severe enough to cause total central blindness or deafness, the neurological syndromes may be overlooked and the child may be said to have no organic disease If mentally handicapped children were examined with the same precision as adults with suspected organic brain disease, I am sure that the organic basis of severe mental (i e , cognitive) defect could no longer be doubted Only the recognition and diagnosis of the *special* organic nature of a child's mental handicap will give us the understanding and the insight necessary for devising special medico educational methods to compensate for the weakened or lacking perceptual modalities

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[1] Lock F R, Greiss, F C *Amer J Obstet Gynec* 1955 70, 861

[1] Petch, C P In the press

St Lawrence's Hospital,
Caterham, Surrey

LISE GELLNER

THYROID CANCER AFTER RADIOTHERAPY

SIR,—In the excellent annotation in your issue of Dec 17 you remark that a survey of the relationship between X-ray treatment in infancy and the development of thyroid cancer seems to be called for

I recently agreed to join with Dr Theodore Winship, of Washington, and Mr Frank Rundle, of Sydney, in carrying out such a survey, and I would be very grateful if particulars of any cases of thyroid cancer in children under fifteen years of age could be sent to me at New End Hospital, London, N W 3

London, W 1

RAYMOND GREENE

X RAYS FROM TELEVISION SETS

SIR,—In view of research work now going forward and of our knowledge of the effects of radiation upon tissues, it seems appropriate to raise the question of whether the great increase of television-viewing in the public generally does not bear some relation to the rather startling increase in the incidence of leukæmia and lung carcinoma Every television set contains a cathode ray tube and every such tube emits radiation when "on" I know of no investigation which has been undertaken on the effects on tissues of whatever radiations such tubes emit, but I see no reason to suppose they differ from those emitted by an X-ray cathode tube Very small quantities of radiation over a long period are, I believe, carcinogenic If there is the slightest possibility that the emanations from the average television tube are carcinogenic, then the matter calls for the most immediate and complete investigation

London, N W 3

N CHISHOLM

*** We understand that Dr Chisholm's important question can be answered reassuringly—for television-viewers at any rate The television sets at present in general use are of low voltage, and the manufacturers see to it that the tube is screened in such a way that no significant quantity of radiation escapes But technicians and others who regularly handle sets with the screening removed may be repeatedly exposed to low-energy X rays, and the risk they run in this way deserves close attention —ED L

FIRST-AID TREATMENT OF THE UNCONSCIOUS PATIENT

SIR,—Recently some first aid textbooks have been criticised for their recommended treatment of insensibility, and the neurosurgeons have very kindly advised as to improvement in this treatment The St John Ambulance Association has accepted their ruling and has issued to its members a supplement to their textbook *First Aid to the Injured* giving the revised treatment

The essential point made is the great danger of pneumonia due to the inhalation of secretions, blood, or vomit into the respiratory passages, and the treatment now includes the following rules

1 If breathing is obstructed in any way by blood, secretions, or vomited matter, lay the patient on his side in the three quarters prone position (half-way between side and face down position) and ensure that the throat and lungs are free from obstruction

2 Support the patient in this position with a pad in front of the chest If no pad is available draw up the patient's upper knee

3 If there is still any tendency to choke, the patient should be placed in the full prone position with the head lower than the feet and turned to one side

4 Keep a continuous and careful watch on the patient

St John Ambulance Association,
10, Grosvenor Crescent,
London, S W 1

A C WHITE KNOX
Principal medical officer

STAFFING LABORATORIES

SIR,—I am glad that other pathologists beside me are concerned at the proposed new gradings in laboratories After two years' bitter labour the Whitley Council has delivered itself of a ridiculous mouse

I think that it was in 1946 that laboratory technicians last had a reasonable salary award There have since been minor adjustments, but I doubt whether the salaries of senior technicians especially have kept pace with their responsibilities and standards

If the new gradings are to be forced upon us, we, as pathologists, will have to bear the opprobrium of their imposition on individuals Although our advice in this matter appears to have been ignored the technicians who will suffer will blame us The great danger is that the new gradings would tend to produce in time a kind of second class senior technician who works in a second class laboratory In my opinion this idea cannot be too strongly condemned It would certainly not benefit either patients or staff

May I make an earnest plea to the Whitley Council to think again and to try and achieve a more generally acceptable result ?

Group Pathological Laboratory,
Lakin Road, Warwick

A P PRIOR

SIR,—Dr Taylor (Dec 24) is rightly concerned about the difficulty of staffing laboratories in the smaller hospitals, but he is on debatable ground when he says without qualification "Remuneration in the higher grades of technology should depend on individual merit" All will agree that it is proper that the most meritorious candidate should be appointed to a vacant post, but merit awards to holders of posts have not been such a success in hospital medical staffing that we should lightly approve an extension of the principle to laboratory staffs

The only equitable method of rewarding specific senior posts is to grade them according to the technical standard necessary for the work to be carried out efficiently, and this must depend on the technical skill called for by the work involved, and also the amount of responsibility entailed in the supervision of other technologists and the training of students and juniors—in short the "rate for the job," arrived at after consideration of all aspects of the case by persons, including the pathologist-in-charge, whose experience qualifies them to express an informed opinion

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[1] Gellner L *Biology* 1951 16 130, and unpublished papers
[2] Gellner L *Spec Sch. J* 1955, 44, 12

When this had been done, a state would develop in which the more able men would be stimulated to apply for the higher-grade senior-technologist posts and would be at an advantage as candidates for such posts by reason of their superior experience and ability, while the less outstanding men would be absorbed into the less responsible posts, and would not have to compete for these against candidates of outstanding merit, who might be tempted to apply if the remuneration depended on the successful candidate's individual merit rather than on the nature of the work

Regional Transfusion Centre
Brooklands Avenue
Cambridge

C B V Walker

CHILDREN IN HOSPITAL

Sir,—It was pleasant to read the account by Professor Illingworth and Dr Holt (Dec 17) of the kind and sensible régime at the Sheffield Children's Hospital

Their description of the all too common outbursts of rage and grief in child patients, following a visit by a parent, will be familiar to all who have worked in a children's ward These emotional cataclysms tend to be so harrowing in the case of younger children that, on this score alone, it might be difficult to persuade an observer who was unversed in the subtleties of child psychology that the encouragement of frequent visiting was anything more than an act of faith

The ultimate value of frequent visiting cannot be assessed simply by observing children and parents during a period of inpatient care I would urge Professor Illingworth and his colleagues to extend their valuable work to include the study of a child's behaviour before and after his hospital stay A controlled series could be obtained from the study of children who have the misfortune to be admitted to those few remaining hospitals where visiting is restricted or forbidden In surveys of this nature one cannot help believing that the assistance of a children's psychologist and psychiatrist would materially help the pædiatricians However well developed the sense of responsibility may be in the latter, without a psychological training it is difficult to describe, let alone interpret, any child's behaviour

Department of Psychological Medicine,
University of Durham,
Queen Victoria Road
Newcastle upon Tyne 1

Joseph Neville

HORDER MEMORIAL TRUST

Sir,—By the death of Lord Horder—who would have been 85 this month—the medical profession and the public have lost a very great doctor His former house-physicians at St Barthomomew's Hospital believe that there are many of his colleagues and former pupils, patients and friends, and those interested in the many activities to which he gave his support, who would like to contribute to a fitting memorial

With this object in view, his former house-physicians are asking for funds to inaugurate the Horder Memorial Trust, which has the approval of his family and the support of the Royal College of Physicians and of the Treasurer and Governors of the former voluntary hospital of St Bartholomew with which Lord Horder was so long associated The College and Governors have agreed to act jointly as trustees

It is proposed to found a travelling fellowship or professorship in clinical medicine—the science of healing at the bedside—for members of the medical profession, and if money permits to endow a lectureship in this subject at St Bartholomew's Hospital Throughout his long life, both as practitioner and teacher, Lord Horder always emphasised that a doctor's most important work is done at the bedside of his sick patient, and it is felt that a Trust of this nature will best serve to keep his memory alive, and will be of lasting benefit to the profession and therefore to the public also

Cheques, &c, should be made payable to the Horder Memorial Trust and sent to Sir George Aylwen, Bt, c/o St Bartholomew's Hospital, London, E C 1

London

G Aylwen
W Russell Brain
Geoffrey Bourne
Edward Cullinan
E M Darmady

Appointments

Brinkley Diana M M B Lond D M R T whole time asst radiotherapist, Addenbrooke's Hospital Cambridge
Maxwell, William, M B Belf, D T M asst M O, Flintshire
O'Dwyer J P M B N U I, M R C O G obstetrician and gynæcologist, U S A F Hospital South Ruislip Middx
Rohan T M B, M B Belf asst M O H and school M O Rotherham

The Hospital for Sick Children, Great Ormond Street, London

Airey, D M M.B N Z D C H M O, Tadworth Court
Barrie Herbert M D Lond asst medical registrar
Cothay, Delia M H H M B Lond house-surgeon
Cottom, D G M C B M Oxfd, M R C P asst medical registrar
Donovan D F M D Dubl D C.H house physician
Kennedy W P, M D D C H house physician
Perkin, Hyman M.B Cape Town house-surgeon
Shanks Jean M, B.M Oxfd registrar, department of clinical pathology

East Anglian Regional Hospital Board

Batty Shaw Anthony D M Oxfd M R C P consultant physician, Norfolk and Norwich Hospital group
Blundell, J A M B Lond D A senior anæsthetic registrar, Peterborough Memorial Hospital
Fieldus, P L M B Lond medical registrar Newmarket General Hospital
Inman, G K E M B Sheff, D M R D consultant radiologist, Peterborough and Stamford area
Kabraji D K, M S Bombay surgical registrar, North Cambridgeshire Hospital
Pargiter R A, M B Lond, senior registrar in psychiatry, Suffolk mental hospitals
Sheldon C S M B Lond registrar in psychiatry Fulbourn and Addenbrooke's Hospitals
Sochocky Serhij M.D Lwow M R C.S surgical registrar, Papworth Hospital
Thacker C K M M B Lond, D T.M & H medical registrar Papworth Hospital

Birmingham Regional Hospital Board.

Corbett F H, M R C.S whole time asst psychiatrist Stallington Hall Hospital Stoke-on Trent
Elkes O C M B Lond whole time asst psychiatrist, All Saints' Hospital Winson Green, Birmingham
Flewett T H, M D Belf whole time consultant pathologist, Birmingham (Selly Oak) group
Maclay D T, M D Glasg, D P M whole-time consultant in child psychiatry, Herefordshire and West Bromwich child guidance clinics, All Saints' Hospital Winson Green, Birmingham
Roberts, Henry, M D Lpool, M R C O G part time consultant in obstetrics and gynæcology West Bromwich group
Wynford Jones, H M R.C.S whole time senior casualty officer, Birmingham (Selly Oak) group

Manchester Regional Hospital Board

Begg W G A., M B *Glasg*, D P.M deputy medical superintendent and asst psychiatrist (S H.M O), Springfield Hospital, Manchester
Davidson, S W, M B Edin, F R C S E consultant traumatic and orthopædic surgeon, Macclesfield and district hospitals

Colonial Appointments

Baldacci, L M D Bologna M O, Gold Coast
Cookson G A H, M.B Dubl M O Kenya
Dutal G M M D M.O, Northern Region Nigeria
Edmonds, C M D M.B resident M O Kenya
Fenwick, K W H M B *Durh* M O, Kenya
Galea, J, M D Malta M O, Somaliland Protectorate
Garland A P, M B Lond M O Tanganyika
Gracey, T L M B Belf, D.P H asst bacteriologist medical department Jamaica
Lawrence E P M B Camb M O Uganda
Lothe, F M B Sheff pathologist, medical department Uganda
Smith C J C M B Edin, F R C S E M O, Tanganyika
Stansfield D M B Lond M O, Sierra Leone
Tewfik G I M B Lond, D P.M specialist alienist, Uganda
Williams Margaret S I, M B Lond. resident M O, Uganda

Obituary

RENÉ LERICHE

MD, Hon FRCS, Hon FRCSE

Professor Leriche died at his Mediterranean villa at Cassis on Dec 29

Born in 1879, he received his education at the University of Lyons, and throughout his long life Lyons and its medical school retained the first place in his loyalties In his early years his surgical interests were wide His Thesis in 1906 was on resection of the stomach for carcinoma, and in 1909 he published with Poncet two volumes on surgical tuberculosis During his service with the army in the war of 1914–18 he became interested in fractures, and wrote discerningly on their treatment During this period also he began that study of vascular conditions which was to be the absorbing interest of his life After the war he practised in Lyons until 1924, when he was appointed professor of clinical surgery in the University of Strasbourg

His inaugural lecture at Strasbourg set the pattern for all his many and important contributions to the literature of surgery He had watched uneasily a tendency to overestimate the value of operative techniques, and in this address on "Physiological Surgery" he elaborated his own view that a patient must be studied as a whole, with the particular object of restoring function to diseased parts In formulating this approach—at the time somewhat unorthodox—he had been influenced by the writings of Claude Bernard, and to the end of his life this influence was to permeate and pervade his practice, and his papers and books

[Blanc & Demilly Lyons

During the fourteen years Leriche was in charge of *Clinique Chirurgicale* "A" in Strasbourg, he had always a number of pupils drawn from all over the world, many of whom now occupy important academic positions in their own countries It was a period of active and productive research, chiefly upon problems relating to the circulation, conducted both in his wards and in the experimental laboratory

Leriche was wholly disinterested in putting at the disposal of his staff both his vast clinical material and the profusion of ideas for research born in his fertile brain To his great natural resources of mind he added intellectual liberalism and receptiveness, the latter fed by frequent visits to surgical centres in Europe and the Americas He rapidly became a national figure, receiving all the honours his professional colleagues in France could bestow upon him, and also an international figure in his own right and in virtue of the dissemination by his disciples of his views and practice

In 1937 he accepted the position of Professeur au Collège de France Although this is the premier chair in France, it has the great disadvantage that the professor is not provided with clinical facilities in any teaching hospital in Paris, for the remainder of his active years Leriche's clinical work was private, and was done in his consulting rooms and in the American Hospital at Neuilly Each year the professor must deliver and publish a course of lectures Leriche's first volume was the well known "Surgery of Pain" a physiological essay in the Hunterian tradition In his next book he returned to an earlier interest, the physiology and pathology of bone The war interrupted these courses After it, his lectures dealt with vascular problems and, steadfast in his conviction regarding the correct approach to surgery, the title of each volume began with the words "Physiologie Pathologique " Each volume until the last in *La Philosophie de la Chirurgie* (1951) he reaffirmed his original concept of surgical practice, and recorded critically the modifications his own opinions had undergone in the light of his experiences in Strasbourg and Paris He was now an older statesman France had rewarded him by electing him to the Institute in the Academy of Sciences, he was the moving spirit (and a past president) of the International Society of Surgery, and he travelled widely both to lecture on surgical topics and to give advice on academic matters Two years ago he had an illness which curtailed many of these activities

In the operating theatre Leriche was deft without ever striving for the spectacular, always on the watch for some immediate problem in hominal physiology a friend described him as a peripatetic "why?" He was a superb expositor, clear and logical, it has been said that one did not require to know a word of French to follow what he was saying At the council table his disinterestedness and sincerity often rescued a discursive discussion—even an argument—from foundering, in a short speech in which he would unerringly go to the root of the matter at issue His interests in life were catholic He was a voracious reader and his apartment in Paris was full of objects of art, often the work of his grateful patients

Leriche was a good friend to this country and to its surgeons, who were always assured of a warm welcome He was an honorary fellow of the Royal College of Surgeons of England, of the Royal College of Surgeons of Edinburgh, and of the Royal Society of Medicine And in 1939 he was awarded the Lister medal, one of the most prized of his many distinctions

This memoir would be incomplete without some mention of the part played in his life by his wife, who watched over him with the most loving care, conserved—so far as was in her power—his exuberant energy, and delighted to share with him a gracious hospitality To her, as was inevitable, he dedicated his "Philosophy of Surgery"

A great leader, and one hard to replace, has passed from the world of surgery A suitable epitaph perhaps would be "L'homme est toujours plus grand que le chirurgien"

S A writes

I am glad he died at Cassis which he loved He had a house there among the rocks and pines of this small and sunny harbour Here he grew his own vines, and he was proud to offer his own wine to favoured friends in Paris

A characteristic picture of him would be at one of his clinics before 8 o'clock in the morning He would arrive at high speed in a small motor car, quite often on the wrong side of the road, or looking backwards and talking to a passenger He would bounce out of his car, and be half way up the corridor, with his assistants running behind trying to catch what he was saying He was small and round, gay and lively He had very bright intelligent eyes which twinkled over the tops of his half rimmed glasses He wore a plain grey suit and spotted bow tie, and was surprised that people in London knew he was French although he wore a suit of English worsted He was always interested in everything, full of ideas and energy In teaching he preferred to answer questions by posing others and getting one to supply one's own answer, often with much teasing He was a very eloquent lecturer, both in French and in English, but had in recent years refused to speak English after hearing himself speak on a recording a friend had made of one of his lectures in London

He never failed to stress the importance of honesty, and clarity, in writing notes, or research, and he liked statements to be put down plainly He thought diagrams and graphs were over emphasised, and ' appeal to the eye, not the intellect " By his precept he encouraged an inquiring attitude of mind It was a great privilege to have worked for a man who, by his work, his writings, and his personality, revealed himself as truly great

MALCOLM WATSON

Kt, M D, LL D Glasg, Hon F R F P S, D P H

Sir Malcolm Watson, who died at the age of 82 on Dec 28, was one of the outstanding characters of tropical hygiene during the past half-century He had been a pioneer in the control of malaria and for long was pre-eminent in its practice

[Press Portrait Bureau

He was already mature when he went to the Malayan Medical Service in 1901, being aged 27, having the M B Glasg and D P H, and having travelled as a ship's surgeon Ten years later his name was known throughout the world He found Malaya in a very critical condition on the one hand there was the promise of flowing prosperity from the wide expansion of the rubber industry, and on the other the threat of ruin from the devastating malaria epidemics which decimated labour forces and might well have brought the expansion to an end The transmission of malaria by mosquitoes had recently been demonstrated by Ross, but there was no practical experience of its control Watson set out at once to gain that experience and he set out with an ingenuity which has ever since remained unrivalled Almost alone he did not allow the aetiological discovery of Ross to blind him to the great fund of epidemiological knowledge which preceded it He saw malaria as occurring in certain types of surroundings whether of forest, brackish waters, clear streams, or other characteristics, the influence of which was explicable in terms of Ross's discovery though the surroundings remained the fundamental cause He developed techniques for modifying the surroundings or alternatively of recognising their danger and moving villages to safer areas He acquired no mean knowledge of civil engineering, working out mechanisms of tide control and a variety of forms of drainage By this breadth of outlook and combination of knowledge he whisked malaria away from place after place, turning literal death-traps into healthy sites The new Port Swettenham, on which work had been abandoned and which he sanitated by tidal control, was one of his earliest triumphs, to be repeated in different forms in many other places The peril which had threatened Malaya's prosperity was removed and that country became an outstanding example to the world, up to the time of the Japanese occupation, by the application of Malcolm Watson's principles This precedence over others was no mere temporary phase, for Malaya remained consistently twenty years ahead in this respect

He left government service and settled into private and consultant practice in Malaya in 1907, being called in to advise on many developments of industrial, municipal, and general natures, including the sanitation of Singapore in 1911 and the Perak River Hydro electric Scheme—the success of which gave him particular pleasure His success was generally acclaimed he received the gold medal of the Rubber Growers' Association in 1911, he was knighted and elected LL D of Glasgow University in 1921, received the Stewart prize of the British Medical Association in 1927, the William Jones gold medal of the Asiatic Society of Bengal in 1928, the Mary Kingsley medal of the Liverpool School of Tropical Medicine, in 1934, and the Albert medal of the Royal Society of Arts in 1939

In 1928 he left Malaya to become director of the malaria department of the Ross Institute, under the director-in-chief, Sir Ronald Ross, whom he succeeded in 1933, remaining in the post until his retirement in 1942 In these posts he set out to extend to other parts of the world the principles he had developed in Malaya, his first attempts were in Ceylon and India where he established a branch of the institute, the work of which showed that the principles were transferable though the techniques needed to be modified to local conditions His great interest lay in Africa and particularly in the Rhodesias, where a malaria-free settlement was built up in the Copper Belt under his advice, and he visited and advised in many other places in Africa, Europe, and the Americas He was a great believer in the benefits which industrial development could bring to the tropics and set himself to further them by advising industry on health matters and training its employees

Despite his success there was always controversy about Watson he did not conform to the patterns or practise many of the techniques which seemed to be dictated by the new scientific age, but again and again he achieved brilliant success where others could not Controversy raged round the question " Why ? " The answer lay in his combination of a general epidemiological approach with the narrower entomological approach which most people followed He had a great sense of fun, he enjoyed every minute of his work, he enjoyed his triumphs, his controversies, and even his failures because they always taught him something which would bring success another time He had in fact a very full life

He was married twice in 1900 to Jean Alice Gray who died in 1935, by whom he had three sons, and in 1938 to Constance Evelyn Loring by whom he had one daughter

G M

HENRY PRATT NEWSHOLME

M A, D M Oxfd, B Sc Lond, F R C P

For fifty years and more, the name of Newsholme has held an honoured place in the public-health service To the family tradition which his uncle Sir Arthur Newsholme began to establish in the '90s, Henry Newsholme, as medical officer of health and professor of public health in Birmingham, steadily added his own individual contribution

He was the son of the Rev B Pratt Newsholme, of Secunderabad, India, and he was educated at Brighton Grammar School and Balliol College, Oxford As a student he had a brilliant career, and in 1907 he took a first-class in the natural science school at Oxford and graduated B SC Lond with first-class honours He continued his medical studies at St Thomas's Hospital, qualifying in 1910 After holding house-appointments there he was in 1911 appointed an assistant school medical officer under the London County Council Later he held appointments at Brighton and Southend-on-Sea, and under the Surrey County Council During the 1914–18 war he served with the R A M C in France and Italy In 1915 he took his M D

After the war he was appointed M O H for the North Riding of Yorkshire, and in 1923 for Croydon In 1927 he succeeded Sir John Robertson at Birmingham and in the same year he was elected F R C P

At Birmingham Newsholme continued with outstanding success the development of the public-health services which Robertson had so soundly established *Perhaps* the most notable achievement of his years of office was the collaboration, without fusion, of the public-health and school medical services which had grown up separately His factual annual reports, each written as an essay in the best English style, won wide recognition He was able to record a state of health in which the city could justly take pride For years, despite unfavourable local circumstances, the infant-mortality rate, for instance, was below that for England and Wales But Newsholme also made important contributions to the theory of public health He read widely, as his bookshelves even in his office showed. In his own writings his religious and philosophical outlook was applied to his professional preoccupations and in 1929 he published *Health, Disease and Integration*, in 1933 *Evolution and Redemption*, in 1937 *Christian Ethics and Social Science*, and in 1951 *Matter, Man and Miracle*

In 1939 he and his wife were received into the Roman Catholic Church Of this important side of his life G A writes "Newsholme had been brought up in a religious household and his life was guided by his own firm faith and an essential spirituality which showed itself in a cheerful readiness to help others in times of trouble, sorrow, or crisis"

Another colleague who spent the troubled war years with him at Birmingham, recalls how he insisted on sharing to the full the war-time dangers and responsibilities of the health department

"For five years he shared equally with two junior medical members of his staff the exacting Civil Defence duties at central control This meant sleeping at the Council House each night for one week out of three

"He had a great deal of human understanding and was at all times courteous and kind But he was excessively shy and retiring by nature and I had the impression that, because of this, he was not always completely at ease in his position as head of a large and important public health department There was nothing of the 'showman' about him and he preferred to travel third class rather than first, and to walk or go by public transport rather than in a corporation chauffeur driven car"

From 1937 to 1941 Newsholme also held the chair of hygiene and public health He retired from his civic appointment five years ago, and he died on Dec 21 at the age of 70 His widow survives him with five children

OCTAVIA MARGARET SOPHIA LEWIN

M.B Lond

Dr Octavia Lewin, who died in London on Dec 27, graduated in medicine some sixty years ago She leaves a long record of independent but practical work Within the profession she will be chiefly remembered for her views on nasal hygiene and correct breathing As a member of convocation of London University, a school manager of the London County Council, and a governor of Bedford College, she also did much for education

She was born at Ware, the daughter of Spencer Robert Lewin, and was brought up in Wimpole Street She was educated at Queen's College, London, Girton College, Cambridge, and the Royal Free Hospital After qualifying in 1896 she held house-appointments there Her interest in diseases of the ear, nose, and throat led her to take a clinical assistantship at the Central London Throat and Ear Hospital. Later she was appointed rhinologist to the London County Council

During the 1914–18 war she worked in French hospitals and later as aural surgeon at the Endell Street Military Hospital When she gave up her work with the London County Council she continued to teach her methods of nasal hygiene and breathing exercises at the Westminster Health Centre, to which she was medical adviser She also wrote many articles and letters to the press describing her methods She was a member of the British Homœopathic Society and in 1945 she was elected a member of the Faculty of Homœopathy

L N writes

Octavia Lewin was a member of a large family who were left motherless when she was three years of age She early learned to be independent and fearless, and she retained these characteristics all her life When working as throat and ear specialist for the L C C she was convinced that lessons in breathing correctly should be given before tonsil and adenoid operation instead of after, as then practised She sacrificed a lucrative appointment rather than give up her pioneering method, which she taught at free clinics connected with the Westminster Health Society She insisted on only air being allowed into the nasal passages and deprecated all douching and syringing with liquids She taught people how to sneeze correctly, so that the expiratory blast blew away the excess mucus secreted in catarrh of nasal passages This was followed by voluntary blowing with mouth shut and head well down "Shut your mouth and save your life" was one of her repeated admonitions She invented all sorts of methods to train children to keep their mouth shut instead of being what she called "gapers"

Her many other interests kept her always young in mind and she was a storehouse of all sorts of original ideas in the home Her unfailing kindness and love for children was always practical She was a rare character and beloved by many

Mr L V. CARGILL

Prof Arnold Sorsby writes

"Lionel Vernon Cargill was associated with the Royal Eye Hospital for some fifty-five years In the early years he brought to it a keen and searching mind and superb technical knowledge and skill In the later years he was the elder statesman, guiding the hospital through a difficult period, increasing its bed complement from some 50 to 130, and initiating the research chair in ophthalmology at the hospital and the Royal College of Surgeons In all these activities he was the upright man of clear and decisive action

"His long life extended over the Victorian and Edwardian periods, and the turbulent years of two world wars Professionally he saw the transformation of ophthalmology from a minor branch of general surgery into an independent and significant specialty, and in this transformation he played his part, as is shown by his early publications and his services as ophthalmic surgeon to several general hospitals His work for the Society of Apothecaries and at King's College School, Wimbledon, were as valued and as disinterested as his more strictly professional activities"

Prof T B DAVIE

Two of Dr Davie's South African colleagues write

"His enthusiasm, energy, determination, and courage had made him a leading figure in academic affairs in South Africa He was one of those exceptional men who really enjoyed committee work The reasons were obvious to all who served with him his clarity of vision allowed him to crystallise for others the most complex administrative problems, and from his insight flowed solutions which gave him satisfaction, and which were invaluable to the university In the South African Council for Scientific and Industrial Research he served as a member of the council and as chairman of its medical and dental research committee It is not insignificant that during his term of office there was a steady increase in the output of medical research sponsored by the C S I R As member of the National Council for Social Research he was able to play his part in the development of research in fields other than that of science Since the recent establishment of the university advisory committee to the Minister of Education, Arts, and Science, Dr Davie had served on it as representative of the committee of university principals, and for this important position the South African universities could have chosen no better delegate He was also a trustee of the Max Sonnenberg University Trust, the Abe Bailey Trust, and the Isaac Ochberg Education Fund, and he was member of the governing councils of several public institutions and of many scholarship committees Through all this work and through his public statements he soon became known as a man who fought fearlessly for the principles he considered right Foremost among these he ranked the principles of academic freedom of universities, a freedom which he considered fundamental in a civilised world

"Despite his eminence he remained approachable by all He was always ready to listen to their problems and to give his guidance to members of his staff or to students In addition to his many official duties he found time for innumerable public engagements He was keenly interested in South Africa and its affairs, its history, its people, its flora and fauna Even his stamp collection had a South African bias

"Throughout his busy life he never forgot that he was a doctor' His medical school and medical research benefited greatly from his counsel, and he retained an interest in the affairs of the medical profession, being a strong advocate of the College of Physicians and Surgeons now being established in South Africa It was often said that he did the work of three men This is hardly an overstatement, yet for years he had been afflicted with arthritis which but for his indomitable spirit would have been incapacitating In part this achievement was due to the help he received from his wife The gap he leaves will be difficult to fill, but the example he set will remain vivid and living for many years to come"

S B, *who was one of his students, writes*

"Clarity, enthusiasm, and a robust humour were Davie's characteristics as a teacher He was the best I have known, and one of the best men It is easy for a teacher to display his knowledge and wit at the expense of a student, but though I saw Davie have a hundred opportunities of this kind, I never saw him take one Himself seemingly an extrovert, he seemed to have an intuitive knowledge of the minds and souls of others—springing perhaps from his most endearing quality, an ebullient and childlike innocence He gave us his knowledge and he made us laugh with him I once made a ludicrous, but unfortunate, mistake in a pathology viva For a moment my fate seemed to hang in the balance The external examiner looked grave Then Professor Davie threw back his head and burst into enormous laughter, and brushing the mistake aside, the three of us went happily on He knew and I knew that I was not going to let him down again

"After the war I had occasion to ask his help in a small personal matter I did not think he would remember one out of the thousands of students he had known, and was he not, in any case, head of the University of Cape Town? But he did remember me, and he did help me, though then an ill man, grappling with issues a thousand times more important than my small business Like many teachers, he inspired respect in his students, but much more he inspired affection The keynote of his life was youth he looked young, he thought young, and it was to the young that he devoted most of his days I am sure that many will remember all their lives this noble man, whose death has saddened as much as his life rejoiced us"

Diary of the Week

JAN 8 TO 14

Tuesday, 10th

ROYAL COLLEGE OF PHYSICIANS OF LONDON Pall Mall East, S W 1
5 P M Dr R T Brain Clinical Vagaries of the Herpes Virus (Watson Smith lecture)

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields W C 2
3 45 P M Dr Leslie Foulds Experimental and Histological Studies of the Responsiveness of Mammary Tumours to Hormones (Imperial Cancer Research Fund lecture)

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
8 P M *Psychiatry* Prof L S Penrose, F R S Prospects of Genetical Research in Mental Illness Dr J Fraser Roberts Preliminary Results of two Surveys on Mental Deficiency

INSTITUTE OF DERMATOLOGY, Lisle Street W C 2
5 30 P.M Dr R G Cochrane Hansen's Disease

CHELSEA CLINICAL SOCIETY
8 30 P M (Rembrandt Hotel Thurloe Place, S W 7) Dr A A Mason Theory and Practice of Hypnosis

MANCHESTER MEDICAL SOCIETY
5 P.M (Medical School, University) *Surgery* Mr R R Simpson Shakespeare and Surgery

Wednesday, 11th

ROYAL SOCIETY OF MEDICINE
4 30 P M *Physical Medicine* Dr W A Fell, Squadron Leader C V Wynn Parry Dr W D Fletcher Injuries in Sport

INSTITUTE OF DISEASES OF THE CHEST Brompton S W 3
5 P M Sir Russell Brock Surgery of Septal Defects

INSTITUTE OF DERMATOLOGY
5 30 P M Dr H Haber Specific and Foreign Body Granulomas

MIDLAND MEDICAL SOCIETY
8 15 P M (154, Great Charles Street Birmingham, 3) Dr A B Hegarty Depressive States

NOTTINGHAM MEDICO CHIRURGICAL SOCIETY, 64 St James's Street
8 30 P M Mr F W Law Exophthalmic Ophthalmoplegia

MANCHESTER MEDICAL SOCIETY
4 30 P M *Medicine* Dr Richard Schilling Byssinosis in Lancashire Cotton workers

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242 St Vincent Street Glasgow, C 2
5 P M Prof Thomas Symington Some Endocrine Aspects in Relation to Modern Surgery

Thursday, 12th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P M Sir Geoffrey Todd Chemotherapeutic Control in the Treatment of Fibro nodular Pulmonary Tuberculosis (Marc Daniels lecture)

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Dr E R Williams The Skull at Birth (Hunterian lecture)

ALFRED ADLER MEDICAL SOCIETY
8 P M (11, Chandos Street W 1) Dr D J West Homosexuality and Social Psychiatry

Friday, 13th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330 Gray's Inn Road, W C 1
3 30 P M Mr G H Howells Sinusitis—Acute and Chronic

INSTITUTE OF DERMATOLOGY
5 30 P M. Dr Cochrane Hansen's Disease

Notes and News

SHORTAGE OF MENTAL NURSES

ADDRESSING a meeting in Shrewsbury last month, Dr M J Brookes drew attention to the acute shortage of nurses in Shelton Hospital, of which he is the medical superintendent This hospital, built 112 years ago to accommodate 176 patients, has been expanded, and its present statutory accommodation is for approximately 750 patients Nevertheless, over 1000 patients are in residence There are only 67 full time nurses and 48 part-time nurses—i e, the equivalent of about 91 full time nursing staff—whereas the ideal establishment would be 270 This means, in practice, that 3-4 nurses look after 50-60 patients, whereas the ideal figure would be 1 nurse to every 4 Dr Brookes appealed particularly for local help, though he would also be glad to have nurses from other parts of the country Recruitment, however, was unfortunately limited to the local district because of inadequate residential accommodation for nurses

The *Shrewsbury Chronicle* of Dec 9, in reporting this appeal, draws its readers' attention to the fact that the Ministry of Labour and National Service allows young men deferment from National Service if they are willing to start training as nurses before they are 18½ Under this arrangement, made in 1947, men who have completed their training are given an opportunity to work as nurses during their period of National Service

DISCUSSION GROUPS AND SMALL CONFERENCES

THE World Federation for Mental Health and the Josiah Macy, jun, Foundation, of New York, are the joint sponsors of a small international working conference on the Functioning of Discussion Groups and Small Conferences which is to be held in Eastbourne from Jan 31 to Feb 6 Varying methods of group discussion are increasingly employed at meetings, but, as they are not always as productive as they might be, it has been suggested that a useful manual might be produced as a result of the working conference Dr Brock Chisholm, who is a member of the executive board of the federation, is to be in the chair at the conference

HOSPITAL NEW YEAR

MANY administrators and doctors will face 1956 with more confidence because they have on an accessible shelf the current edition of the *Hospitals Year Book*[1] In it they will once more find in orderly array particulars of all hospitals and hospital authorities in Great Britain and Northern Ireland, the blood-transfusion services, Government departments, and statutory bodies The useful indexes to statutory instruments and official circulars have been brought up to date In his annual review Mr J F Milne, the editor, discusses the inadequacy of the proposed capital expenditure on hospitals, the problems of our mental hospitals, and the shortage of staff at all levels in all kinds of hospitals He believes that despite these difficulties the quality of the service offered to the patient has improved, "especially in endeavouring to see that he is treated as a person and not simply as a case"

University of Cambridge

The following degrees were recently conferred

M.D—I M P Dawson, Errington Ellis, J R Ellis, R M Forrester, C S McKendrick, *F N Macnamara, Adolf Polak Iris Watkins, *D N White

M.B—H W Kirkpatrick

B Chir—Joyce F Baron R W Beard, R B Bennet M S Bethell A E Boyo, R M Buckle, N L Burrell, D S Carmichael S B Carter R A Catterall J D Charters J H Clark M N Cox J F Crewdson, M W L Davis J H Eckersley, P H Evans A G Fraser, C G Geary, Mary R Glyn John I P Grant Whyte Rosemary C Hayball, P J E Hubbard, C N Hudson Rachel E Hudson, M H Heycock, Frank Heyes J D Jenkins Donald King Price, J H L Lloyd Thomas J F Marsden J J Mather W O Mavor, D L Miller, J D McCaldin A S MacKenzie, D J Moorhouse A M Morgan, N H Moynihan, J F M Newman K E A Norbury, R E Nottidge, B W G Orr M A Pallister E H O Parry Katrina M Parry, H W Parry-Williams Helen J Pegg B S Phillips, N B Pride, M B Reddington, R L Rothwell Jackson A G Strube, A H Sears, J A Tait, D G Twyman J V Williams

* by proxy

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[1] Hospitals Year Book 1955-56 Institute of Hospital Administrators 75, Portland Place, London W 1 1955 Pp 116 47*s* 6*d*

Society of Apothecaries of London

At recent meetings of the court of assistants, with the master, Dr Neville Finzi, in the chair, Sir Horace Evans and Mr Alan Brews were elected to seats on the court, and it was resolved to confer on Sir James Paterson Ross the freedom of the society, honoris causa

The following were elected to the livery.

J B M. Coppock, A C Frazer, L J Wallace, A M Rackow

The following were elected to the freedom of the society by redemption

J D A Gray A J C Gormley, W D R Thompson, Elizabeth A King Turner

The following diplomas were granted

M M S.A—H A Evans, C J Goosen

L M S.S.A—A H Sears, M K C Lu, B M Hellings Evans J F Popper, R N *Gardiner, St J Dowling C* P K Watson, B H Gooch, R Dawkins, R C Rintoul, G B Middle, R D Sandfield, A H Atkinson, R M Burton

D I H—R H R *Aston*, J *G S Coetzer* J M *Davies*, A P Dikshit, H Miller, K N J Pocock, V G Springett

Liddle Prize

An award of this prize (£200) is to be made in 1958 The subject chosen for the essay is *the social and economic aspects* of epilepsy Further particulars may be had from the dean of the London Hospital Medical College, Turner Street, E 1

Nuffield Dental Fellowships

One of the aims of these fellowships is to enable graduates in medicine and science to qualify themselves to undertake teaching and research on dental health and disease Further particulars will be found in our advertisement columns

British Association of Plastic Surgeons

The following officers have been elected for 1956

President, Mr Wilfred Hynes, hon treasurer, Mr R P Osborne, hon secretary, Mr J P Reidy, other members of the council Prof T P Kilner Mr D N Matthews Mr Rainsford Mowlem, Mr R J V Battle, Mr P H Jayes, Mr J S Tough, Mr A B Wallace, and Mr H P Pickerill

Research into Ageing

Entries for the 1955–56 Ciba Foundation awards for research on basic problems of ageing should reach the foundation not later than Feb 10, 1956 Information about the awards may be had from Dr G E W Wolstenholme, the director of the foundation, 41, Portland *Place, London*, W 1

Royal Society of Medicine

The next award of *the Colyer prize will be made in* November It is offered for the best original work in dental science completed during *the previous seven years* by a dental surgeon who has qualified from a dental school in Great Britain or Northern Ireland not more than seven years ago Applications should be submitted to the prize committee of the society, 1, Wimpole Street, London, W 1, not later than June 30

Institute of Diseases of the Chest, London

Clinical demonstrations will be given by Dr N Lloyd Rusby and Mr T Holmes Sellors at the institute (in the grounds of Brompton Hospital, Fulham Road, S W 3) on Fridays from Jan 6 to March 23 Open lectures will be given on Wednesdays, from Jan 11 to March 14 All the meetings are open to doctors without fee and will be held at 5 P M

Reciprocal Agreement with New Zealand

A reciprocal agreement on *social security* between the United Kingdom and New Zealand was signed in Wellington on Dec 20 It will come into operation on April 1, 1956

Under the agreement the Ministry of Pensions and National Insurance will treat people who come to the United Kingdom from New Zealand as if they had paid contributions to the National Insurance scheme while they were in New Zealand, so as to enable them to qualify for retirement pensions, widows' benefits and sickness and unemployment benefits People who go from the United Kingdom to New Zealand will continue, as at present to receive any retirement pension or widow s *benefit for which* they may have qualified under the National Insurance scheme The New Zealand ministry of social security will, however treat them as if they had been resident in New *Zealand* while they were living in the United Kingdom so as to enable them to satisfy the conditions for New Zealand benefits, and will take into account the amount of any National Insurance benefit *to which* they are entitled The agreement also provides for the payment of sickness and unemployment benefits under the New Zealand schemes to people from this country

Anyone who thinks he may become entitled to benefit under the agreement should apply to his local Pensions and National Insurance office

General Board of Control for Scotland

Mr A A Templeton, C B E, J P, has been appointed a commissioner of the board in place of Sir Robert Bryce Walker, who has resigned

Dietetics Congress

The second International Congress of Dietetics will be held in Rome from Sept 10 to 14, 1956 Further particulars can be had from the Associazione Dietetica Italiana, via dei Penitenzieri n 13, Rome, Italy

Ministry of Health *Appointments*

Mr Robert Turton, the Minister of Health, has appointed Mr P Benner *to* be his *private* secretary and Mr E F Cooper to be his assistant private secretary He has appointed Mr W M F Vane to be his parliamentary private secretary

Anglo-French Exchange Bursaries

Short-term grants for work in France are offered again this year to British doctors and medical research workers by the *Institut National d'Hygiène in Paris* *Application forms* can be had from Dr G W Wolstenholme, director of the Ciba Foundation, 41, Portland Place, London, W 1 The closing date for applications is Feb 4

Modern Aspects of Rheumatic Disease

The British Postgraduate Medical Federation and Empire Rheumatism Council have arranged a consultants' conference on this subject from March 22 to 24 in London Sir Francis Fraser will *give the opening address* at 2 15 P M on Thursday, the 22nd Further particulars may be had from the general *secretary* of the Council, Tavistock House, (N) Tavistock Square, W C 1

Symposium on Venereal Diseases

The first International Symposium on Venereal Diseases *and the Treponematoses will be held in Washington, D C* from May 28 to June 1 It will be sponsored by the United States Public Health Service and the World Health Organisation Further particulars may be had from Dr C A Smith, division of special health services, Public Health Service, Department of Health, Education, and Welfare, Washington, 25, D C

National Association for Mental Health

The annual conference of this association will be held next year at Harrogate on April 12 and 13, under the chairmanship of Sir Charles Morris, vice chancellor of the University of Leeds The theme chosen is Mental Health and Personal Responsibility, and the speakers will include Prof G R *Hargreaves, Prof T Ferguson* Rodger, and Dr Mary Burbury Further particulars may be had from the secretary of the association, 39, Queen Anne Street, London, W 1

Fellowships in Clinical Research

The Medical Research Council invite *applications for* fellowships tenable at centres in the United Kingdom during 1956–57 from medical graduates who wish to prepare themselves for a career in clinical research

The awards will be made for one year in the first instance and will be renewable annually to a maximum of three years in all Stipend will be at the rate of £950–£75–£1100 per annum, with superannuation. Applications must be sponsored by the head of the appropriate department in the candidate's university or medical school and an undertaking will be required that a suitable academic post in a clinical department will be available to the candidate in that institution on satisfactory completion of the period of study under the fellowship Forms of application may be had from the secretary of the council, 38, Old Queen Street, London S W 1, to whom they must be returned not later than March 1 1956

Oxford Graduates Medical Club

A dinner will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, W C 2, on Friday, Jan 20, at 7 30 P.M., when Mr E A Crook will be in the chair Tickets (25*s*) may be had from Mr Selwyn Taylor, 3, Roedean Crescent, Roehampton, S W 15

CORRIGENDUM *Argentaffinoma*—In the articles and our annotation last week the name of Dr Albert Sjoerdsma was *incorrectly* spelt

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Births, Marriages, and Deaths

BIRTHS

TALBOT—*On Dec 31* at Kings College Hospital to Rosalyn (nee Carrick) and John M Talbot—a son (Derek Michael)

LIFE
(BIOLOGICAL, NOT BIOGRAPHICAL)*

ROBERT PLATT
M.D Sheff, M Sc Manc, F R C P
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF MANCHESTER

WHEN Christopher Wren was making his experiments on blood transfusion and the intravenous injection of fluids, and 70 years or so later when that clergyman Stephen Hales was demonstrating and measuring the blood-pressure of the horse, an educated gentleman (and there were such) could comprehend the whole of science, and even contribute to it by his own observation and experiment

Yet I suppose even in the 17th century a reservation would have to be made for mathematics, which had already reached considerable maturity and complexity, especially in its application to astronomy and to navigation, so much older is it than the rest of science Napier, whose logarithms to base *e* still do not enter into the daily thought of most of us, died in 1617

Even in the 19th century, amateurs such as Mendel and Galton made observations which were the starting-point of a new science Today it becomes harder and harder to do so, although still not impossible, as we see for instance when technical advances bring the amateur into unexplored territory as with Hillary to Everest or Cousteau to the depths of the sea

Yet physics has split from chemistry, and even chemistry itself has split into so many fragments that the specialist in each branch has difficulty in understanding the language of his colleagues In medicine you need no reminder of how difficult it is becoming (as a colleague of mine has said) for one man to understand both cardiology and electrocardiography at the same time The difficulty is not simply that knowledge has increased in extent and complexity The point is that as we begin to explore any part of our own subject in greater depth we at once feel the need of knowledge and techniques which belong to sister sciences, and are not readily at our command For all these reasons it is a good thing from time to time to try to observe, if only as an interested spectator, some field of knowledge other than our own, and occasionally to be prepared to discuss it—even, as Schrödinger (1945) says in a similar context, "at the risk of making fools of ourselves" We cannot of course hope to become expert in other men's specialties, but we can see them from a point of view determined by our own interest, background, and training, and in doing so we may occasionally ask a new question even if it is unlikely that we supply an answer It is with these considerations in mind that I shall speak on some fragments of biological knowledge which I personally find interesting

Life at a Standstill

Our bold colleagues the surgeons, with the help of their equally enterprising anæsthetists, have been making tentative studies in hypothermia They have, I believe, reduced the human body-temperature, without disaster, to between 21° and 25°C, at which level the heart is slowed and so is cellular metabolism; and tissues can thus be deprived of their blood-supply for a longer period than would be normally compatible with survival

Biologists, who by recourse to animal experiment can usually be a move ahead, have succeeded in reducing the temperature of rats and hamsters to 0°C, and I have myself seen the experiments of Anjus and of Audrey Smith (Smith 1954) at the National Institute for Medical Research, at Mill Hill As the animal's temperature is progressively reduced, respiration and circulation are arrested The continuous record of the electrocardiogram slows down and then comes to a standstill Yet the blood does not coagulate Animals may be kept in an ice-bath in this state for an hour or so with a rectal temperature of −5°C In some cases crystals of ice appear in the tissues Yet when the animals are warmed they come to life again and behave like normal animals The reviving process needs some care and skill because it is important that the periphery is not warmed too rapidly, the process is carried on by diathermy As the temperature rises, artificial respiration is carried out for a short time until spontaneous breathing is re established The animals do not suffer from frostbite unless the tissues have been handled and the joints flexed while they were in a frozen state These experiments represent, I suppose, an extension of the natural phenomenon of hibernation, but they seem to me to pose certain questions on what constitutes life, at any rate in the mammal If our definition requires that the heart should be beating, and the blood circulating and the individual regularly exchanging carbon dioxide for oxygen, then clearly these animals are dead I am sure that they are legally dead, though physiologically they must be still alive

But really all that is new is that this vital standstill takes place in a mammal That life in the form of the seed of a plant can exist potentially for hundreds of years is of course well known Equally remarkable, though perhaps not so dramatic, is the fact that mammalian germ cells—for instance in rabbit ovaries—can be kept for a month or more at −79°C and by grafting into another animal can be made to function and produce new individuals And this brings us to one of my main topics which is the transmission of life from one generation to the next

Transmission of Life

I suppose the supremely important outcome of Mendel's work was that he showed *heredity to be* particulate where Darwin would have thought of it as blended For although Mendel's work was *published in* 1866, during Darwin's lifetime, it lay unheeded in an obscure journal (the Proceedings of the N[illegible] Verein in Brünn) until it was rediscovered in 1900 [illegible] after Darwin's death Darwin would have thou[illegible] each individual as a blend of its father and mot[illegible] two wines might be mixed in a bottle D[illegible] have expected (as you or I might) that if *you* [illegible] and dwarf peas you would get plants int[illegible] *between the two* Mendel showed that you did[illegible] obstinately remained either tall or dwarf and [illegible] proportions dependent upon the genetic [illegible] their parents If we want a simile for Mende[illegible] late inheritance we can think of [illegible] coloured beads in a bottle † Each bead [illegible] inherited *either* from father or from [illegible] l *individual inherits a* different assort[illegible] r either parent, and so the pattern of th[illegible] e *variable, and every individual* is [illegible] beads themselves, or the genes [illegible] de simile), are transmitted unchange[illegible] ei *millions of generations* [illegible] m

And one of the most fascinatin[illegible] hat *inheritance is that, like* mar[illegible] nce *equally well not only to mice* [illegible] hem *also to* plants and in fact t[illegible] can *sexually* Sex itself is of [illegible] to *inheritance*, and you will [illegible] of the X and Y chromo[illegible] *species* being the homo[illegible] [illegible] XY Since [illegible] germ-cells, which are haploid (that is containing only a single and not a double number of chromosomes and genes), all human ova are X whereas sperms are either X or Y. All the cells of the human body contain in their nuclei a replica of the 24 pairs of chromosomes, including of course the XY or XX pair which determine sex. It is therefore not surprising that recent work has established that certain sex differences can be discovered in somatic cells. An individual's sex may in fact be diagnosed from his leucocytes or more clearly by a skin biopsy.

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* Presidential address to the section of medicine of the Manchester Medical Society, April 6, 1955 Also used at a meeting of the Royal Australasian College of Physicians, Dunedin, Sept 23, 1955

† [illegible] recollect who e[illegible]

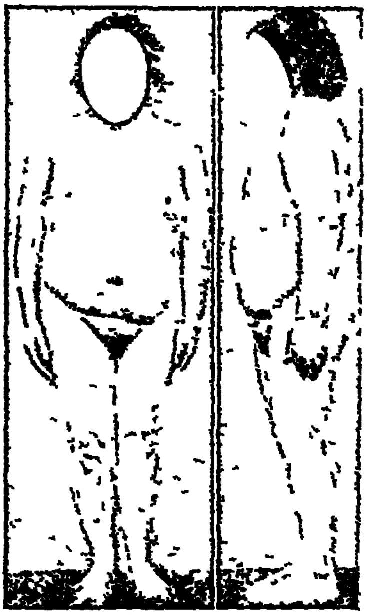
Fig. 1—A case of Turner's syndrome in which the genetic sex was male.

It has lately been found that in certain cases of ovarian agenesis, including those known as Turner's syndrome in which other congenital abnormalities coexist, the sex as determined by skin biopsy is male (fig. 1). These people appear to be female, but at the age of puberty they fail to develop secondary sexual characters. Examination shows an infantile vagina and uterus and no ovaries. Under the influence of œstrogens they can be transformed into apparently normal females except that, having no ovarian tissue, they are incapable of having children. One of our patients who was treated in this way (fig. 2) is successfully filling the female rôle of marriage to the satisfaction of both parties. It was only some years later when Polani, Hunter, and Lennox published their paper (Polani et al. 1954) that we discovered by skin biopsy that she is *genetically male*. Needless to say, this information has been kept to ourselves.

Biological Advantages of Sexuality

While on the subject of sex we may briefly consider the reasons in favour of sexual reproduction. Obviously sex is not necessary for the continuance of a race. Many primitive organisms divide and reproduce without sexual differentiation. Even in higher animals parthenogenesis may take place. The drone bee has no father. Loeb in 1899 was able to make starfish eggs develop without fertilisation. Bataillon in 1911 produced tadpoles from frog spawn by artificial stimulation. Gregory Pincus, in 1939, after a large number of experiments, produced three fatherless rabbits (Pincus 1939).

Why then has sexuality been adopted by all the higher species?

The union of two individuals has two major effects. One is that by Mendel's law of independent assortment, separate characters previously found in two different individuals may meet in the next generation and appear together in the same individual. Sexuality thus produces the new variants on which the process of evolution can act by natural selection. Darwin, who thought heredity to be a blending of characters instead of a reassortment, was aware of this difficulty to the acceptance of his theory of evolution, for a blended heredity would lead to uniformity. Tall and dwarf peas, for instance, would in the subsequent generations all end up as medium in height. He therefore postulated that sudden unpredictable variations, or mutations as we would now call them, were very important for evolution. We can now see that this is not so. Sex plus particulate inheritance—the gene system in fact—produces most of the necessary variation. Natural selection will favour the survival of new and advantageous products of sexual reproduction. Inbreeding within a small population will tend to limit the number of variants and new patterns, whereas outbreeding will increase them. This is no doubt one reason why we find in Nature many devices to discourage inbreeding, such as "*the heterostyly of the primrose and the Table of Kindred and Affinity of the Prayer book*" as Haldane (1954) observes.

Sexuality has, however, another major effect, somewhat in the opposite direction. It provides that all individuals are diploid—that is, they have a double set of genes and chromosomes. This makes for stability in the race, for new mutations, which are usually disadvantageous, are usually recessive and are not immediately apparent. It has, in fact, been calculated that a new mutation occurring today, either spontaneously or as a result of all the radiation at present being released in the world, would be unlikely to show itself for some 500 years. But this is no reason why we should neglect the problem, and of course a cousin marriage might bring two mutant recessive genes together much more quickly. One hesitates to think what might be the result of a cousin marriage in Hiroshima, or for that matter a marriage of cousins whose common grandmother had been a radiographer.

I have said that each individual is unique, a new pattern being formed although the genes themselves are transmitted unchanged. But both statements, of course, require qualification. Identical twins are the exception to the uniqueness of pattern, and mutations are the exception to the unchanging nature of genes.

It is now well known that there are two kinds of twins—those in which the fertilised ovum has split into

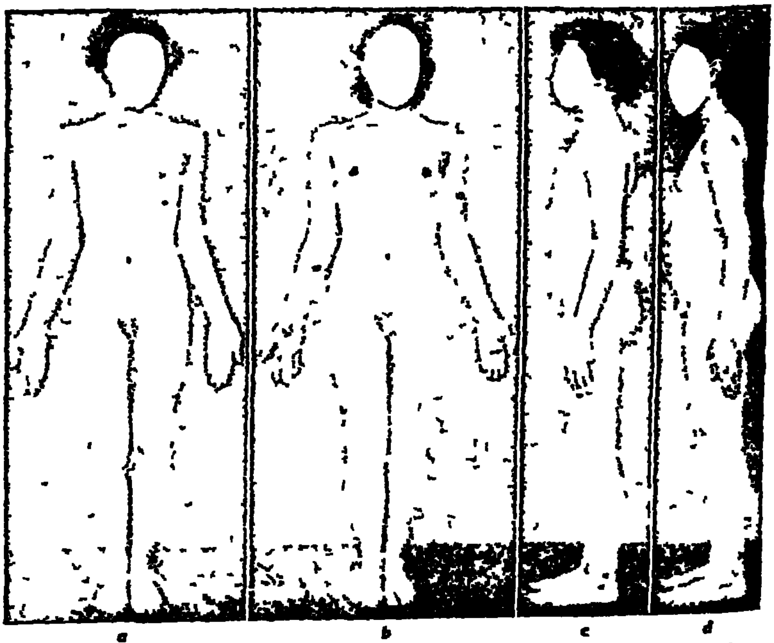

Fig. 2—A case of ovarian agenesis in which the genetic sex was male. *a* and *c* before treatment; *b* and *d* after treatment with œstrogens.

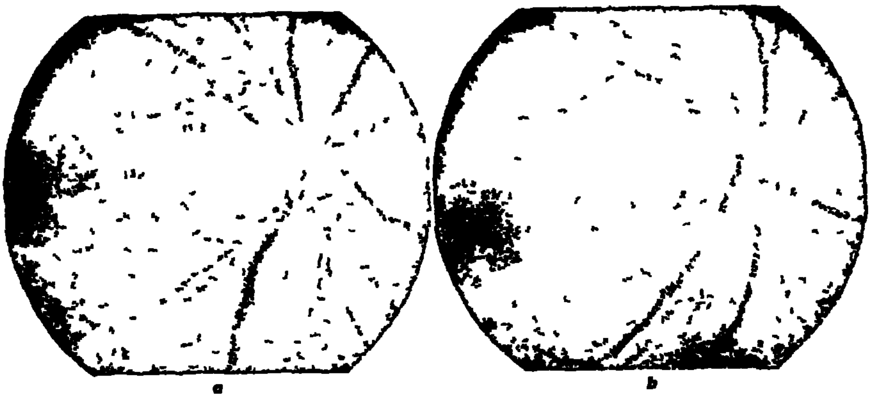

Fig 3—Retinal photographs from the identical twins illustrated in fig 4

two before going on to its normal embryological development (the so called uniovular or identical twins), and those in which two ova are fertilised by two sperms at the same time, and are simply brother and sister (or two brothers or two sisters) sharing the uterus at the same time. It is not so well known that there may be a third type of twin (obviously a theoretical possibility) in which the ovum splits into two before fertilisation and the two halves are fertilised by separate sperms. (Or alternatively the second polar body of meiosis is fertilised as well as the ovum.) In this case most characters transmitted from the mother would be identical in the two twins, whereas those derived paternally would be dissimilar in expected proportions. Not very uncommonly the resemblance between twins is far stronger than the resemblance which is usual between two siblings, and yet they differ in some obviously inherited characteristic such as hair or eye colour. No one, so far as I know, has made any important study of this problem. If a great enough number of twins, together with their two parents, could be assembled, and their blood groups examined, there might be statistical evidence of the existence of this type of twin. Taking the MN groups, for instance, the combination MN in one parent and N in the other should yield equal numbers of MN and N in the offspring. If twins are identical, all their blood-groups will of course be identical, but if there are significant numbers of dissimilar twins derived from one ovum and two sperms, there should be a greater likelihood of the twins inheriting the same group where the mother is the heterozygote than where the father is.

Coördination of Development

An interest both in retinal photography and in twins has led me with the help of Raymond Lawton to study the retinæ of identical and non-identical twins. The pattern of each retina is unique for each individual: it is as distinctive as his fingerprints or electrocardiogram. Hence, if identical twins had identical retinæ, retinoscopy would have been a ready and very useful method of distinguishing between uniovular and binovular twins. However, it turned out differently. Although with practice one can often pick out from a number of retinal photographs those which belong to a pair of identical twins, the vessels after they have left the disc are usually very unlike. One can in fact easily tell one twin from the other with an ophthalmoscope, even when it may be socially very difficult to do so (figs 3 and 4). It looks as if the genes lay down the general plan but not the full detail of our architecture, and that after a certain stage of development some kind of controlling or coordinating mechanism is in operation, as if "the organism knew in advance what it wanted" as Graham Cannon has said.

This kind of phenomenon has led some biologists, such as Cannon and the late Frederic Wood Jones, to wonder if Darwinian selection can account for all evolution and all the adaptations found in Nature. Take the development of the human eye for instance, says Cannon (and I hope I do not misrepresent him): it is inconceivable, he says, that it should develop without some process of coordination regulating the simultaneous development of retina, vessels, lens, and so on. Right, say the orthodox biologists, then no doubt there are inherited coordinating genes, which are so to speak in charge of the process. Then, says Cannon, those genes must have been evolved before the human eye could develop, so that the control of the process was laid down before the organ appeared. In other words Lamarck perhaps was somewhere near the truth when he postulated that it is the need of a new organ which results in its production.

Acquired Characteristics

There are, however, experimental as well as philosophical doubts as to the adequacy of orthodox views on evolution, and here the study of the genetic behaviour of primitive organisms such as moulds and bacteria has been very important. Why do tubercle bacilli become resistant to streptomycin, for instance? Do they learn to adapt their metabolism to it so that it is no longer harmful? If so, they clearly pass on this acquired characteristic to future generations. Or is this only Darwinism on a shorter time scale? Do a few bacilli exist from the beginning which by some natural mutation have all along been resistant to streptomycin? If so, they will survive when all their fellow bacteria are killed off and the new generations will come to be composed only of resistant strains developed by selection from these mutants.

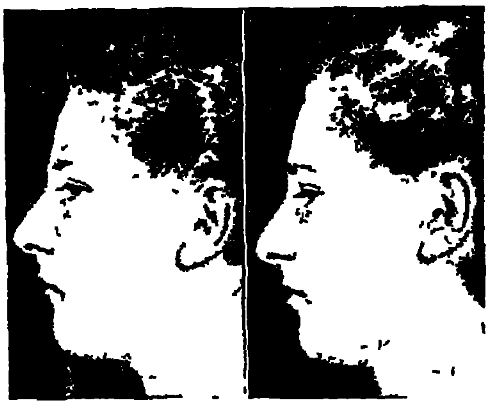

Fig 4—See fig 3

It is difficult to plan crucial experiments to decide between these alternatives. There is no doubt whatever that certain bacteria and moulds can be "trained" in the performance of certain biochemical processes: that is, they can be trained to do without a certain substance or to accept one which is normally poisonous to them. There is equally no doubt that this acquired ability can be passed on to future generations. The difficulty is to tell whether a new skill has been acquired, or an existing one developed, and in transmission to decide between true nuclear inheritance and protoplasmic transfer, and, in some cases, to exclude the possibility of virus transmission. Despite the difficulties, there seems to be evidence which satisfies such authorities as Haldane and

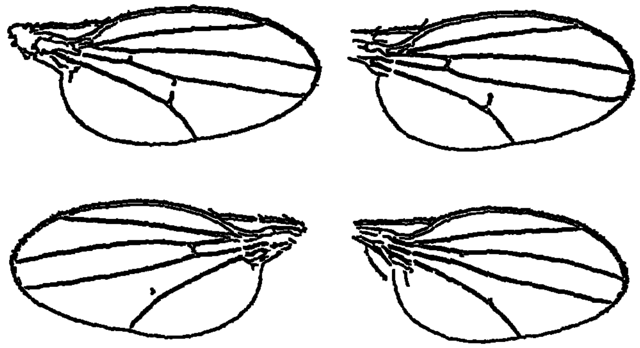

Fig 5—Defect in the posterior cross veins in the wings of *Drosophila melanogaster* (see text) (*Reproduced from* *Endeavour*)

Hinshelwood that in some cases the hereditary transmission of an acquired characteristic has been proved in the bacterial world

In higher forms of life, Waddington's recently reported transmission of an acquired characteristic in drosophila is important (Waddington 1952) If these flies are exposed to a temperature of 40°C for a few hours at a certain stage of their development, about 40% show a variant in the veins of the wing (fig 5) If now those which show the abnormality are bred among each other, in about twelve generations flies begin to appear (and eventually reach a prevalence of about 80%) in which the cross vein-less *abnormality occurs without the* application of the environmental stimulus The implication for evolution is this evolution by selection does not merely act on a series of chance variants but also affects the sensitivity of individuals to react to an environmental stimulus Thus if we may jump a long way from Waddington's experiment we see that, starting with a race of white *men who easily adapted to sunshine* by pigmentation, we might, by the action of selection in a tropical environment, end with a race of Negroes

Before leaving the subject of the transmission of acquired characteristics I must refer again to the possibility of virus transmission in some instances in plants and bacteria, and there is at least one instance of virus transmission *in the mammal Bittner studied* strains of mice susceptible to breast cancer In some strains a very large proportion of the adult female mice developed breast tumours He found, however, that if the mice of a non-susceptible strain are suckled by a mother of a susceptible strain and vice versa, transmission of the tumour tendency is by the milk line and not by the ordinary rules of heredity *It now seems certain that a* virus is transmitted in the milk, which gives rise to breast cancer in later life The possibility that this happens in the human species has not been ruled out

The study of genetics in simpler organisms such as bacteria and fungi has given rise to other discoveries By exposing fungi such as neurospora to X rays a large number *of mutant strains can be produced, each of which* seems to give rise to a specific and single block in the synthesis of certain amino acids Thus normal stocks of neurospora will grow on a minimal medium consisting of water, inorganic salts, glucose, and a trace of biotin The mutant strains fail to grow, but will do so if given the specific amino acid which they now fail to synthesise or in some cases a *precursor* In this way a good many metabolic pathways have been mapped out, some of which probably have an important *bearing on* cell metabolism in higher animals Indeed, mutations in the human subject, giving rise to "inborn errors of metabolism" are, as Archibald Garrod recognised years ago, blocks in the sequence of cell biochemistry

The Nuclear Material

The main substance of the nuclear genetic material appears to be desoxyribonucleic acid (D N A), and work by Watson and Crick (1953), which is rather exciting, though I do not profess to understand it, suggests a molecular structure for this compound which gives at the same time an inkling of how *nuclear material may* duplicate itself D N A, they postulate, consists of a *double chain arranged in helical* form (fig 6) The two chains are held together by hydrogen bonds between the organic bases which are part of the molecule, and in which, for physicochemical reasons, only certain linkages are possible Thus adenine must pair with thymine, and *guanine with cytosine If the two chains* come apart, as they presumably do before reproduction, each acts as a template on which another chain forms according to the design necessitated by the structure of the existing chain The original work should be consulted At the 1954 meeting of the British Association Dr Chayen cast doubts upon the likelihood of D N A being the essential substance of genes, but it is clearly associated with them It is not itself a protein, though it has a molecular weight of 1–4 million

Some very interesting observations have lately been made on the genetic functions of this substance D N A, *which seems to be just as important in the genetics of* bacteria as it is in man Hotchkiss (1953–54) and others have shown that unencapsulated relatively avirulent pneumococci can be made into virulent encapsulated organisms by transferring D N A from killed organisms of the encapsulated type Now the capsules consist largely of polysaccharides, so it is definitely not the capsular substance which is being transferred, but the genetic control of its development

Perhaps even more remarkable, the same workers have shown that drug resistance in pneumococci—for instance, resistance to penicillin or streptomycin—can be transferred to non-resistant strains by transfer of an extract which contains D N A but as far as possible is freed from all other components of the resistant organisms The resistance so transferred is then transmitted through succeeding generations

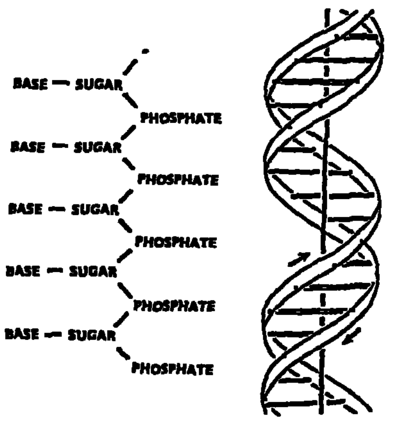

Fig 6—Structural formula of desoxyribonucleic acid (see text)
(*Reproduced from* *Nature*)

Obviously I am even less well equipped to discuss *these matters of* bio physical-chemistry *than I* am most of the rest of the material of this lecture, but having got so far I would like at least to allude to some of the work of Krebs on cellular metabolism (Krebs 1953), for one cannot consider life simply as a beginning and end without even asking how it is maintained in the individual The beauty of Krebs's concepts is that, like others we have *been discussing, they appear to be as applicable* to protozoa as to the higher mammals, and probably with reservations to plants and *bacteria as well* He shows how the initial phase in energy production is the breakdown of large molecules of foodstuffs into smaller units The next phase is the partial oxidation of these into only three substances—acetyl co enzyme A α ketoglutaric acid, and oxalo acetic acid The utilisation of these provides the energy which is built up into that universal storage *battery of* chemical energy A T P (adenosine triphosphate) which seems *to* be the source of all readily available energy for body processes *It seems certain* that A T P (or in some cases I T P —inosine triphosphate) supplies energy for the osmotic work of cells, for the contractile phase of muscular work (Weber 1953–54), and probably for the resynthesis of acetylcholine hydrolysed during nervous conduction (Nachmansohn 1953–54)

Disease and Natural Selection

Having thus skated on some extraordinarily thin ice I shall pass on to matters which I can understand rather better—back to human disease and the end of life Now that so many of the hazards of infancy, and the infective disorders of the young, have been mastered by the progress of scientific knowledge, more of us die of what we think of as the great constitutional diseases—atheroma (with coronary occlusion and myocardial infarction), hypertension, and cancer When we use that old-fashioned term constitutional, we infer that there is something inherent in the make up of the individual which, no doubt along with environmental influences such as cigarette smoking and being a doctor, renders the person liable to a disease which does not seem to be determined by such obvious external factors as trauma or infection Though we know little enough of these diseases, two things at least are clear about their ætiology One is that hereditary factors are important (They may not be very apparent in most cases of cancer, but critical investigations have usually revealed them in some form In hypertension they are much more in evidence, and I have myself contributed to the investigation of this phenomenon) The second is that they all tend to occur not so much in old age as in what we euphemistically call middle life, 45–60 years old We all know exceptions, but no one of us would deny that cancer and severe hypertension are commoner at 55 than they are at 35

As both Medawar (1951) and Haldane (1954) have pointed out, if a disease is partly determined by heredity and if the age of its onset is also under hereditary influences, then natural selection will gradually determine that it occurs more and more in the post-reproductive period, which we may call 45–60 when most of us have finished having families For a man or woman who had one of these disorders in a form in which it occurred at the age of 30 would on the average have fewer children to whom to pass on the hereditary influence

So it seems that the reason why these diseases attack us in so-called middle life is that evolutionary processes have pushed their incidence back towards that age After the reproductive period, so far from being selected out of the population, selection will if anything tend to favour these diseases (as Haldane somewhat cynically remarks), since the survival of a race will be favoured by not having too many elderly folk for the young ones to support And so you may infer that the prevalence of coronary thrombosis among physicians is really Nature's answer to the problem of the Senior Registrars

Clonal Ageing

My last topic is clonal ageing, and I am glad to see that there has been a revival of interest in this subject

A clone is a group or family of individuals all derived from a single cell In primitive organisms such as paramecium, and in plants, where reproduction may be sexual or asexual, a single fertilised cell, the result of sexual conjugation, may divide and divide again by a series of mitoses until a large number of individuals have resulted They then undergo, all at the same time, some ageing process, and unless a further sexual conjugation has taken place, the line will give out and the cells will reproduce no longer Sonneborn (1955) has explored the reasons for this in paramecium, and finds it to be due to inaccurate copying processes in mitotic division

You may ask what bearing this has on higher organisms But if you think of yourselves you will realise that every cell in the human body is the result of the asexual mitotic division of another cell, and that, in turn, of another cell, and so on until we get back to the single fertilised ovum from which we all originated It often gives me some quiet satisfaction to realise that whatever you may think of yourselves biographically, biologically you are nothing but a lot of clones If geriatrics ever becomes a science it may owe more to professors who study paramecium than to those who work at the bedside, important though the latter's work may be in a social and humane context

Life and Death

In conclusion I return to Schrodinger's introduction to his little book "*What is Life?*" In it he quotes Spinoza as saying "There is nothing upon which a free man ponders less than death, his wisdom is to meditate not on death but on life" If by this Spinoza meant what I think he meant, then I disagree, for I believe that a wise man, at any rate when he reaches the post reproductive age, should meditate now and then upon death, if only to face it courageously should it announce its coming in advance Though perhaps not with the morbid preoccupation of Charles Morgan's *Sparkenbroke*, I nevertheless find death a fascinating subject, and perhaps at some future time I may be permitted to address you on that theme If so I shall of course be under the handicap of not being able to speak from personal experience

I am grateful to Professor Waddington and the Editor of *Endeavour*, and to Dr Watson and Dr Crick, and the Editors of *Nature*, for permission to use figs 5 and 6

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SEROLOGICAL EPIDEMIOLOGY OF POLIOMYELITIS

DISTRIBUTION OF IMMUNITY TO POLIOMYELITIS VIRUS

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Over the last eighty years the incidence of poliomyelitis has much increased, especially in Scandinavia (where the first large epidemics were observed), North America, Australasia, and Western Europe Epidemics have occurred elsewhere, particularly in some island communities, but in the main have not been so large as in the above-mentioned areas

In those countries where epidemics occur frequently there has been a shift in the age group attacked Whereas poliomyelitis most often affected children younger than school age in the earlier part of the present century, it now most often affects children of school age, adolescents, and young adults This change has not been noted in those countries where epidemics either have not occurred or have only occurred in the last few years

The countries principally affected by epidemic poliomyelitis are those where the standard of living is high, and Olin (1951) suggests that in these countries the chances of coming into contact with the virus at an early age have been reduced, compared with the chances in the underdeveloped countries of the world. This being so, contact with the virus takes place at a later age in highly civilised countries; and, as with many other viruses, when infection does take place, the manifestations are more severe than they would have been if infection had taken place earlier in life.

Serological surveys have shown that contact with the virus of poliomyelitis does take place at an early age in the underdeveloped areas of the world (Paul et al. 1952, Paul 1954), and that in America (e.g., Melnick and Ledinko 1953) early infection with the three types of poliomyelitis virus does not take place to the same extent as in Cairo and North Africa.

In this country poliomyelitis has occurred in wide spread epidemic form only since 1947. The reasons why epidemics appeared later in this country than in other countries with a high standard of living are not clear. Serological surveys may shed some light on this problem.

Present Investigation

Bradley (1954) notes that eighteen areas in England and Wales did not notify cases of poliomyelitis in 1922–52 inclusive. The largest area had a population of 9400; the others had much smaller populations. Bradley suggests that these areas escaped because they had not been exposed to the virus. It was decided to investigate Betws-y-Coed in North Wales because no notification of poliomyelitis had been received from there since poliomyelitis became notifiable in 1912. Liverpool, where poliomyelitis occurs annually, was used for comparison.

Sera obtained from children in both Betws-y-Coed and Liverpool were examined for antibodies to the three types of poliomyelitis virus. The child population was surveyed because they are less likely than adults to have acquired antibodies to poliomyelitis virus outside the areas in which they live. Furthermore, the level of serum antibodies to poliomyelitis virus in the child population reflects the recent prevalence of the virus in the community.

During these surveys attempts were made to isolate poliomyelitis virus from the sewage of Betws-y-Coed. The methods of ammonium sulphate precipitation (Gard 1940) and ultracentrifugation (Melnick 1943) and a combination of the two (Melnick 1947) were used without success.

AREAS SURVEYED

Betws-y-Coed is a village in North Wales with a population of about 750 (Registrar-General's estimate for mid-1954), this figure having varied only slightly in recent years. The village is a popular holiday resort, many people visiting it for the day in addition to those staying for longer periods. All children of school age up to 11 years attend the local county primary school. Some children then proceed to a grammar school in a neighbouring town, the remainder continuing to attend the local school until they reach the age of 15. Apart from the holiday trade the principal local occupation is agriculture, and some of the children attending the primary school live either on farms or in houses outside the village. The village's water supply comes from a reservoir in the neighbouring hills and is chlorinated. The school and all the houses in the village have satisfactory drainage, the untreated sewage effluent being discharged into a river about ¹/₂ mile below the village.

Liverpool is an industrial port with a population of about 786,000 (Registrar General's estimate for 1954). Some of the population live in tenements, and there are still some overcrowded slums in the city. Apart from this the general housing is moderately satisfactory. Poliomyelitis has occurred with increased frequency during the last few years, the largest outbreak being in 1951, when 135 cases were notified.

POPULATION EXAMINED

In Betws-y-Coed samples of blood were obtained during the winter of 1954–55 from children attending the local infant-welfare clinic and the county primary school. Their ages ranged from 7 months to 14 years. Of an estimated child population of 176 aged 0–14 years, serum was available from 78.

In Liverpool, children's sera were obtained from hospital laboratories to which they had been sent for other investigations. No child with a history of poliomyelitis was included in the survey. The age range was the same as that for Betws-y-Coed. 71 sera were examined from Liverpool.

METHODS

Sera were obtained by venepuncture or by heel puncture according to the child's age. After inactivation at 56°C for 30 minutes sera were examined initially at a dilution (after addition of virus suspension) of 1:10. Those sera from Betws-y-Coed which neutralised one or more types of poliomyelitis virus were re-examined at a final dilution of 1:100, whereas those which did not neutralise at 1:10 dilution were re-examined at a final dilution of 1:2 against the appropriate virus types.

Tissue cultures used for examining sera were either of rhesus monkey kidney or of HeLa cells. Most of the sera were examined by using cultures of monkey kidney, and all the serum titrations were done in these cultures. Two types of monkey-kidney cultures were used: fragment cultures and cultures of trypsin-dispersed kidney. The latter were set up by the method first described by Dulbecco and Vogt (1954) and modified by Youngner (1954). Before fragment cultures were used for neutralisation tests or for virus propagation, the fragments were shaken off the roller tube wall, leaving the sheet of epithelial outgrowth behind. The culture medium used for most of the tests was that described by Melnick et al. (1954), except that Earle's balanced salt solution was used instead of Hanks' solution. HeLa cells were maintained as described by Syverton et al. (1954), except that trypsin dispersion of cells before subculture was abandoned in favour of dispersion of cells by simply pipetting the cell suspension (obtained by scraping the cells off the tube wall) up and down until most of the cell clumps were broken up. A modification of the medium described by Kret (1955) proved satisfactory for maintaining the cells when they were being used for either neutralisation tests or virus propagation.

Virus strains were: type 1, Mahoney strain; type 2, Y SK strain; type 3, Saukett strain. They were received from the Central Public Health Laboratory, Colindale. Virus pools were made by passage of the three strains in cultures of monkey kidney or HeLa cells, and the same pools were used throughout these tests. The titres of the aliquots of each pool were determined before their use in the neutralisation test. The 50% infectious dose for tissue culture (TCD50) was calculated by the method of Kaerber (1931).

Tissue culture neutralisation test.—Serum neutralisation tests were set up by the method described by Ledinko et al. (1952). Equal volumes of diluted inactivated serum and a suspension containing 200 TCD50 of the appropriate type of virus in each 0.1 ml. were mixed and allowed to stand at room temperature for 1 hour. Mixtures of each serum with each of the three types of poliomyelitis virus were set up. After 1 hour 0.1 ml. of each virus-serum mixture was pipetted into each of two tissue-culture tubes from which the culture medium had been removed. 0.1 ml. of a mixture of serum and balanced salt solution was pipetted into one culture tube, which acted as a serum control. With each test six cultures were used for virus controls, two tubes being inoculated for each type of virus, the final dose of virus being the same as in the neutralisation tests—i.e., 100 TCD50. Cultures were left at room temperature on the bench for 30 minutes to ensure maximal contact of the inoculum with the cells. At the end of this time cultures received 1 ml. of medium and were then placed in a roller drum at 37°C and after 5 days examined by low-power microscopy. The presence of antibody was indicated by the absence of "cytopathic" changes in the cultures, which changes were evident in the virus control tubes. Positive sera of known antibody content were not available when the testing was begun.

RESULTS

Betws y-Coed

The distribution of antibody to any type of poliomyelitis virus in relation to age is shown in fig 1 Only 8 of the children were without antibody to one or more types of virus, and 5 of these were aged less than 2 years Infection with type-1 virus has been commoner than with any other type (fig 2) Antibodies to this virus type were present in some sera from even the youngest children, indicating that infection with type-1 virus had taken place in the village within the year preceding this investigation

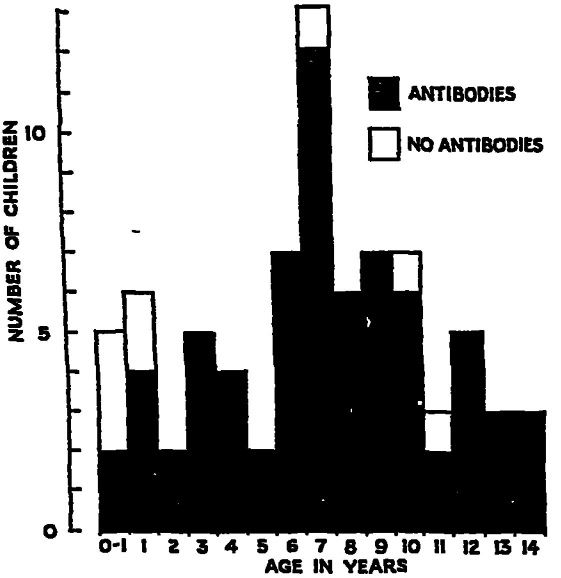

Fig 1—Numbers of Betws-y Coed children with and without antibodies to poliomyelitis virus in a final serum dilution of 1 10

The distribution of antibodies to type-2 virus is shown in fig 3 Except one child, aged 8 months, who had antibodies to all three types of poliomyelitis virus at a titre of 1 10, no child aged less than 2 years had antibodies to type 2 virus It appears that infection with type-2 virus either had not taken place or had been very limited in distribution during the two years preceding this investigation

Antibodies to type 3 virus were the least common in sera from Betws y-Coed (fig 4) Except in the child already mentioned they were not present in the sera of children aged less than 3 years Table I shows the numbers of children with antibodies to one, two, or all three types of poliomyelitis virus in each 5 year age-group The figures show that the age group 5–9 years had the highest proportion of children with antibodies to two or three types of poliomyelitis virus (83%) Even in the age group 0–4 years 8 (36%) of the 22 children examined had multiple antibodies, illustrating again the widespread infection with poliomyelitis virus in this community

TABLE I—NUMBERS OF CHILDREN EXAMINED FROM BETWS-Y-COED WITH SERUM ANTIBODIES TO ONE OR MORE TYPES OF POLIOMYELITIS VIRUS (1 10 SERUM DILUTION)

—	Age-group (yr)			Total
	0–4	5–9	10–14	
No of children examined	22	35	21	78
No of children with antibody to a single type of virus	9	5	6	20
No of children with antibodies to two types of virus	4	15	5	24
No of children with antibodies to all three types of virus	4	14	8	26
No of children with no antibody	5	1	2	8

After the sera had been tested for antibodies, inquiries were made into family relationships It was found that 44 of the sera had been obtained from 2 or more children from each of 17 families None of the children coming from these family groups had escaped infection with at least one type of poliomyelitis virus, and within each family the children had antibodies to at least one virus type in common In 9 family groups the children within each family had been infected with the same virus types In 4 families the youngest child lacked antibody to one type which the elder children had, and in one other family the youngest child had antibody to one more virus type than had the elder children Although antibodies to all three types of virus were found among children living in isolated dwellings, antibody to type-1 virus was less common among them than among the village children (Of the 15 children living outside the

TABLE II—TITRES OF SERUM ANTIBODIES TO THE THREE TYPES OF POLIOMYELITIS VIRUS IN BETWS Y-COED CHILDREN

Virus type	No of sera having highest titres of		
	1 2	1 10	1 100 and over
1	1	40	14
2	1	23	27
3		19	18

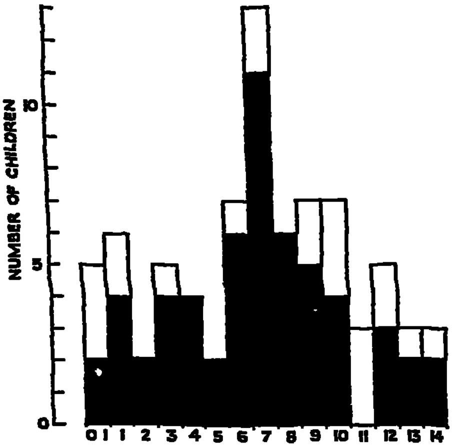

Fig 2—Numbers of Betws-y Coed children with and without antibodies to type-1 poliomyelitis virus in a final serum dilution of 1 10

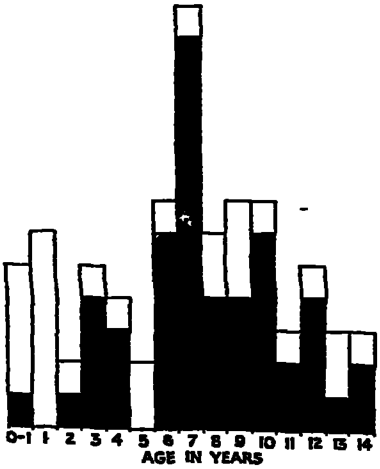

Fig 3—Numbers of Betws-y-Coed children with and without antibodies to type-2 poliomyelitis virus in a final serum dilution of 1 10

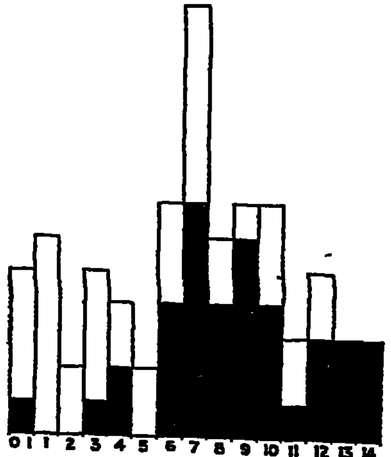

Fig 4—Numbers of Betws-y-Coed children with and without antibodies to type-3 poliomyelitis virus in a final serum dilution of 1 10

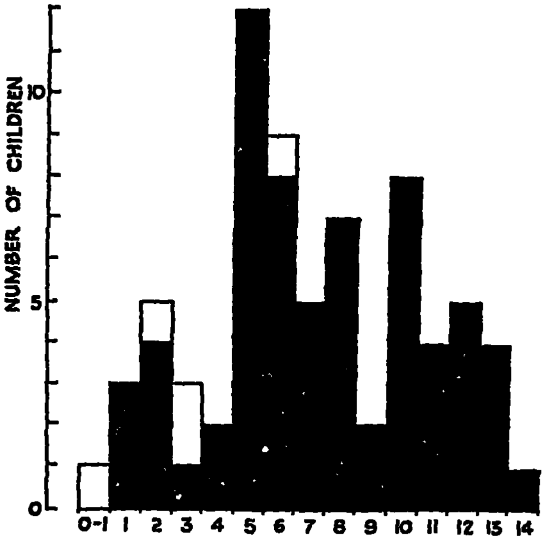

Fig 5—Numbers of Liverpool children with and without antibodies to poliomyelitis virus in a final serum dilution of 1 10

village 14 were aged 6–13 years, and, if the numbers of these children with *type 1* antibodies are compared with the numbers of children living in the village and having *antibodies to type-1 virus, it appears that*, whereas 5 of 14 children living outside the village had antibody to type 1 virus, 32 of 37 *children in that age group* living in the village had antibody to that virus type)

Table II shows the titres of serum antibodies *to the* three types of poliomyelitis virus found in Betws-y-Coed Titres of 1 100 or over were less common for antibodies to type-1 virus than for antibodies to the other two types This might well depend on the strain of type 1 virus used in the tests

Liverpool

The numbers of children examined in each age group with or without antibodies to one or other of the three types of poliomyelitis virus are shown in fig 5 As was noted for Betws y-Coed, the children with no antibodies to poliomyelitis virus were mainly in the younger age-groups Of the 71 Liverpool children examined 66 (93%) had antibodies to one or other of the types of poliomyelitis virus This shows that, in this area also, infection with *the virus of poliomyelitis* has been extremely common in recent years Figs 6–8 show the numbers of Liverpool children *in each age group* with antibodies to the three types of virus It can be seen that infection with each type of virus has taken place in almost every age group, there being no suggestion that any one type had been absent from the community in recent years Infection with types 1 and 2 has been more common than infection with type 3 virus Thus, whereas 45 children were infected with type-1 virus and 46 with type 2, only 29 children had antibodies to type 3 virus

Table III shows the numbers of Liverpool children in each five-year age group with antibodies to one, two, or all *three types of poliomyelitis* virus In the youngest age group (0–4 years) none of the children examined *had been infected with all* three types of virus, but 5 had been infected with two types Infection with more than one type of virus appears to have taken place in similar proportions of children in the 0–4 and 10–14 age groups in both areas surveyed, but in the age group 5–9 years it had apparently been less common in Liverpool than in Betws y-Coed

Discussion

The extent of infection with the three types of polio myelitis virus in *both of the* areas surveyed, revealed by tests for neutralising antibody, is compared in figs 9–11 with that in *children in two other communities*—Cairo in Egypt (Paul et al 1952) and Winston Salem in the U S A (Melnick and Ledinko 1953) In Cairo clinical infection appears to be uncommon, whereas Winston Salem had an epidemic of poliomyelitis shortly after the collection of the sera from which the results illustrated were obtained

Fig 9 shows that in Betws-y-Coed antibody to type 1 virus was more commonly found than in Cairo and in Liverpool For type 2 virus the rate and extent of infection in Betws y-Coed and Cairo appear to be similar, except that the 1-year old group in Betws y-Coed had not yet experienced infection with this type of virus

TABLE III—NUMBERS OF CHILDREN EXAMINED FROM LIVERPOOL WITH SERUM ANTIBODIES TO ONE OR MORE TYPES OF POLIOMYELITIS VIRUS (1 10 SERUM DILUTION)

—	Age group (yr)			Total
	0–4	5–9	10–14	
No of children examined	14	35	22	71
No of children with antibodies to a single type of virus	5	12	9	26
No of children with antibodies to two types of virus	5	15	6	26
No of children with antibodies to all three types of virus		7	7	14
No of children with no antibody to poliomyelitis virus	4	1	0	5

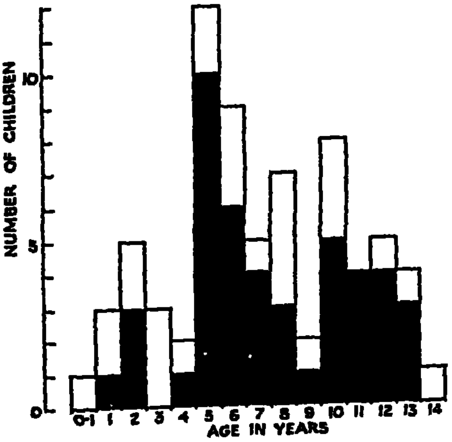

Fig 6—Numbers of Liverpool children with and without antibodies to type-1 poliomyelitis virus in a final serum dilution of 1 10

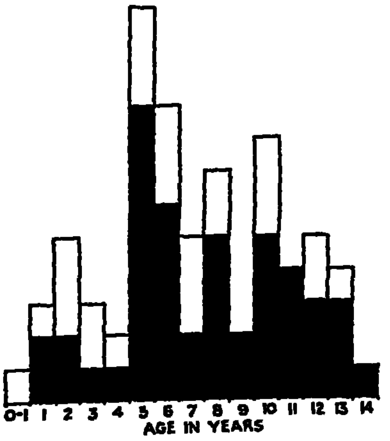

Fig 7—Numbers of Liverpool children with and without antibodies to type-2 poliomyelitis virus in a final serum dilution of 1 10

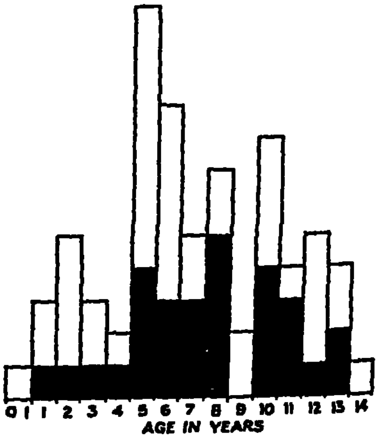

Fig 8—Numbers of Liverpool children with and without antibodies to type 3 poliomyelitis virus in a final serum dilution of 1 10

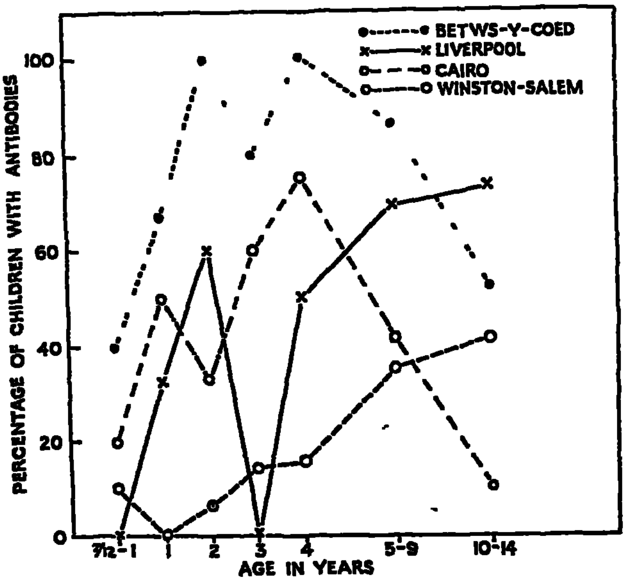

Fig 9—Prevalence of antibodies to type-1 poliomyelitis virus in different populations

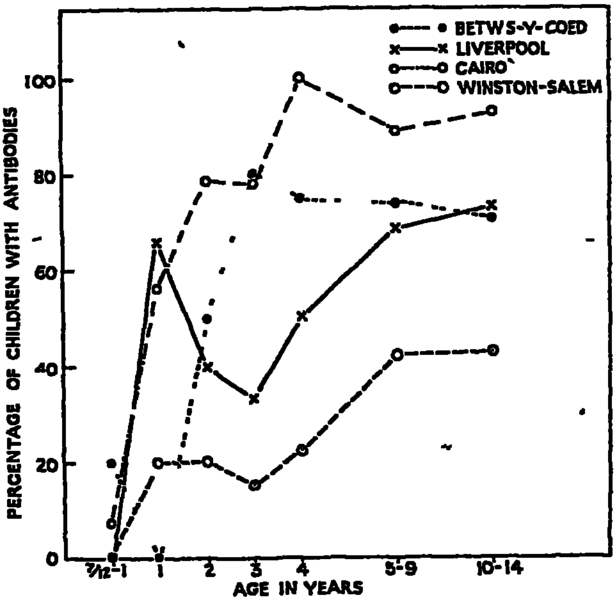

Fig 10—Prevalence of antibodies to type-2 poliomyelitis virus in different populations

(fig 10) Liverpool children showed less evidence of infection with type-2 virus Infection with type-3 virus has apparently been less common in the two areas surveyed than in Cairo (fig 11) Infection with all three types of virus appears to have been less extensive in Winston Salem than in Betws y-Coed and Liverpool, although the difference for type 3 is not so obvious

The results of the examination of children within families in Betws-y-Coed agree well with the findings of others who have shown that poliomyelitis virus is rapidly spread to susceptibles within the family (Zintek 1947, Brown et al 1948, Bhatt et al 1955, and others)

The reasons for the absence of notifications of clinical poliomyelitis from Betws-y-Coed are not clear It is quite conceivable that clinical non-paralytic infection has taken place without being recognised, indeed, it is very dubious whether abortive infection is ever recognised in the absence of an epidemic The absence of a frank paralytic case is not easy to explain but may be related to the small size of the community and possibly to the high rate of infection at an early age

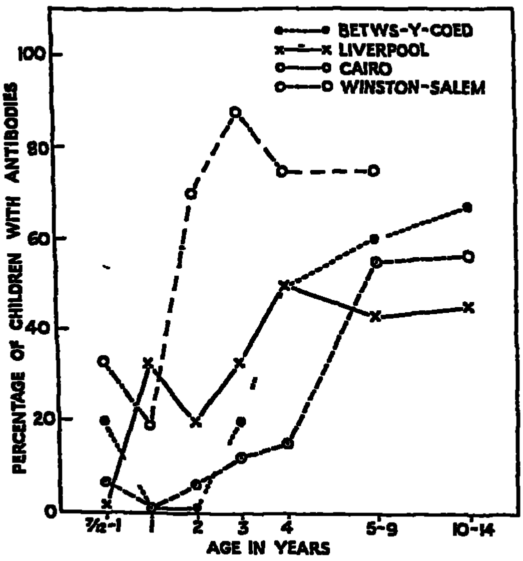

Fig 11—Prevalence of antibodies to type-3 poliomyelitis virus in different populations.

This survey therefore shows that, in both areas, infection with all three types of poliomyelitis virus, and especially with types 1 and 2, must have been widespread How far these findings are applicable to the country as a whole cannot be estimated, but the finding that infection has been more widespread at an early age in this country than in America may partly explain the lower incidence of clinical poliomyelitis in Britain

Summary

The sera of children from Betws-y-Coed and Liverpool were examined by tissue culture methods for antibodies to the three types of poliomyelitis virus

Infection with all three types of poliomyelitis virus has apparently taken place recently in both areas, infection with types 1 and 2 predominating

Although clinical infection with poliomyelitis virus has been observed in Liverpool, no case has been reported from Betws-y-Coed

The findings are discussed in relation to the incidence of poliomyelitis in the two areas and to similar serological surveys in other countries

I wish to thank Dr D E Parry-Pritchard, county medical officer of health for Caernarvonshire, and Dr T Heber Pierce, divisional medical officer of health for North Caernarvonshire, for their coöperation, Mr J Glynn Hughes, Mr C A Kortegas, M S I.A, and Miss E Williams, health visitor, for their help at Betws y-Coed, and Dr E G Hall, Dr J S Elwood, and Dr C A St Hill, and Sister S Hetherington for supplying sera from Liverpool children

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CONTINUOUS INTRAGASTRIC MILK DRIP IN TREATMENT OF UNCOMPLICATED GASTRIC ULCER

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THE treatment of gastric and duodenal ulcer has generally been based on the assumption that gastric juice, by virtue of its peptic activity, is one of the factors which prevent healing of the ulcer—if, indeed, it has not been assumed to be the principal factor in causing the initial breach in the mucosa The Sippy régime aimed at eliminating peptic activity by neutralising the hydrochloric acid in the gastric juice, and it may possibly have had this effect throughout most of the day if administered according to Sippy's instructions

Sippy (1915) gave hourly feeds of milk, eggs, and purées from 7 A M to 8 P M and sufficient alkali midway between each feed to prevent free hydrochloric acid appearing in the juice immediately before the next The last feed was followed by half-hourly doses of alkali for 2–2½ hours and the gastric contents were aspirated two or three times in the night so long as "excessive night secretion" persisted (i e, an amount of more than "about 10 c c")

The régime was onerous for the patient and required constant nursing attention, for practical reasons it has seldom been followed according to Sippy's exact instructions Any less strict technique is certainly inadequate to produce continuous neutralisation Nicol (1939), for example, found that hourly feeds of milk and vegetable purée, with 1 drachm of alkali four times a day, not only failed to neutralise the gastric contents but had less effect than an ordinary light diet, given at 2–3 hourly intervals

Nicol gave a powder consisting of 1 part of heavy magnesium carbonate, 1 part of calcium carbonate, and 2 parts of sodium bicarbonate In addition he gave ½ oz of olive oil and atropine sulphate gr 1/200 thrice daily

A more promising technique was introduced by Winkelstein (1932, 1933), who tried to achieve neutralisation over the whole 24 hours by giving patients a continuous intragastric drip of milk, to each quart of which was added 5 g of sodium bicarbonate With this method ulcers which would not respond to standard forms of treatment have healed rapidly (Winkelstein et al 1942) Other investigators have also reported good results with the treatment (Clark 1950, Garlick 1949), and have particularly stressed the rapidity with which otherwise intractable pain is relieved Reports of controlled trials of the method are, however, lacking

Method

We have tried to assess the therapeutic effects of continuous intragastric milk drip by means of a controlled trial The investigation was conducted in three parts, which were similar in general outline but differed in detail in the administration of the drip and in the use of ancillary treatments In each part of the investigation patients with fresh gastric ulcers were admitted to hospital, and then, if considered clinically suitable for inclusion in the trial, they were divided at random into two groups Patients in one group were kept in bed and given a standard medical régime, while patients in the other group were treated in the same way but were also given a course of milk drip

Parts A and B of the investigation were carried out in the course of a long-term research into the treatment of gastric ulcer In these parts the two main treatment groups were further divided into subgroups of four patients, and each member of a subgroup was allocated at random, in a similar way, one of four combinations of two ancillary treatments, thus (1) treatment X and treatment Y, (2) treatment X alone, (3) treatment Y alone, or (4) neither additional treatment With this experimental design it is possible to assess the effect of three forms of treatment on the same group of patients The results obtained with milk drip can be compared directly with the results obtained without milk drip, since both groups are comparable in respect of the proportion of patients receiving ancillary treatment Similarly the results obtained with each of the ancillary treatments can be compared with the results obtained in the corresponding control groups of patients who did not receive them Possibly the different treatments might have a synergistic effect on one another, so that although no effect was produced by one alone an effect might be produced by two or more in combination The existence of such an effect can, however, be recognised from inspection of the results, and if present can be allowed for in the analysis Details of the type of patient admitted to the trial, of the method of allocation to the treatment groups, and of the basic method of treatment, apart from the special methods under investigation, are described in a previous paper (Doll and Pygott 1954)

In *part A* of the investigation the main ancillary methods of treatment were the administration of 'Robaden' and of cabbage juice Another treatment used in a small group of patients was the routine administration of atropine (dry extract of belladonna gr ½ in pill form three times a day)

In *part B* of the investigation the additional forms of treatment consisted in the substitution of a normal hospital diet, less fried food, for the standard "basic" and "convalescent" gastric diets (Doll et al 1956), and advice to smokers to stop smoking The results obtained with robaden and with cabbage juice and the results obtained by varying the standard diet have been reported separately (Doll and Pygott 1954, Doll et al 1956) These treatments appeared to have no effect on the rate of healing of the ulcers Insufficient patients have been treated with atropine, or by advice to stop smoking, to enable any conclusion to be reached about their value No suggestion of any "interaction" has been observed between them and treatment with milk drip, and, in view of the way in which the investigation was designed, it is believed that any effect attributable to them can be ignored in making the comparison between the patients who were given milk drip and those who were not

In *part C* of the investigation no other ancillary treatment was under investigation, and all patients in both drip and control groups were given a modified Meulengracht diet, patients in the control group were given, in addition, 4 g of an alkaline powder every 2 hours during the day

The alkaline powder comprised sodium bicarbonate 3 parts, calcium carbonate 3 parts, light magnesium carbonate 3 parts, bismuth carbonate 1 part

The results of treatment were assessed subjectively by recording the patient's description of his symptoms, and objectively by measuring the change in the size of the ulcer niche A barium meal examination was made immediately after the patient's admission to hospital and

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* We regret to have to record that Dr Price died on Nov 28—Ed L

2–4 days before the specific treatments were instituted A second barium-meal examination was made after the completion of the courses of treatment, exactly 4 weeks after the first examination The method by which the size of the ulcer niche was estimated, and the precautions taken to ensure, so far as possible, that the results of the radiographic examinations before and after treatment were comparable, have been described previously (Doll and Pygott 1954)

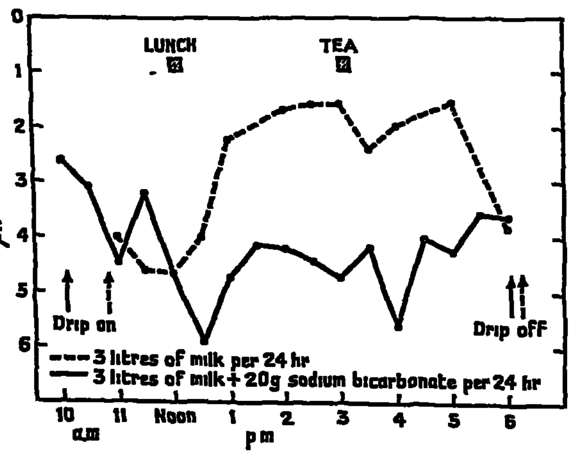
Administration of Milk Drip

The ordinary apparatus used for other forms of drip infusion was connected to a piece of thin rubber tubing, which was passed into the stomach through the nose or, if preferred by the patients, through the mouth Surgical drainage tubing $^1/_{20} \times {}^1/_{40}$ in was used instead of a Ryle's tube because it was thinner, more pliable, and more readily tolerated by the patient The tube was kept in the stomach for the whole period of 24 hourly administration of the drip, save that patients were allowed to remove it for half an hour after breakfast when they got up to wash Most patients, however, preferred to disconnect the tube from the drip apparatus and to keep it in situ The same meals were served to patients on the drip as to the control patients not on the drip, and all were encouraged to eat as much of the meals as they could

In *part A* of the investigation patients on drip were given by this method 6 pints of milk every 24 hours for 2 weeks, the daytime drip was then stopped and they were given 2 pints of milk by drip at night only for a further period of 10 days In *part B* the same course was given but sodium bicarbonate was added to the milk In *part C* the alkalinised milk was given day and night for 3 weeks and the period on night drip only was omitted

The Addition of Alkali

The primary object of milk drip treatment is to reduce the acidity of the gastric contents to such a level that the peptic activity of the juice is eliminated over the whole of the 24 hours To be certain of doing this the pH must be raised to a level of about pH 4 In fact, milk given continuously between meals does not generally have this effect, and a considerable amount of alkali has to be added before a satisfactory level can be ensured (see figure) Observations in the medical unit at St Mary's Hospital showed that in patients with gastric ulcer the addition of 20–40 g of sodium bicarbonate to the daily ration of milk was usually sufficient, but that in a few such patients (3/15) a daily dose of 60–160 g was necessary Patients with duodenal ulcer generally required 80–100 g (Price and Sanderson 1955)



pH of the gastric contents during the administration of continuous intragastric milk drip, with and without added sodium bicarbonate

TABLE I—COMPARABILITY OF PATIENTS ON ADMISSION WITH REGARD TO PRESENCE OF PAIN, BODY-WEIGHT, AND SIZE OF ULCER

Characteristic	Part A		Part B		Part C		Whole trial*	
	Drip	Control	Drip	Control	Drip	Control	Drip	Control
Pain on admission								
Present	30	27	21	24			51	51
Absent	10	13	11	8			21	21
Initial weight								
Under 7 st	5	0	2	3			7	3
7 st –	4	11	7	8			11	19
8 st –	12	6	9	6			21	12
9 st –	8	12	2	4			10	16
10 st –	6	6	7	4			13	10
11 st +	3	2	3	6			6	8
Not recorded	2	3	2	1			4	4
Av all patients (st, lb, oz)	8, 11 12	9, 1, 3	8, 13, 5	9, 0, 11			8, 12 8	9, 0, 15
Initial size of ulcer niche (sq mm)								
10–24	7	15	10	7	0	0	17	22
25–49	16	12	7	9	0	4	23	25
50–99	10	5	6	8	4	2	20	15
100 +	7	8	9	8	6	4	22	20

* Data for the presence of pain on admission and for the initial weight are not available for part C of the trial

van Goidsenhoven et al (1954) have shown that, although well marked chemical alkalosis may develop, doses of sodium bicarbonate of this order may safely be given to patients with peptic ulcer for periods of up to 3 weeks, so long as there is no evidence of pyloric stenosis, renal failure, or cardiac failure

The present investigation was started before the work of van Goidsenhoven and his colleagues was completed, and in *part A* milk drip was given alone without the addition of alkali In *parts B and C* a routine dose of 40 g of sodium bicarbonate a day was added to every 6 pints of milk It was realised that this dose would not produce the desired degree of neutralisation in all cases, but it was chosen in order to assess the therapeutic effect of a standard dose which could be given routinely in the absence of facilities for frequent estimation of the pH of the gastric contents In *part C* two patients received larger doses (80 g and 140 g a day) because their pain was not controlled on the smaller doses In *parts B and C* of the investigation patients in whom there was evidence of pyloric stenosis or of important renal disease were considered unsuitable for treatment with the alkalinised drip and were excluded from the trial

Initial Comparability of Patients

In the absence of certain knowledge of the clinical features which affect prognosis (Doll and Pygott 1952, 1954), the only precautions taken to ensure that the patients given the different treatments were comparable before treatment was started were (1) the exclusion from the trial of patients who had been treated previously, and (2) the allocation of the specific methods of treatment for each patient at random The results of treatment have been assessed by recording the change in size of the radiographic ulcer niche, the change in the patient's weight, and the duration of the patient's symptoms The initial comparability of the patients in the different groups with respect to the characteristics immediately relevant to these measures is evident from table I, which shows that

(1) Equal proportions of the patients on drip and not on drip continued to complain of pain on admission (51/72 in each case)

(2) The average initial body weight was somewhat lower in the drip series The effect of this difference is considered later, in the analysis of the results

(3) Rather more of the patients in the control series had very small ulcers (22/72, compared with 17/72) Complete

healing is more likely when the ulcer is small, but an increase in the size of the ulcer is also commoner in small ulcers, so the average amount healed, expressed as a percentage of the initial size, is practically the same as for large ulcers The difference between the initial sizes of the ulcers in the treated and control groups is not great, and it is unlikely to have materially affected the results

Results

The results are summarised in tables II–IV Table II shows, for each of the main groups, the numbers of patients in whom the ulcer had completely or partly healed after a month's treatment and the average amount healed, expressed as a percentage of the initial size of the ulcer, for the whole group In each part of the investigation the proportions of ulcers which healed completely in a month were similar for the patients on milk drip and for the control patients not on milk drip, in all parts taken together the proportions were identical (20/82) In parts B and C of the investigation (in which alkali was added to the milk) the proportions healed by two-thirds or more were also similar (27/42, compared with 28/42), and so were the average amounts healed

TABLE II—PATIENTS GIVEN MILK DRIP AND CORRESPONDING CONTROL PATIENTS RESULTS OF TREATMENT ASSESSED RADIOGRAPHICALLY

Part of trial	Treatment	No of patients	No of patients in whom niche was				Average amount healed (%)
			Healed	Two thirds or more healed	Less than two thirds healed	Larger	
A	Drip	40	10	17	9	4	69 7
	Control	40	9	8	16	7	50 7
B	Drip	32	8	11	13	0	69 5
	Control	32	8	13	9	2	65 8
C	Drip	10	2	6	2	0	80 2
	Control	10	3	4	3	0	82 8
All parts	Drip	82	20	34	24	4	70 9
	Control	82	20	25	28	9	60 5

In part A (in which no alkali was added), on the other hand, more ulcers healed by two thirds or more among the patients on milk drip than among the control patients not on drip (27/40, compared with 17/40) In view of the fact that the difference appears in only one of the three parts of the trial, that the response to the drip in part A was no better than in parts B and C, and that the response to treatment in the control group was appreciably worse than in parts B and C, it seems most likely that the difference was due to an unfortunate play of chance in the selection of patients for the control group[1]

Table III shows the effect of treatment as assessed subjectively by the patients' symptoms in parts A and B of the investigation detailed records were not kept in part C More patients on milk drip were completely free of pain than in the control group not on milk drip (36/72, compared with 25/72), but the difference is not large and could reasonably be attributed to chance ($\chi^2 = 3\ 44$, $n = 1$, $0\ 05 < P < 0\ 10$) The measure of symptomatic relief shown in table III is, however, not a sensitive one and the impression was obtained that pain, when present, became less severe and less frequent *immediately* after the drip was instituted Several patients on drip who complained of pain, complained of it only during the periods when the drip was stopped or when the *drip bottle ran empty* 2 patients in part C of the trial continued to have pain when given the standard milk-alkali mixture The gastric contents in these patients were found to have an acidity below pH 3 5 while they were on the drip, and the amount of alkali was, therefore, increased Freedom from pain was eventually achieved with daily doses of 80 and 140 g

TABLE III—PATIENTS GIVEN MILK DRIP AND CORRESPONDING CONTROL PATIENTS RESULTS OF TREATMENT ASSESSED SYMPTOMATICALLY

Part of trial	Treatment	No of patients	No of patients		
			Pain-free	With occasional pain	With daily pain for a week or longer
A	Drip	40	21	9	10
	Control	40	15	16	9
B	Drip	32	15	14	3
	Control	32	10	15	7
A and B	Drip	72	36	23	13
	Control	72	25	31	16

Patients on the drip tended to gain weight more rapidly than the control patients, this was particularly true of patients on alkalinised drip Weight changes after 1 month's inpatient treatment are shown in table IV Data for 3 patients have been excluded because the presence of major intercurrent disease is likely to have affected them (1 patient on drip in part A with generalised dermatitis and 2 control patients in part A with pulmonary tuberculosis), adequate records for 5 others are missing The differences between the numbers of patients gaining different amounts of weight in the two treatment groups are statistically highly significant (parts A and B taken together, $\chi^2 = 30\ 26$, $n = 3$, $P < 0\ 001$) Gain in weight tended to be greater for patients with a low initial weight, and on the average the patients on drip had a lower initial weight (table I) This, however, cannot have accounted for the results The initial difference between the series is eliminated if the 10 patients who weighed under 7 st are excluded, the average initial weight in both series is then 9 st 2 lb 11 oz, and the average gain in weight is 6 lb 14 oz for the drip series and 3 lb 6 oz for the control The greater gain in weight may have been partly due to water retention, particularly among the patients on alkalinised drip The secondary fall which follows the cessation of treatment with large doses of fluid and alkali was illustrated by van Goidsenhoven et al (1954) In the present investigation, however, the final weight was recorded, not immediately after the period on continuous drip, but at the end of a subsequent period of 10 days during which the drip was confined to 2 pints of milk at night only No records are available for the weight a week or so after all treatment had been stopped, but nearly all patients were weighed (as outpatients) 2–3 months after discharge These outpatient records show that the average increase in weight over the initial inpatient record was still 15 oz more for patients who had been treated with milk drip than for the control series, and 1 lb 5 oz more if patients with an initial weight of under 7 st are excluded These differences are not statistically

TABLE IV—PATIENTS GIVEN MILK DRIP AND CORRESPONDING CONTROL PATIENTS CHANGES IN WEIGHT AFTER ONE MONTH

Part of trial	Treatment	No of patients	No losing weight	No gaining weight			Average gain in weight		No of patients excluded
				0–4 lb	5–9 lb	10 lb +	lb	oz	
A	Drip	38	2	11	20	5	6	13	2
	Control	37	6	21	10	0	2	15	3
B	Drip	30	0	2	17	11	8	6	2
	Control	31	4	10	17	0	4	3	1
A and B	Drip	68	2	13	37	16	7	0	4
	Control	68	10	31	27	0	3	8	4

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[1] Considered as the results of a single trial, the difference between the proportions 27/40 and 17/40 is statistically significant ($\chi^2 = 5\ 05$, $n = 1$, $P = 0\ 03$) The trial was, however one of a set of three, and in these circumstances the standard level of significance is not appropriate In any set of three trials, one or more will show a difference attributable to chance with a probability of as little as 0 02 once in 20 times, and 0 02 should, therefore be taken as the appropriate level of significance for the results of one of the trials taken alone

significant but, in the absence of more detailed data, it seems reasonable to conclude that some of the increase in weight associated with milk-drip treatment was probably due to an increase in body-tissue [2]

Side effects

The drip treatment was carried out without difficulty The great majority of patients grew accustomed to the presence of the tube after a few hours, and although a few continued to find it unpleasant the discomfort was in no case so great that the treatment had to be abandoned Several patients complained of mild heartburn which they had not noticed previously and which ceased when the tube was removed (In 1 patient, not in the present series, diarrhœa appeared to be produced by the drip and was sufficiently severe to necessitate abandoning the treatment)

In none of the patients on alkalinised drip did renal failure develop, nor were any symptoms observed which could be attributed to alkalosis specifically The biochemical effect of prolonged administration of such large doses of sodium bicarbonate in man is discussed by van Goidsenhoven et al (1954)

Discussion

The failure to demonstrate a beneficial effect on the healing of gastric ulcers with continuous intragastric milk drip is disappointing Even the addition of alkali to the milk in sufficient quantity for the acidity of the gastric contents to be kept, in the majority of patients, above pH 4 throughout the 24 hours failed to have a recognisable influence on the healing process It is, of course, possible that the continuity of the drip was not maintained with the same exacting attention to detail under conditions of routine treatment as in the course of the experimental observations which have been referred to Regular tests of the pH of the gastric contents were not made during the trial, and in some or all of the patients the acidity may occasionally have fallen temporarily to below pH 4 Nevertheless such occasions cannot have been of more than short duration in the majority of the patients in parts B and C of the trial, and it is unlikely that any more complete neutralisation has been achieved in any other reported series It would seem, therefore, that, unless very short periods of exposure are effective, peptic digestion cannot be of prime importance in maintaining the activity of a gastric ulcer and that, under conditions of bed rest in hospital, further treatment aimed at the complete elimination of peptic digestion is unlikely to help the ulcer to heal

It is not suggested that continuous neutralisation does not relieve the pain of peptic ulcer There is good evidence that, when an " active " ulcer is present in the stomach, pain can often be reproduced by instilling an acid fluid, and conversely that pain, when present, can be abolished constantly by withdrawing the gastric contents or by their neutralisation (Palmer 1927, Bonney and Pickering 1946) The present investigation confirms the impression that pain is relieved more readily by a continuous milk drip than by the standard medical regime, and we therefore accept intragastric drip as a useful adjunct to the treatment of those rare cases in which the pain does not respond to rest in bed

The present data throw no light on the value of milk drip in the treatment of duodenal ulcer Acid secretion is usually increased in quantity in patients with a duodenal ulcer, while it is usually close to normal in patients with gastric ulcer (Ihre 1947, James and Pickering 1949) It is, therefore, possible that peptic digestion may play a more important rôle in the production or maintenance of the activity of duodenal ulcers, and conclusions drawn from the treatment of patients with a gastric ulcer cannot be applied automatically to the treatment of patients with a duodenal ulcer

The more rapid gain in weight obtainable with a milk drip may be, in some circumstances a positive indication for its use

Summary

The value of continuous intragastric milk drip in the treatment of gastric ulcers has been investigated by means of a controlled trial which covered 164 inpatients in two hospitals 82 received the drip treatment, and 82, who were otherwise treated in the same way, did not In 40 patients the drip consisted of 6 pints of milk a day without any added alkali, in 40, 40 g of sodium bicarbonate was added to each 6 pints of milk, in 2 the dose was increased to 80 and 140 g

The proportion of ulcers which healed in the course of a month was identical in the two treatment groups (20/82) The average amounts healed, expressed as a percentage of the initial size of the ulcer, were also similar

The impression was received that pain was relieved more rapidly with milk drip than without it, and an alkalinised milk drip is considered a useful adjunct to the standard treatment in patients whose pain persists after rest in bed

Patients given milk drip gained, on the average, more weight than patients not given the drip (7 lb 0 oz, compared with 3 lb 8 oz), and a slight advantage (15 oz) was still preserved 2–3 months after discharge

We are grateful to Dr F Avery Jones and to Prof G Pickering for their advice and for allowing us to treat patients referred to their clinics, and to the staff of the gastro enterological and radiological departments of the Central Middlesex Hospital and of the medical unit and radiological department of St Mary's Hospital for help in the management and examination of the cases One of us (A V P) was working with a grant from St Mary's Hospital research fund

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[2] For all cases $t = 0\,88$ $n = 131$, $P > 0\,10$ excluding cases with an initial body weight of under 7 st. $t = 1\,24$, $n = 121$, $P > 0\,10$

CONTINUOUS INTRAGASTRIC MILK DRIP IN THE TREATMENT OF UPPER GASTRO-INTESTINAL HÆMORRHAGE

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FURTHER hæmorrhage in patients who are being treated in hospital for hæmatemesis and melæna is a danger signal A continuous intragastric milk-drip has been claimed to hasten the healing of peptic ulcer (Winkelstein 1949) An indwelling Ryle's tube has been recommended in the management of upper gastro-intestinal hæmorrhage to facilitate the early diagnosis of re-bleeding (Chandler and Watkinson 1953) If either of these suggestions is well founded deaths from hæmatemesis and melæna might be prevented These suggestions have been tested in a study described here

Material and Method

In a series of 100 consecutive cases of gastro-intestinal hæmorrhage a Ryle's tube was passed to between marks

TABLE I—DISTRIBUTION OF CASES BY DIAGNOSIS AND AGE GROUP

—	Milk drip (50 cases)	No milk drip (50 cases)
Diagnosis		
Duodenal ulcer	18	18
Gastric ulcer	8	8
X ray neg	16	17
Postop and miscellaneous	8	7
Age group (yr)		
<50	21	21
50–69	17	22
70 +	12	7

II and III Alternate patients were treated with a continuous intragastric milk drip of 6 pints of non citrated milk each 24 *hours*, no sodium bicarbonate was added to the milk Otherwise the patients were treated routinely by a puree diet, alkalis for symptomatic relief of pain sedation, blood replacement, and emergency operation if necessary 3 patients, all aged 70 years, would not tolerate the tube The following data were charted for 72 hours results of hourly aspirations of the stomach, pulse-rate each hour, blood-pressure every 4 hours, and presence of shock, pallor, or overt bleeding

Results

The final diagnosis and the distribution of cases by age groups were used as criteria for assessing the comparability of the two groups (table I) There was a remarkably even distribution, except for slight weighting of the milk-drip series by a greater number of patients over 70 years of age

The value of a milk drip was assessed by comparing in the two groups the number of deaths, the number of massive further hæmorrhages as shown by alteration in the pulse-rate and blood-pressure, sweating, and overt hæmorrhage, the number of patients requiring emergency operation, and the number of patients in whom fresh blood was aspirated *after previous aspirations* that were clear or contained altered blood and in whom no other signs of hæmorrhage were noted ("tube re-bleeding") The results are shown in table II

There is no significant difference between the results obtained in the two groups In only 1 case did aspiration give warning of massive hæmorrhage, and this was 45 minutes before other signs appeared In all other patients signs developed simultaneously with the aspiration of blood In 10 patients mild re bleeding, as shown by aspirations, occurred in the absence of massive re bleeding

TABLE II—DEATHS, MASSIVE FURTHER HÆMORRHAGES, EMERGENCY OPERATIONS, AND "TUBE RE BLEEDING"

—	Milk drip (50 cases)	No milk drip (50 cases)
Death	5	3
Massive further hæmorrhage	12	16
Emergency operation	7	4
"Tube re bleeding"	2	8

Discussion

There is no evidence that a milk drip prevents recurrence of massive hæmorrhage The series described by Ashby and Whitehouse (1955) suggested that a milk drip tends to diminish the duration of bleeding, but the evidence is open to criticism since a retrospective control group was used Ashby and Whitehouse claimed "early reassurance, confidence and freedom from shock" among patients treated with a milk drip, but this is not substantiated by the present series

I have not found an indwelling Ryle's tube of value in giving warning of impending massive hæmorrhage after admission If note had been taken of tube re bleeding in this series there would have been many false alarms It seems that massive re bleeding usually occurs suddenly

It has been suggested that a Ryle's tube might be useful in keeping the stomach empty of blood, but it does not have this effect after massive hæmorrhage, as anyone will agree who has attended an emergency partial gastrectomy and seen the large amount of clot which has to be evacuated from a dilated stomach Even a large stomach-tube or duodenal tube has proved inadequate in such cases

Summary

100 cases of upper gastro intestinal hæmorrhage were managed with an indwelling Ryle's tube

Alternate cases were treated with a continuous intra gastric milk drip

The two groups were found to be well matched for age and cause of bleeding

The two groups did not differ in the incidence of massive further hæmorrhage

An indwelling Ryle's tube is of little value in giving warning of an impending further massive hæmorrhage

I thank Dr F Avery Jones for his encouragement and advice

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THE ÆTIOLOGY OF CLEFT VERTEBRAL ARCH IN SPONDYLOLISTHESIS

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THE term "spondylolisthesis," in its wider sense, embraces all conditions in which the body of a lower lumbar vertebra, with or without an intact vertebral (neural) *arch, is displaced forwards on the succeeding* vertebra The term thus used is not strictly in accordance with its literal meaning—i e, "slipping vertebra" It was introduced by Kilian (1854) to denote a displacement forwards of the entire fifth lumbar vertebra

Lambl (1858) described some cases of spondylolisthesis in which there was a breach in the bony continuity of the vertebral arch between the superior and inferior articular processes, and this part of the arch he appropriately called the pars interarticularis In such cases of spondylolisthesis the body of the vertebra carries forward with it the pedicle, the transverse process, and the superior articular processes, while the inferior articular process, the lamina, and the spinous process remain in situ

Most Continental workers now accept this bone lesion of the arch as an essential feature of spondylolisthesis, whereas English speaking workers prefer the *more comprehensive application of the term* It is in accordance with such an interpretation of spondylolisthesis that Newman (1955), in an analysis of 204 personal cases, remarks that only about half of them showed a breach in the arch

The present non *clinical contribution to the literature* of spondylolisthesis is concerned only with those cases in which there is a cleft in the vertebral arch, and it is submitted as additional evidence that such a lesion, when present, does not result from a failure of *fusion* between two centres of *ossification This hypothesis* has in the past received considerable support and appears to stem from the claims of Schwegel (1859) and Rombaud and Renault (1864) that there are double ossific centres in each half-arch Various other workers have supported the idea of double centres, but no convincing evidence for them has ever been advanced

All critical observations have substantiated the view that a cleft in the pars interarticularis is the result of fracture of an ossified arch

Rowe and Roche (1953) have produced convincing evidence in support of this assertion in an analysis of 509 stillborn and neonatal cadavers (73 of their own and the remainder previously published) they did not find a single instance of a breach in the bony continuity of the vertebral arch, although in adults the generally accepted figure of such a breach in the arch of the fifth lumbar vertebra is about 5% Their analysis also showed that the 5% prevalence is attained by the twentieth year and thereafter remains fairly constant

Stewart (1953), however, reports from the examination of 786 skeletons of Alaskan natives that there is in them an increase in the incidence of the defect during adult life, and he believes that this is mainly due to the combination of unusual postural stresses and a high accident rate

We believed that a study of ossification in the vertebral arch might contribute towards a solution of the ætiology of a cleft in the pars interarticularis , and, since spondylolisthesis is restricted to the lumber region, the observations recorded here are limited to that part of the vertebral column

The critical stages in the early ossification of the vertebral arches of the lumbar vertebræ are while the fœtus increases in its crown-rump length from 75 mm to 130 mm Our observations were made on serial sections of seven fœtuses between these lengths, and to clarify the exact position of the ossific process three reconstructions were made Observations were also made on other younger and older specimens to verify certain findings

Observations

In each half of the vertebral arch a well-marked sequence of changes take place which are always most advanced in the first lumbar vertebra and least so in the fifth vertebra in any one fœtus The pattern of ossification in the arch of the fifth lumbar vertebra differs in no way from that in the arch of any other lumbar vertebra The vertebral arch of the fifth lumbar vertebra in a fœtus about 70 mm long is formed of cartilage, but by the 75-mm stage a small region of the cartilage in the anteromedial part of the pars interarticularis has become calcified At this stage the cartilage of the vertebral arch is avascular and in this feature differs from the bodies of the vertebræ, which show numerous vascular canals before ossification. These canals show as clear spaces in the bodies of the vertebræ seen in fig 1 The calcification in the arch is indicated, in sections stained with hæmatoxylin and eosin, by the deep purple of the intercellular matrix and by an increase in size of the lacunæ containing the cartilage cells, whose cytoplasm has become swollen and vacuolated

After this localised calcification has taken place, a thin lamina of subperiosteal bone is laid down on the anteromedial aspect of the pars interarticularis directly overlying the calcified cartilage in a manner that is essentially similar to the first deposition of bone in the shaft of a long bone Thereafter the calcified cartilage is invaded by blood-vessels and partly destroyed and excavated With increase in size calcification of the matrix extends in all directions from its initial focus, upwards and downwards into the roots of the articular processes, forwards into the pedicle, and backwards and laterally towards the posterior and lateral aspects of the pars interarticularis, and gradually reaches the perichondrium in these regions Wherever the calcification reaches the surface of the cartilage the perichondrium assumes an osteogenetic function, and subperiosteal bone is deposited

The sequence of this process may be seen, in some measure at least, in a single sagittal section of the lumbar vertebræ of a 101 mm fœtus (figs 1 and 2) This section passes through the lateral part of the body of each vertebra, the pedicle, the superior and inferior articular processes, and the pars interarticularis The process of ossification has just begun on the anterior aspect of the

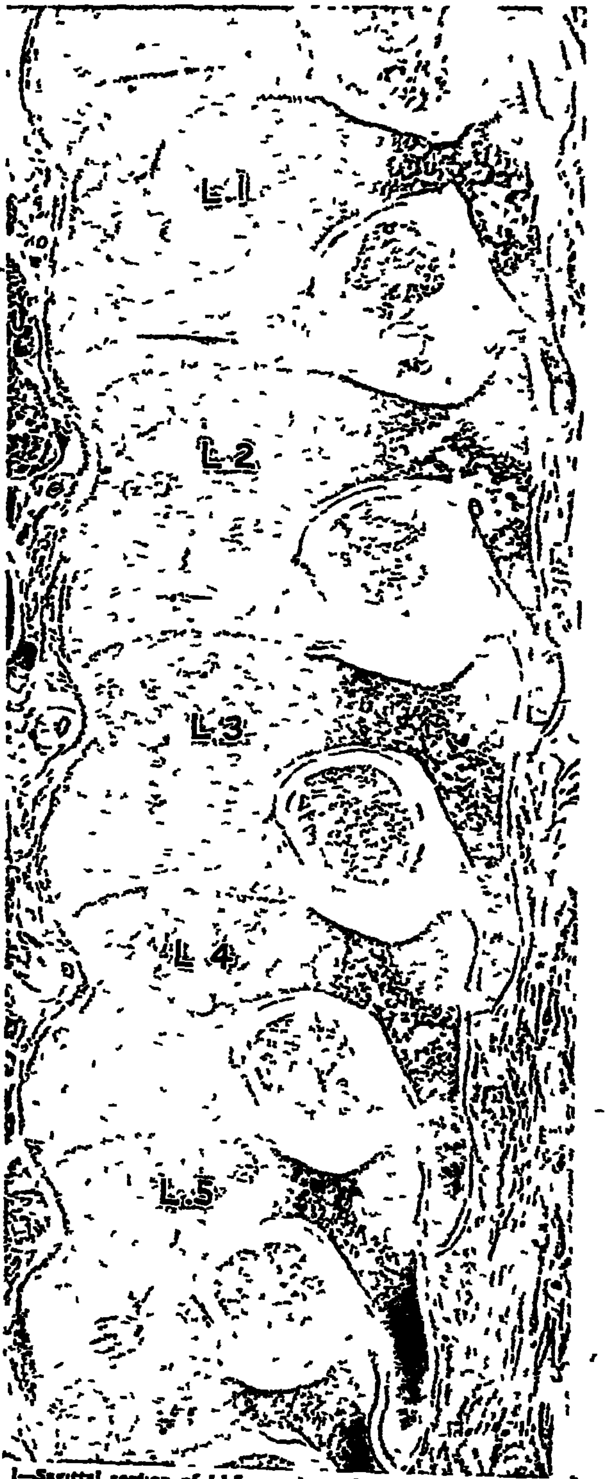

Fig 1—Sagittal section of L1-5 vertebræ of 101 mm (crown-rump) fœtus through bodies pedicles, superior and inferior articular processes, and pars interarticularis Ossification is most advanced in L1 vertebra and least in L5 (×10)

pars interarticularis of the fifth lumbar vertebra, where the bone is seen as a dark lamina lying in front of the calcified cartilage (fig 2c) In the first lumbar vertebra the process of ossification is much more advanced, and the lamina of bone has circumscribed the pars interarticularis, therefore in a sagittal section (fig 2a) bone is seen on both the front and the back of this region While *the deposition of subperiosteal* bone continues, there is massive excavation of the central cartilage of the pars interarticularis (fig 2*a*), and this is as characteristic *a feature of ossification of the* vertebral arches as it is of ossification of the diaphysis of a long bone Small islets of calcified cartilage remain, however, within the subperiosteal collar of bone, and upon these the primary medullary bone of the trabeculæ is laid down

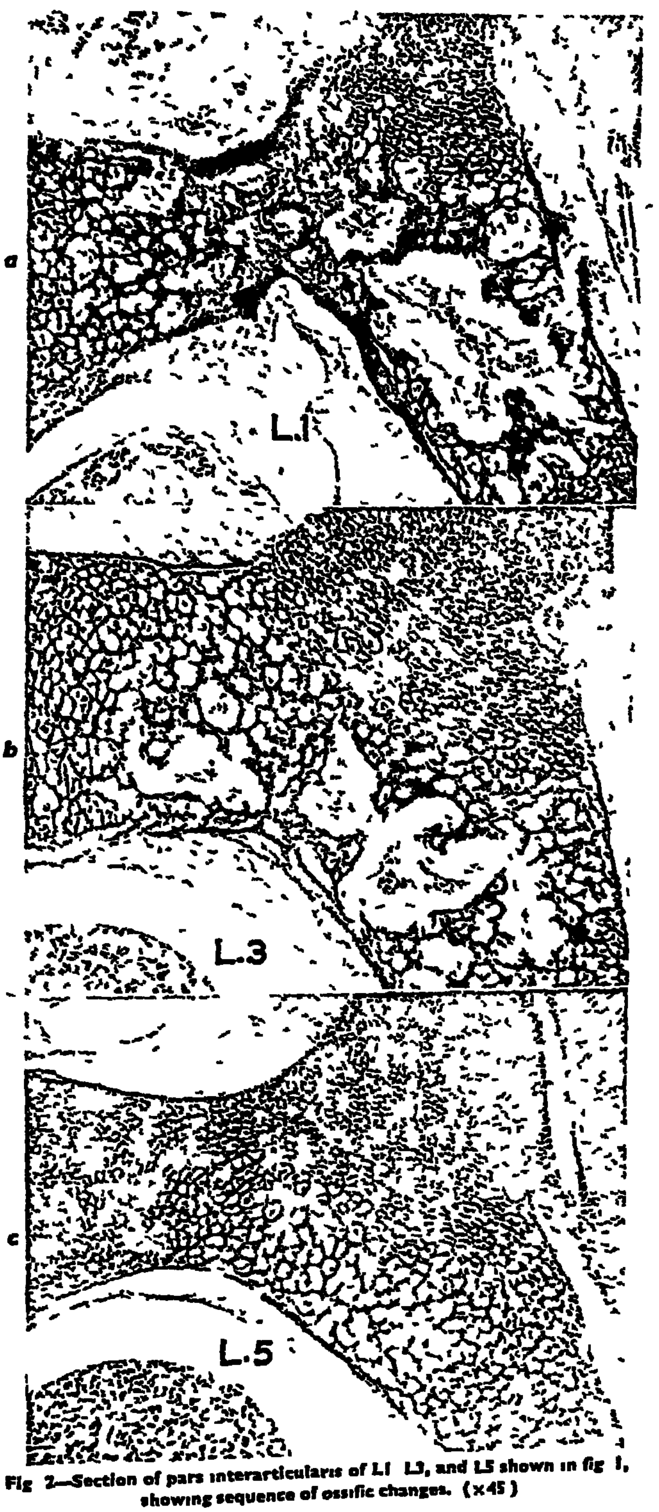

Fig 2—Section of pars interarticularis of L1 L3, and L5 shown in fig 1, showing sequence of ossific changes. (×45)

Reconstructions of lumbar vertebræ of three fœtuses (75 mm, 93 mm, and 101 mm long) show that the calcified cartilage, along with the first-formed bone in the pars interarticularis, together constitute a hemispherical mass This is contradictory to the finding of Willis (1931), who states that the single centre is shaped like an hour glass, a form which, he suggests, may have given the impression to some workers that there are two separate centres in the arch

By the time the fœtus has grown to a crown rump length of about 130 mm the ossification in the vertebral arch of the fifth lumbar vertebra has reached a stage comparable *to that of the first vertebra in the 101 mm* specimen (fig 2*a*) The pars interarticularis is represented by a relatively thin shell of compact bone through which pass numerous vessels Within the primitive medullary cavity are islets of calcified cartilage on which bone is being deposited

Sections through the pars interarticularis of older fœtal and postnatal vertebræ show great variations in the thickness of the cortical bone and in the density of the medullary trabeculæ in specimens of about the same age

Conclusions

Our observations indicate that ossification in a vertebral arch closely resembles ossification in the diaphysis of a long bone In both of them calcification of the cartilaginous matrix is followed by deposition of bone at the surface immediately beneath the periosteum, but only where calcified cartilage has come into apposition with the perichondrium Thereafter ossification continues by thickening and extension of this subperiosteal bone, while the calcified cartilage enclosed and supported by this shell of bone is gradually removed The bone of the medullary trabeculæ is, in the first instance, laid down on the small islets of calcified cartilage that temporarily persist The one difference is that in a long bone the calcification of the matrix begins within the central part of the diaphysis, whereas in the vertebral arch it begins eccentrically on the anteromedial aspect of the pars interarticularis

This pattern is opposed to endochondral ossification as typically seen when a secondary centre or centres of ossification appear within the cartilaginous end of a long bone to constitute an epiphysis There one, two, or more ossific centres may appear within the substance of the cartilage, but there is no primary formation of surface bone as has been described in the ossification of the vertebral arch, nor can there be an accompanying massive destruction of the cartilage within a well defined primary bony collar

These observations are in striking contrast to the statements of Hitchcock *(1940) referring to ossification* of the vertebral arch "This (the ossification) is preceded as in all endochondral ossification elsewhere by the invasion of vessels *from the laminar arteries*" and "The periphery of the isthmic (interarticular) region remains cartilaginous up to and after birth"

As long as Bardeen's (1910) statement is perpetuated that ossification in the vertebral arch is endochondral, and his figure (after Quain), showing this ossification within the substance of the cartilage of the arch, continues to be reproduced, so too will there be misapprehension about possible anomalies in the neural arch Bardeen's statement *that sometimes in the fifth lumbar* vertebra there are two centres for the arch (for which he gives no authority) is in our opinion inconsistent with the manner in which the arch is ossified

All our observations confirm that the whole pars interarticularis is involved in the sequence of changes which take place, and that the process extends from its initial focus in the pars interarticularis to include the whole of the corresponding half of the vertebral arch Furthermore, the bone is laid down as a continuous layer beneath the periosteum wherever calcification of the cartilaginous matrix has extended as far peripherally as the perichondrium Friberg (1939), in photographs of reconstructions of fœtal vertebræ, shows that the first-formed bone is on the anteromedial aspect of the pars interarticularis, in a site almost identical with that which we have observed in our specimens Friberg did not, however, refer to subperiosteal deposition of the first bone, nor did he draw what we believe to be important and pertinent conclusions from it This formation of surface bone is accompanied by such a massive destruction of the underlying cartilage that to postulate that either one or two primary ossific centres appear in this very cartilage is tantamount to assuming that the pattern of ossification is different from that which has appeared so constantly in all our sections and bears a close resemblance to the ossification shown by Friberg (1939) in photomicrographs of fœtal vertebræ

This pattern of ossification is basically opposed to the appearance of either single or double primary endochondral ossific centres within the vertebral arch, and this in turn is in full accordance with the failure of Rowe and Roche (1953) to discover a single instance of cleft vertebral arch in over 500 stillborn and neonatal cadavers If a cleft vertebral arch is caused by a congenital factor, we believe that *it is not due to two centres of ossification but to weakness in the bone of the pars interarticularis of the vertebral arch*

Summary

The pattern of ossification in the vertebral arch of the *fifth lumbar vertebra is similar to that in the arches of* other vertebræ

The site of the initial ossification in the vertebral arch of the fifth lumbar vertebra is indicated by the calcification of the cartilage in the anteromedial part of the pars interarticularis

The bone is first deposited subperiosteally and gradually forms a collar round the pars interarticularis

The laying down of subperiosteal bone is accompanied by much excavation of the underlying calcified cartilage

Ossification in the vertebral arch is not endochondral and *does not appear to be consistent with double ossific* centres

Our sincere thanks are due to Mr J Brown, of this department, for the microscopic sections and photographs

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“ If men value their liberty they are well advised to understand the customs and institutions in which it is grounded and they must be vigilant in its defence But, though recognising it to be above price, they should no more make a fetish of it than a wise man does of his health He learns the principles of hygiene, takes reasonable precautions against abuse, and then gets on with the important things of life which his health permits him to pursue ”—*The Times*, Dec 28, 1955, p 7

THE GENESIS OF THYROID ADENOMAS

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IT is generally accepted that both diffuse and nodular enlargements of the thyroid gland are ultimately due to alterations in the secretion or the activation of the thyrotropic hormone, no matter whether the primary cause is a goitrogenic agent, lack of goitre-preventing factors, or another, unknown, source of deficient synthesis of thyroid hormone (“ inborn error of metabolism ” of Hutchison and McGirr 1954)

Why, in one and the same gland, the increase tends to be *local rather than uniform is not* understood For this reason we investigated the underlying conditions in hypothyroid goitres

Material

The subjects of the study were two siblings, a boy aged 17 years (case 1) and his sister aged 12 (case 2), with familial sporadic cretinism and goitre, who have been reported in detail elsewhere (Zondek et al 1955)

Both had very voluminous diffuse goitres in which five (case 1) and three (case 2) nodules, varying in size from that of large cherries to that of peaches were embedded, and both showed the clinical picture of childhood myxœdema

The administration of a total dose of 960 µg (case 1) and 820 µg (case 2) of tri iodothyronine within eight and nine days respectively led to the disappearance of the myxœdema The response *of the goitres to therapy was, in both patients,* consistent with the well known fact that diffuse thyroid enlargements respond more readily than nodular ones in case 1 reduction of the total volume of the thyroid gland was *first noted after 240 µg (two days) and in case 2 after 80 µg* (one day) of tri-iodothyronine, and the nodules started to decrease after *360 µg (three days) and 520 µg* (six days) respectively

Subsequently there was in both patients a striking decrease of the diffuse and nodular areas alike In case 1 three of the five nodules were no longer palpable after 840 µg of tri-iodothyronine (seven days), the fourth disappeared later under treatment with thyroid gland (7 g in ten weeks), but the fifth, which at that time had shrunk to the size of a small hazelnut, subsequently remained stationary despite prolonged intensive treatment with thyroid The three nodules in case 2 considerably decreased in size during treatment with tri iodothyronine and, later, thyroid but, like the fifth nodule of case 1, did not disappear completely

Present Investigation

After a state of clinical remission had been maintained for some time, both patients were allowed to relapse so that we might possibly find out how the release of the goitrogenic agent from the suppressive action of thyroid hormone would affect the structure of the thyroid gland

Results

In case 1 a clinical relapse was accompanied by renewed and rather rapid formation of a goitre, which again was partly diffuse and partly nodular Diffuse enlargement seemed to precede the formation of the nodules Four nodules reappeared in the converse order of their disappearance They occupied exactly the same sites as before treatment with thyroid Their size had nothing to do with the rate and intensity of either their regression or their reappearance All the nodules, including the fifth, which had never entirely disappeared, attained their former size within sixty nine days after the withdrawal of therapy Repeated administration of thyroid produced a response identical with that produced in the first therapeutic trial Along with clinical remission the four nodules in the same sites as those that disappeared under treatment with tri-iodothyronine and, later, thyroid again disappeared completely, so far as could be ascertained by careful palpation The fifth nodule also behaved in the same manner as the one in the same site in the first therapeutic period although reduced to the size of a hazelnut it did not disappear even after prolonged treatment with thyroid gland and was subsequently removed surgically Histological examination (Dr H Ungar, of the Hadassah Medical School) showed a typical colloid adenoma surrounded by a thick fibrous capsule There was no fibrosis or calcification within the adenoma tissue which might have accounted for its resistance to therapy

In case 2 withdrawal of therapy caused both the diffuse and the nodular parts of the goitre to enlarge progressively Renewed administration of thyroid produced considerable regression of the nodules, which, however, exactly as in the first therapeutic trial, did not subside entirely One of them was removed and also showed the structural properties of a colloid adenoma, again without degenerative changes (Dr Ungar)

Radio-iodine studies during the first period of observation showed in case 1 a total uptake of 14 3% by the thyroid gland after forty eight hours Nodular and diffuse areas behaved exactly alike, except that one nodule collected two or three times as much iodine as did the other tissues (Dr A Hochman, of the Hadassah Medical School) The more active nodule was one of the four which had completely regressed under treatment with thyroid—in other words, it responded to therapy and to its subsequent withdrawal exactly in the same manner as did the less active nodules Conversely, the nodule which did not respond completely to therapy showed the same functional behaviour as the nodules which did respond

Conclusions

On the strength of these observations we postulated that in case 1 the regression of the thyroid adenomas under treatment with thyroid was independent of their functional state Rather must we assume that local differences in responsiveness to the goitrogenic agent—presumably the thyrotropic hormone—accounted for the formation, size, and possibly the nature of the nodules Similar reasoning appears to apply to case 2, in which the nodules did not disappear completely even after prolonged and intensive treatment with thyroid It seems that a regional increase in sensitivity to the goitrogenic stimulus may go so far as to render the tissue refractory to even large doses of thyroid hormone, whereas in other areas of the same gland much smaller amounts suffice to counteract the stimulating agent

According to the peripheral theory of Zondek (1924) the quality and intensity of hormonal activity is modified by the state of responsiveness of the peripheral target-organs, in which respect the electrolytic conditions of the cell surfaces were assumed to play an important part (Zondek and Reiter 1923, Zondek and Ucko 1924–26) This conception apparently also holds good for endocrine structures in so far as they represent hormonal target-organs

Two questions have not yet been answered (1) will it be possible to discover the nature of those inherent factors which determine the local responsiveness of the thyroid tissue to the goitrogenic stimuli? and (2) may the administration of thyroid substances which suppress the goitrogenic stimuli succeed not only in reducing the volume of nodules but also in protecting them from disorderly growth—i e, malignant degeneration? On the strength of our observations this hypothesis is advanced first of all for adenomas within hypothyroid glands, but it may also apply to euthyroid (non-toxic) adenomas Our deduction is consistent with the results of experimental and isolated clinical observations to the effect that the administration of anti-thyroid drugs may produce, especially under hypothyroid conditions, malignant, even metastasising, thyroid neoplasms (Griesbach et al 1945, Purves and Griesbach 1947, Money and Rawson 1947, Fodor et al 1948, Bielchowsky et al. 1949, Herrmann 1951, Boulet et al 1953)

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> "I likewise saw a man who could not move his hand, it being to his thinking dead".
>
> VALENTINE GREATRAKS, 1666

WE draw attention here to Charcot's *oedeme bleu des hysteriques*, a not uncommon form of "hysterical" affection of joints simulating medical or surgical disease, which is rarely mentioned nowadays in published reports We describe two cases (one following injury), neither of which had been recognised They had been referred to one of us (J P R) with a view to sympathectomy or amputation

Charcot (1890) observed that this disorder is characterised by non-pitting œdema, coldness, purplish discoloration, altered sensation, often total anæsthesia, paresis, and contracture of either hand or foot (fig 1), electrical reactions remain normal He and Pierre Marie (1892) added "trophic derangements among them blister like eruptions" Pain is sometimes, but not always, a feature

Although known by Charcot's name, Brodie (1837) had previously referred to "several cases of this singular affection of the hand and wrist," and Paget (1873) had given a detailed description of it as an example of "nervous mimicry" of organic disease

Hysteria and Hysterical

It is impossible to discuss *oedème bleu des hystériques* without glancing at the history of the term "hysterical" This term has impeded the understanding of mental disorders from earliest times It was once used synonymously with insanity in general, and for "fits" of every kind, and latterly it has been used for somatic symptoms of psychological origin Yet it has resisted all attempts at elimination

> "*The name hysteria should be abolished For it is absurdly* derived and used as a term of reproach, is worse than absurd hysterical is taken by many people that she is silly, shamming, *or could get well if she pleased* call them anything but hysterical" (Paget 1873)

Reynolds (1872) pointed out that "hysterical" meant widely differing things to different people

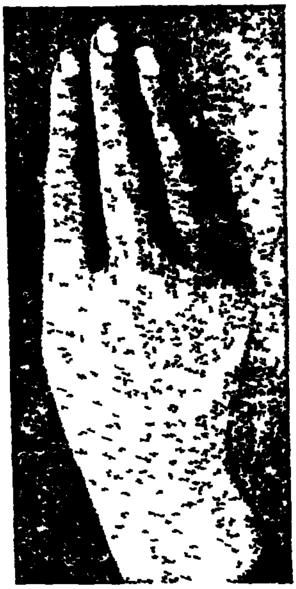

Fig 1—Charcot's original illustration

"'nervous temperament' a mood or disposition of disordered function which cannot conveniently be placed elsewhere simply conveys a doubt as to what is the matter a prevailing conviction that it is nothing very serious"

Allbutt (1869) was "quite sure that by the use of the word hysteria, the medical man not only injured the patient, but damaged his own power to cure"

Unfortunately Charcot elevated hysteria to a disease entity and assembled under *la grande hysterie* a medley of neurological and psychiatric conditions, including epilepsy, hemiplegia, catatonic schizophrenia, malingering, and even fraud He also introduced the misleading factor of hypnotic suggestibility as the hallmark of hysteria

Pathology and Psychopathology

Babinski, in a series of publications in one of which (1896) he described the plantar reflex, demolished Charcot's "hysteria" by demonstrating that lack of diagnostic precision was responsible for purely neurological conditions being termed hysterical But he accepted Charcot's idea that hysteria was due to suggestion, hence only body function subservient to the will could be considered hysterical In a comprehensive survey, he and Froment (1918) suggested calling autonomic symptoms such as œdema "reflex neuroses" in order to emphasise their independent, organic origin, although they agreed that these "reflex neuroses" were usually associated with disturbances of voluntary function, such as paresis, and cleared up with psychotherapy

Roussy and Lhermitte (1918) give the most acceptable explanation of vasomotor and trophic changes found in cases of *oedème bleu*

> "Vasomotor symptoms, fall of the temperature, cyanosis of the paralysed extremities, hyperidrosis, œdema, etc, are the result of functional inactivity, as is proved by their rapid disappearance, when an hysterical paralysis or contracture is cured by psychotherapy"

Today, because we still do not understand how the mind produces somatic symptoms, we are inclined to disregard mental factors Reynolds (1869) had rightly predicted that, if their psychological origin is ignored, such conditions "are theoretically driven into the sympathetic corner, whereas there is nothing to prove that the vaso-motor or sympathetic system is primarily at fault"

Paradoxically, the advent of psychiatry as a specialty in its own right has encouraged this trend, whereas in the past surgeons and physicians dealt with both the body and the mind of their patients, and made valuable psychological contributions, they now leave everything concerning the mind to psychiatrists But the most skilful part—diagnosis and selection of patients—remains their responsibility The psychiatrist labours under similar difficulties he has not the clinical opportunity of comparing organic with non-organic symptoms, and as his training centres largely on mental phenomena, he is ill equipped to deal with patients whose symptoms masquerade as bodily disease Thus patients with somatic symptoms of psychological origin often fall between two stools

Case-reports

Case 1 —A woman, aged 22, shop assistant Left arm in sling, forearm and hand much swollen, skin purplish red, tight, shiny, with several deep ulcers (fig 2A), movement and sensation uniformly reduced, severe pain at times, reflexes, electrical reactions, radiographs, arteriogram, phlebogram, and lymph flow normal

History —Aged 2 adopted by mother's sister, disturbed childhood temper trantrums and sleepwalking In 1946, aged 15, after playing in snow warmed hands in front of fire Both hands red and tight, left appeared swollen Sent to doctor, treated with penicillin and hot bathing Swelling gradually increased, spread up forearm, skin discoloured, ulcers appeared on extensor surface In 1948 admitted to hospital for seven weeks, arm in plaster, penicillin injections Discharged unimproved, outpatient physiotherapy for several months Condition deteriorated

In 1949 referred to one of us (J P R) regarding advisability of sympathectomy or amputation Transferred to psychiatrist (I M) as hysterical paresis

Treatment and progress —Seen eighteen times in eight months Hostile to psychiatric approach "It is not imagination," "I have only been sent for consent to amputation," "Why should I have had so much treatment, if nothing is wrong with my arm?" Clamoured for amputation, complained limb was ugly and disfiguring, but unconcerned about loss of function Bitter about adoption, hostile towards mother who had kept brother "If I had a child I would not get rid of it" Heard of adoption from other children when aged 3, remembers being unable to believe or understand it Consciously devoted to foster-mother, although she was strict, fussy, and possessive During psychotherapy realised she was longing for own mother, whom she called aunt "Perhaps I don't know all the circumstances of the adoption" Wondered whether foster mother had turned her against own mother, accused her of holding on to her Her confused feelings and insecurity were expressed in a recurrent dream she was

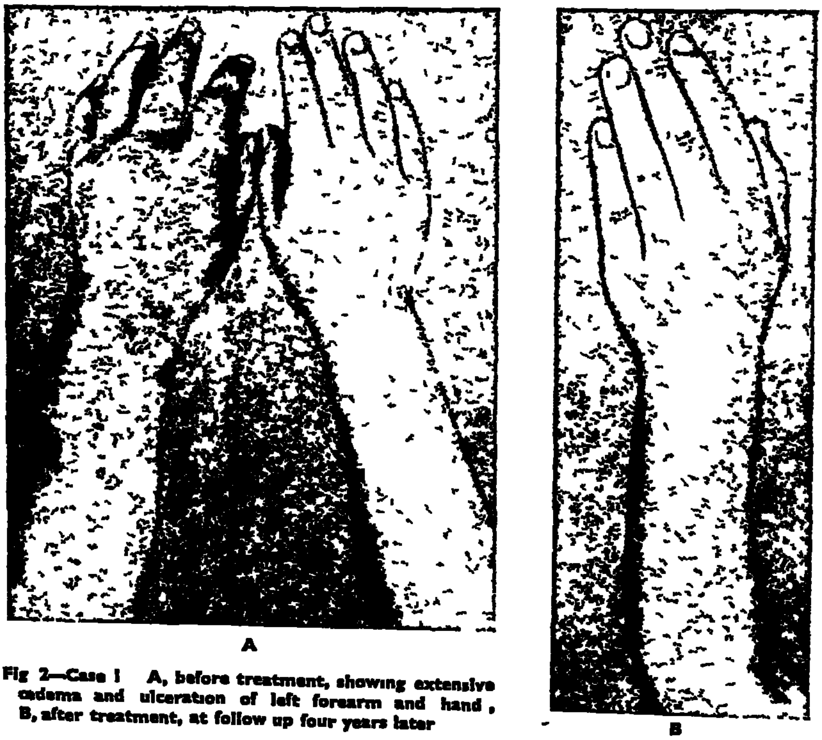

Fig 2—Case 1 A, before treatment, showing extensive œdema and ulceration of left forearm and hand, B, after treatment, at follow up four years later

going to a funeral of either mother or foster mother , she could never tell which Referring to her " two mothers," she said " if only I could cut myself off from this eternal muddle " Later used the same words about her arm, which she wanted " cut off " When it was pointed out that she wished to do with the arm what she had not achieved with her family background, the arm greatly improved , sling and bandage were discarded, colour became normal, ulcers started healing Four weeks later hand entirely normal , full movement, no pain Treatment concluded after two more sessions Four years later working happily as typist, arm and hand remained perfectly normal (fig 2B)

Case 2.—A girl, aged 20, student teacher Loss of movement and sensation in right hand to 2 inches above wrist, contracted, bandaged, and in palmar splint , swollen, reddish blue Reflexes, radiographs, electrical reactions, arteriogram, phlebogram, lymph flow normal

Family and personal history —Father 1914–18 war pensioner, capable only of light work, involved in road accident shortly after patient's accident, with subsequent severe depression Mother handicapped by claustrophobia Patient's early ambition was to teach handicapped children

Present complaint —March, 1952, at college, glass tubing accidentally pierced right hand in mid palm between third and fourth metacarpals Hand bandaged in hospital Because of " pulling sensation " wound explored two days later , no glass found Wound healed " My hand was perfectly all right and I had all sensation, even played netball for about six weeks after accident " May , 1952, hand swelled painlessly, loss of movement index and middle fingers June, 1952, exploration under general anæsthesia several small pieces of glass said to have been removed No improvement In next twelve months four further surgical explorations Patient was told that accident could have been much worse and lucky to have hand at all July, 1953, presented at third hospital with pain and weakness of hand, contracture of fingers, loss of sensation in third and fourth fingers Intensive physiotherapy, but active movement further diminished. Advised to stop using hand altogether, bandage, and use sling while awaiting sixth exploration December, 1953, scar excised, flexor tendons freed from adhesions Slight short lived improvement April, 1954, had to leave training college " in case something happened to my hand " May, 1954, loss of sensation spread to second finger Neurosurgical opinion permanent disability certain, advised to keep hand bandaged to avoid injury Physiotherapy continued, but further deterioration August, 1954, whole hand insensitive, movement grossly restricted, fingers contracted, bluish red (fig 3A) October, 1954, referred to one of us (J P R) for opinion re sympathectomy , referred for psychiatric investigation (I M)

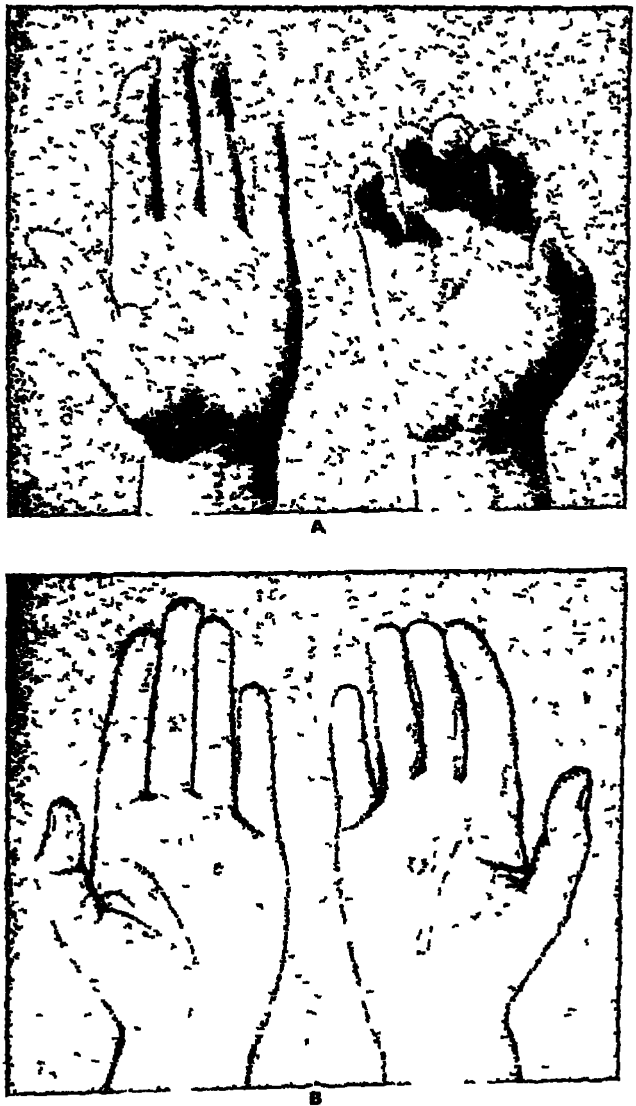

Fig 3—Case 2 A, before treatment, showing swelling and contracture of right hand and scars of injury and operation , B, after five psychotherapeutic interviews

Treatment and progress —Superficially cooperative, but hostile " It is not imagination " Puzzled that surgery, exercises, and physiotherapy had made her worse Believed this confirmed seriousness of original injury " probably it is gangrene " It was explained that the mind can produce somatic symptoms without their being put on or imagined, that attention focused on hand, whether by exercises or bandaging, interferes with normal automatic movement and sensation She wished for amputation " I am almost better without the arm, I could then forget about the accident and all the bother ", " the hand is dead anyway ", " I could get a better job as a severely disabled person " Shock of the accident discussed, and what she thought had happened, also emotional attitude to parents, particularly her intense sympathy with disabled father Advised to discontinue bandaging and sling and to make no conscious effort Later on attempts were made to revive interest in her future and ambition to become a teacher Little direct reference made to arm After third fortnightly interview swelling subsided, movement freer, extension of fingers almost complete, sensation returned except in third and fourth fingers At fifth interview she reported that she found herself using the hand in all activities (fig 3B) Applied for training as occupational therapist and was accepted " as she appeared to have full use of her hand and a firm grip " Relapse ninth interview using hand less coincident with appearing before a committee considering compensation for original injury on sympathetic grounds, negligence having previously been denied Since then improved again, though not prepared to start training till claim settled

Discussion

Differential Diagnosis

Oedème bleu must be differentiated from medical and surgical diseases of joints, central and peripheral nervous disease, dermatitis artefacta, local malignancy, adiposis dolorosa, and peripheral vascular disease

Customarily psychological origin of somatic symptoms is diagnosed only after exclusion of organic disease It is not sufficiently realised that a diagnosis of psychological origin can be made on positive clinical evidence Such cases are by no means uncommon Brodie (1837) found that " at least four fifths of the female patients among the higher classes who are supposed to labour under diseases of the joints, labour under hysteria and nothing else "—a statement endorsed by Paget (1873) and enlarged by Skey (1867) to include " a large proportion of the lower , for much of my practice has been obtained from the wards of St Bartholomew s Hospital "

A carefully recorded history often gives the clue, as when patients have, or have had, other psychosomatic symptoms Cases following minor injuries (e g , the present case 2) commonly have a " latent period " before symptoms appear (Brodie 1837, Horsley 1809) , Turner (1918) spoke of a " phase of incubation " Casual medical remarks often aggravate the condition case 2, when told that she was lucky to have her hand at all, soon lost all power in it , when told she must accept loss of sensation in two fingers, she promptly lost sensation over the whole hand, when advised to wear protective bandage she banged her hand and "took a chunk out of it"

The attitude of these patients to the affected limb differs from that of the organically ill they carry the arm as if it did not belong to them or were not part of them, much as patients with non-organic palsy of the leg drag it without attempting circumduction Mentally they are equally indifferent, they are unconcerned about loss of function and apparently resigned to their condition Indeed both patients clamoured for amputation the first said "I hate this ugly thing", the second insisted that amputation was "the best solution" During examination the patient does not anxiously watch the limb, like patients with organic disease, but looks at the examiner with an expression as of a point scored Paralysis tends to be more complete, anæsthesia more uniform, pain more constant, swelling more widespread, than in organic lesions The condition may remain stationary for years—which, as Babinski pointed out, is unknown in organic affections

Management

Once the condition is recognised as of psychological origin, no attempt should be made to apply physical treatments, which are always taken by patients as confirmation of their belief that their complaint is physical and not mental, making them more refractory to psychotherapy Wilks (1883)

> "could not speak too strongly in denunciation of the old fashion, the plan of treating hysteria by physic instead of moral means which was known to be useless, and yet was followed as a matter of routine It cannot be presented too strongly that the mere absence of treatment by physic is a positive stage towards the cure"

In each of the present cases the patient's condition was aggravated by physiotherapy, immobilisation almost beats the patient at his own game and "always has disastrous results" (Charcot 1890) Local treatment of any kind converts a symptom into a self-perpetuating disease, by preventing "the attention being abstracted from the local symptom" (Brodie 1837) Indeed it is best for patient and doctor not to concentrate on the local complaint.

> "To 'make an effort' is sheerly detestable to the hysterical patient, and as impossible but to exert herself, almost unconsciously, because a motive is supplied, is scarcely felt to be an effort" (Reynolds 1872)

The physician must show "painstaking appreciation of the patient's own feelings, determinate assurance that the disease is no idle fancy" (Reynolds 1872), "It is very erroneous, when patients are charged with imagining or inventing their sufferings" (Paget 1873). It is the essence of the illness that patients cannot see that their symptoms arise from an unconscious idea or emotion (Macalpine 1954), they behave much like patients with frank delusions, who are not amenable to rational argument, objective evidence, or reassurance.

We cannot here discuss details of psychotherapy; we conduct expectant, non-interfering, *face-to-face* interviews Interestingly Charcot himself warned that in these cases "the abuse of hypnotism has been followed by very serious complications" (Charcot and Pierre Marie 1892)

Psychological Significance

"It is not that the muscles are incapable of obeying the act of volition, but that the function of volition is not exercised" (Brodie 1837). "She says, as all such patients do, 'I cannot', it looks like 'I will not' but it is 'I cannot will'" (Paget 1873) Yet there is no lack of will-power in other spheres (It is historically interesting that Paget (1873) suggested "It may be due to mental association, perhaps unconsciously").

Loss of movement and sensation express the idea that the limb is to the patients' "[illegible]" (Greatraks 1666) Hence they avidly accept anything which seemingly confirms this belief This phenomenon misled Charcot into postulating suggestibility as the hallmark of hysteria But patients need not be generally suggestible, they are so within the confines of their morbid ideas

It is the function of psychotherapy to trace out the development of patients' feelings and ideas Case 1 spoke of her arm and her family in identical terms she wanted to cut herself off When the unbearable confusion of love and hate to mother and foster-mother was worked through, the condition cleared up Case 2 was from early childhood deeply affected by sympathy for her invalid father, and concretely expressed this by "suffering with" him—psychologically speaking, she identified with him A striking feature in both was the concreteness of expression achieved in the symptoms, which is characteristic

Psychiatric Significance

These patients illustrate the transition from somatic symptoms arising in the mind to mental illness proper (Macalpine 1954) Concrete thinking as opposed to conceptual, abstract thinking is common in mental disorders The same is true of serious persistent disregard of one's own interest, which our patients displayed by readily accepting their disability, indeed their insistence on amputation may be regarded as a degree of self-mutilation amounting to partial suicide Their inaccessibility to objective evidence and reassurance differs from frank delusions only by their false beliefs being centred on *their body and not on the outside world.* Thus cases of *oedeme bleu* illustrate the early or mild stages of mental *illness*, the disorder still being confined to the patient's relation to himself, to his mind and his body (Macalpine and Hunter 1955) The presenting symptom must not be regarded as a foreign body to be removed; rather it plays a vital part in the mental economy, and if treated in isolation or by physical means patients may be much worse off Other somatic symptoms equally likely to be misunderstood and hence mismanaged may appear, or a frank psychosis may develop This is confirmed by patients in whom the condition alternates with periods of psychosis (Brodie 1837)

Recognition of localised abnormalities such as *oedème bleu* is therefore of immediate practical importance, and their study may advance our understanding of mental illness in general.

Summary

Two cases of *oedème bleu* are reported, and the condition is discussed in its historical, clinical, psychological, and psychiatric aspects.

We thank Mr. N. K. Harrison, of the photographic department, for the figures.

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AFIBRINOGENÆMIA

ASSOCIATED WITH SEVERE UTERINE HÆMORRHAGE FOLLOWING CÆSAREAN SECTION

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A CASE of postpartum hæmorrhage associated with a deficiency of fibrinogen was reported by Kelsey and Muirhead (1955), who found that few such cases had been published We describe here a further case, in which severe hæmorrhage occurred during a lower segment cæsarean section done for prolapse of the cord

Case-report

A woman, aged 38, who had previously borne three children, was admitted as an emergency case to the Gables Maternity Hospital, Peterborough, in labour with a prolapsed cord, at 3 30 A M on Sept 29, 1955 Lower segment cæsarean section was performed at 4 A M The placenta was found attached to the lower segment (anterior wall of the uterus) as a type-1 placenta prævia, the amniotic cavity was incised lateral to the placenta, which was displaced medially A healthy female infant weighing 7 lb 15 oz was delivered Hæmostasis was difficult to achieve, 55 oz of blood being lost during the suturing of the uterine incision A specimen of blood was taken from an arm vein for grouping and cross matching, and an intravenous drip was set up 'Intradex' 2 pints was given, followed by one bottle of 4 3% dextrose and 0 18% saline solution

6 15 a m blood pressure (B P) 80/60 mm Hg, pulse rate 110

7 a m B P 80/60 A few minutes later a report was received from the consultant pathologist that the specimen of venous blood taken during the operation, before the start of intravenous therapy, had not clotted

8 15 a m triple strength plasma (small pool) was given intravenously with 'Synkavit' 50 mg

8 30 a m B P 80 75

9 30 a m B P 116 76

10 15 a m B P 105/75 pulse rate 100

11 15 a m clinical improvement, less bleeding per vaginam and blood beginning to clot

12 45 p m fibrinogen 186 mg given into intravenous drip

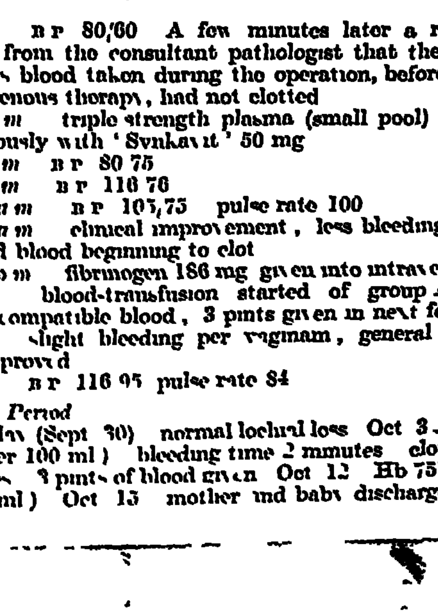
1 p m blood-transfusion started of group A rhesus-positive compatible blood, 3 pints given in next few hours

4 p m slight bleeding per vaginam, general condition much improved

7 p m B P 116 95 pulse rate 84

Recovery Period

Next day (Sept 30) normal lochial loss Oct 3 Hb 58% (8 2 g per 100 ml) bleeding time 2 minutes clotting time 4 minutes 3 pints of blood given Oct 12 Hb 75% (11 0 g per 100 ml) Oct 15 mother and baby discharged well



Paper electrophoresis of plasma a first specimen, not showing any fibrinogen b second specimen showing fibrinogen (level was 312–313 mg per 100 ml).

Electrophoresis

The first specimen of venous blood still failed to clot after 102 hours A second specimen of venous blood was taken at 2 P M on Sept 29, and both specimens were examined in the Department of Medicine, Cambridge University Medical School The results of paper electrophoresis of the plasma are shown in the accompanying figure No clot was obtained with the plasma taken before the administration of any intravenous therapy The plasma taken 75 minutes after fibrinogen had been given contained 312–313 mg of fibrinogen per 100 ml of plasma

Discussion

If the blood ceases to clot, replacement of fibrinogen is urgently needed This can be done either by giving fibrinogen intravenously (fibrinogen can be obtained from regional blood-transfusion centres but is in short supply) or by infusion of plasma of double, treble, or quadruple strength (Barry et al 1955), made up by simply adding respectively a half, a third, or a quarter the usual volume of water This should be sufficient, in most cases, to correct afibrinogenæmia (Scott 1955)

Intradex or a similar preparation should be given to help to restore the blood volume, pending the arrival of fibrinogen from the regional blood-transfusion centre This should be done in spite of the considerable clinical and experimental evidence that dextran can impair the coagulation mechanism In view of this evidence, however, it seems wise to limit the use of dextran to 1 or 2 pints, and to follow this up as soon as possible with transfusion of grouped cross matched whole blood

Small test-tubes should be kept ready in obstetric units to enable the clot observation test to be carried out Weiner et al (1953) say that, even when clotting takes place, it may be followed within an hour by fragmentation and dissolution, and that, if this happens fibrinogen should be given immediately to restore the ability of the blood to clot Multiple whole blood transfusions will not do this

The patient showed clinical improvement at 11 15 A M after the administration of triple strength plasma by intravenous infusion, the clot formed being soft and mushy The fibrinogen (186 mg) was given at 12 45 P M —i e, 4½ hours after the plasma The normal range of plasma-fibrinogen level is about 220–400 mg per 100 ml and in pregnant women near term about 450 mg per 100 ml (range 300–600 mg per 100 ml during labour) We therefore consider that the infusion of triple strength plasma restored the clotting-power to almost normal and that the small dose (186 mg) of fibrinogen restored it to normal

Barry et al (1955) state that when rapid coagulation is essential, pure human fibrinogen 4000–6000 mg should be given intravenously

Summary

A case of afibrinogenæmia associated with massive postpartum hæmorrhage after a lower-segment cæsarean section is described

It was treated by intravenous infusion of fluids and of plasma blood transfusion, and intravenous injection of fibrinogen

We should like to express our thanks to Miss L M Gales matron of the hospital, and her staff, to Dr F E [illegible] consultant anæsthetist to Dr D H [illegible] senior consultant pathologist, to Dr C V B W[illegible] of the regional blood-transfusion centre, Cambridge and to Dr J F M[illegible]ard and Dr M J Ne[illegible] of the department of medicine Cambridge University Medical School

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A HYPERTENSIVE FAMILY

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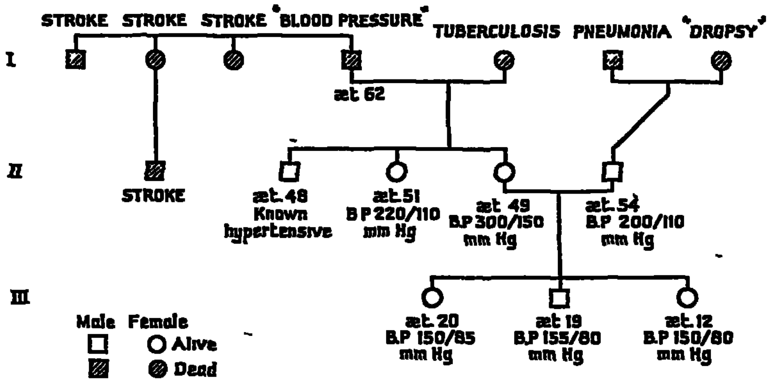
GENERAL PRACTITIONER

IN 1947 Platt stated that he had not yet discovered a family in which all the siblings had essential hypertension and that neither had Weitz Both these workers, however, found a strong suggestion of heredity in essential hypertension in about 75% of cases (Platt 1947, Weitz 1923)

I report here a family with three generations of hypertensive patients (see figure) All the first generation died of stroke except one who died of "high blood-pressure" at the age of 62

All three of the second generation are alive, although somewhat precariously, and all have hypertension I have personally examined two, and I am told that the brother who lives away is having treatment for "blood-pressure" One of the sisters is married to a man with a moderate hypertension (200/110 mm Hg), and they have three children aged 20, 19, and 12 years (third generation) All these three have a systolic blood-pressure on the high side, particularly the girl aged 12 years All the readings were taken with the patients at home resting in an armchair and were repeated several times Urinary albumin was absent in all the third generation and in their mother The others were not tested



A hypertensive family

In the second generation two daughters and a son, all living have hypertension, and a cousin of theirs died of a stroke

Discussion

The normal blood-pressure of children aged 12 years is 102–115 mm Hg systolic and 62–72 mm Hg diastolic (Holt and McIntosh 1940), the blood-pressure of the girl aged 12 years is abnormally high at 150/80 mm Hg The elder girl, aged 20, has a blood-pressure of 150/85 mm Hg and the boy, aged 19, one of 155–80 mm Hg These are the lowest recordings and can be considered higher than normal for children of their ages

On their mother's side of the family there seems to be a dominant gene which has become apparent in all near blood-relations Their father also has moderate hypertension Unfortunately his brothers and sisters cannot be traced All the three children are well

I intend to follow up the third generation as far as possible, but marriage has taken away the eldest girl and the Services the boy, scattering the family, and family reunions are hardly the time for the doctor to appear, armed with his sphygmomanometer, like a spectre at the feast

It is generally agreed that death from apoplexy, be it cerebral thrombosis or cerebral hæmorrhage, is associated with hypertension (Brummer 1947) Thus all the first generation must have been hypertensives

Summary

Three generations in a family have been hypertensive, all those living have hypertension and those deceased had hypertensive deaths

In the third generation, slight but persistent hypertension is noted in a girl aged 12 years, a boy aged 19, and a girl aged 20

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ACUTE CHYLOUS PERITONITIS

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THE presence of chyle and chylous fluid in the abdominal cavity is unusual, and it is particularly rare to find acute peritonitis in association with a chylous ascites I could find no reports of acute chylous peritonitis in British literature, but 27 cases have been described in American and European journals Hoffman (1954) collected 23 cases, and added 1 of his own, Jackson (1953), Olechowski and Froyd (1952), and Kelemen (1954) each described single cases Every case was regarded as an "acute abdomen," and the diagnosis was established at laparotomy

Case-report

A forester aged 27 was admitted to hospital complaining of severe abdominal pain of eight hours' duration The pain, which began soon after he had eaten a breakfast of bacon and eggs, was felt first in the costovertebral angles Later, it travelled round to the umbilical region, and then to the right iliac fossa where it persisted The pain was constant and intense, with occasional exacerbations Nausea was continuous, and the patient vomited once before admission Micturition was normal, and he had had a recent bowel movement, and passed flatus

He had been in another hospital eighteen months previously with "appendicitis," but he was discharged without operation Seven years ago, some tuberculous glands of the right side of the neck were excised

When first seen in hospital, the patient was rolling about in bed and crying out His face was flushed, sweating, and anxious His blood-pressure was 120/78 mm Hg, temperature 97°F, pulse 98, and respirations 34 per min His abdomen was rigid on the right side and there was guarding on the left side There was no abdominal movement on respiration He was tender all over the right side, especially in the right iliac fossa Bowel sounds were diminished Liver dullness was within normal limits There was considerable tenderness on the right side on rectal examination Analysis of his urine was normal White count was 8500 per c mm Straight X-ray examination of the abdomen was normal.

No definite diagnosis was made, but laparotomy was considered essential to exclude acute pancreatitis or perforated duodenal ulcer, with tracking of bowel contents down the right paracolic gutter

Operation —As soon as the peritoneum was opened, the wound was flooded with chyle, of which about 12 oz was aspirated.

The cæcum was completely white, and the ascending colon patchily so, as if milk had been injected under the serous coat The mesentery of the ileum, the mesocolon, the pancreas, and several small areas on the posterior abdominal wall were similarly affected Free chyle lay in Morison's pouch, the right paracolic gutter, and in the rectovesical space A mass was felt behind the stomach, so the wound was enlarged upwards.

There was an irregular, craggy mass, measuring about 3×2×1 cm, on the posterior abdominal wall of the lesser sac, over the 2nd and 3rd lumbar vertebræ, and from the middle of it came a trickle of chyle No other abnormality was found The mass was friable and looked tuberculous, but a neoplasm could not be excluded A small piece was excised for histological examination

Closure of the leakage was difficult, but the opening was patched with a piece of omentum, a large "cigarette" drain was inserted into the lesser sac through the gastrocolic omentum, and the wound closed round it

Pathological Report—"The tissue submitted is a small lymph-node Microscopy shows numerous foci of caseation with surrounding epithelioid cell reaction, and occasional giant cells The appearances are those of tuberculous lymphadenitis The fluid is milky in appearance, alkaline in reaction, and its specific gravity is 1014 There is no change in the fluid on standing, and it is sterile on culture both on ordinary and Löwenstein Jensen media Microscopy shows numerous finely divided fat particles approximately 2 µ in diameter Only occasional lymphocytes are seen in stained smears The appearances are consistent with a chylous effusion"

Subsequent Progress—The patient's pain was abolished as soon as drainage was instituted, and his convalescence was uneventful until the eighth postoperative day, when a small-bowel obstruction developed, and a further operation was carried out Several loops of ileum were found to be adherent, but the loop responsible for the obstruction was easily freed All the subserosal collections of chyle had disappeared Following this, his progress was uninterrupted, and he was discharged on the twenty-fourth postoperative day He was quite well two years after the operation

Discussion

The physiology and pathology of the lacteal system are imperfectly understood, and one can only speculate on the reasons underlying the findings in this case The free fluid in the abdomen was, in the main, pure chyle and not a transudate, as chyle was seen trickling from the mass overlying the cisterna chyli Subserosal collections of chyle were widespread and patchy in distribution, and it is unlikely, therefore, that these were caused by retroperitoneal spread from the tuberculous mass overlying the cisterna chyli It is more likely that the inflammatory mass caused obstruction, not only to the main lymph but also to the collateral channels Lee (1942) showed experimentally that ligature or section of the main thoracic duct alone did not produce chyloperitoneum, because a collateral circulation was rapidly established

Presumably, when the main lumbar channels and the collaterals were obstructed in this patient, back pressure was built up and some of the peripheral lacteals ruptured, allowing chyle to spread in the subserosal layer Subsequently a leak must have occurred in the soft tuberculous mass, and acted as a safety-valve Collateral channels must, however, have opened up after the first operation, because there was no sign of subserous collection of chyle eight days later

The initial lumbar pains were possibly caused by increasing pressure in the main lymphatic trunks and distension in the subserosal layers, the change of site to the right side of the abdomen being due to irritation of the peritoneal cavity by free chyle

Peritoneal reaction following the first operation was sufficient to cause multiple adhesions and obstruction, but the origin of this and of the pain is obscure, because free chyle usually produces little or no pain or reaction in the abdomen or thorax Blockage of the main lymph-ducts by microfilaria causes stasis, distension, and final rupture of the distended lacteals, but no pain, however, this is a gradual process and is not exactly comparable, as it produces transudates also

Possibly chyle, in concentrated form, contains some irritant factor, but Wells (1920) found little to suggest its identity, unless it is a diastatic enzyme

In only 8 of the 27 previously described cases were any lesions found at operation, and in only 3 of those was the lymphatic system affected (Guldmann 1921, Dutton 1930, Jackson 1953)

The prognosis is good in most of the acute case
less satisfactory in chronic cases Only 3 fatal ca
acute chylous peritonitis have been recorded
associated lesions were paralytic ileus (Papenberg
lymphosarcoma (Jackson 1953), and miliary tu
losis (Reboiras and Giralt 1938)

Abnormalities in the abdomen may be correct
operation, but closing the ruptured chylous duct is
difficult The patch technique worked in this patien
the establishment of a collateral circulation was
With regard to wound drainage, 18 of the pa
previously described were drained and 9 were not,
was no appreciable difference in the convalescence
2 groups

Summary

Acute chylous peritonitis was diagnosed at laparot
The predominant feature was a tuberculous obstru
and erosion of the lumbar lymphatic trunks
erosion was closed with a patch of omentum, and rec
was rapid

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Preliminary Communication

THE EFFECT OF PARA-AMINOSALICYL ACID ON HYPERTHYROIDISM

SINCE the first report by Clausen and Kjerulf-Jen
many investigators have reported that in some pat
the prolonged administration of *p*-aminosalicylic
(P A S) is followed by the development of goitre
or without myxœdema Recent investigation by B
et al[2] and Macgregor and Somner[3] has appare
shown the anti thyroid activity of P A S We re
here the effect of P A S on hyperthyroidism,

Calcium P A S *15 g a day by mouth was given*
3 male and 10 female hyperthyroid patients

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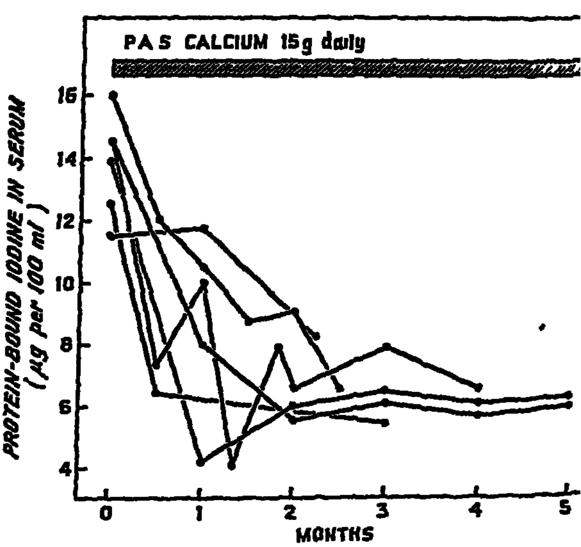

Level of protein bound iodine in patients with either slight or moder
hyperthyroidism, showing decrease to normal range under tre
ment with P.A.S

RESULTS OF TREATMENT OF HYPERTHYROIDISM WITH P A S

Result	Administered longer than 2 mos	Discontinued within 2 mos because of pyrexia	No of cases
Full control	5	1	6
Control→relapse	2	1	3
No improvement	3	1	4
Total	10	3	13

The patients with either slight or moderate hyperthyroidism were improved by P A S The accompanying figure shows that the amount of protein-bound iodine in the serum of these patients decreased to the normal range under the treatment The basal metabolic rate of the patients in whom this happened fell significantly

In 4 patients with severe hyperthyroidism the amount of protein bound iodine in the serum either decreased temporarily or did not decrease at all under the treatment 3 patients with moderate hyperthyroidism in whom the amount of protein-bound iodine in the serum decreased to the normal range relapsed under the treatment (see accompanying table) The 24-hour uptake of ^{131}I by the thyroid glands of the patients who responded to treatment was considerably diminished, but that of the patients who did not improve remained unaltered by the treatment with P A S

3 patients developed pyrexia, during the treatment, this was intermittent and fluctuated between 98°F and 102°F As soon as the P A S was discontinued, the pyrexia disappeared The relation between the severity of the hyperthyroidism and toxicity is indicated in the table, which shows that P A S is apt to be toxic to patients with hyperthyroidism

P A S is an aromatic anti thyroid substance which inhibits the binding of tyrosine and elemental iodine[4] Its anti-thyroid activity may be compared with that of *p* aminobenzoic acid, with which Berman[5] and Goodwin et al[6] successfully treated hyperthyroidism Though the anti-thyroid activity of P A S in euthyroid people is weak according to our experience about half our patients with hyperthyroidism responded to P A S We cannot recommend P A S for all patients with hyperthyroidism, but it may be useful in the treatment of tuberculous patients with hyperthyroidism

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4 Fawcett, D M, Kirkwood S *J biol Chem* 1954, 204, 787
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New Inventions

JEJUNAL-BIOPSY TUBE

JEJUNAL biopsies can be obtained by a modification of the duodenal-biopsy tube described by Shiner[1] Fig 1 shows the component parts of the biopsy tube, and fig 2 a sample biopsy

The tube, which is flexible, measures 161 5 cm in length and 5 mm in diameter The headpiece is 2 5 cm long and has a diameter of 1 3 cm at its widest point The diameter of the biopsy hole is 3 5 mm The knife-cylinder is 9 mm long and is ridged at its distal end An air-hole is situated in one of its ridges extending down the side of the knife-cylinder, thus allowing air to reach the rubber balloon at the distal end of the headpiece. The tailpiece of the tube is essentially the same as that in the duodenal-biopsy tube except that it is longer and allows more play in the movement of the wire, which has to travel a greater length within the flexible tube

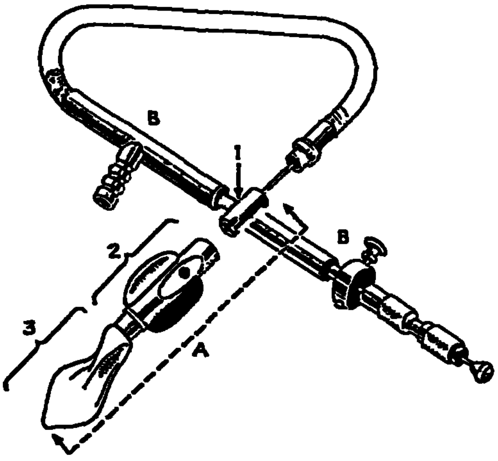

Fig 1—Jejunal-biopsy tube A headpiece (1) knife-cylinder, (2) biopsy head (3) balloon B, tailpiece with lateral exhaust.

The tube is introduced in the same way as the duodenal-biopsy tube and its course is guided fluoroscopically When the first part of the duodenum is reached the balloon is inflated and guides the headpiece along into the jejunum The balloon is an essential part of the jejunal-biopsy tube as it has been found impossible to make the headpiece travel through the third and fourth parts of the duodenum without it

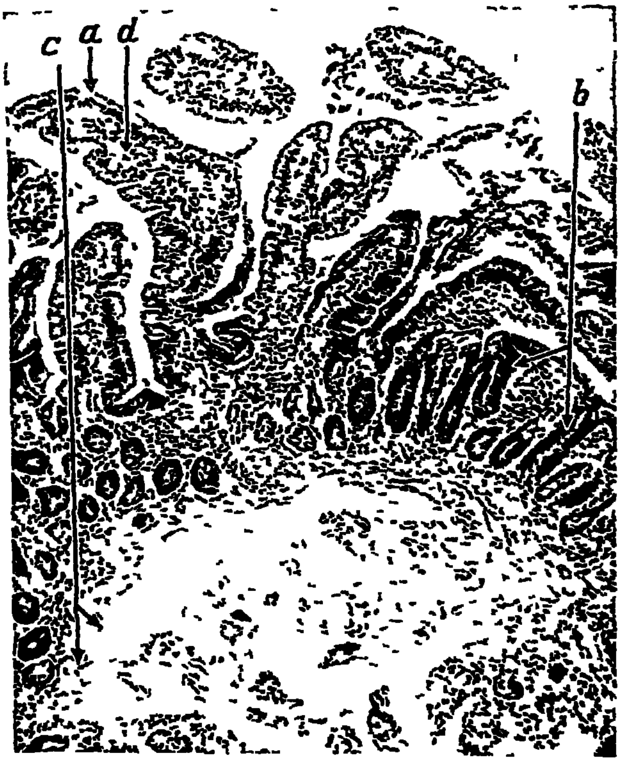

Fig 2—Jejunal biopsy (a) villi (b) crypts of Lieberkühn, (c) muscularis mucosæ (d) cellular infiltration (× 80)

Fig 2, from a specimen taken with the jejunal-biopsy tube, shows the full thickness of the jejunal mucosa with well-preserved villi, and the muscularis mucosæ

I should like to thank Mr G Hawkins, of the Genito-Urinary Manufacturing Company, for his invaluable help in the construction of the instrument

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M R C S, D C H

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Reviews of Books

Munk's Roll

Vol IV Lives of the Fellows of the Royal College of Physicians of London, 1826–1925 Compiled by G H BROWN, M A, B LITT London Royal College of Physicians 1955 Pp 637 *42s*

William Munk's *Roll of the Royal College of Physicians of London* was first published in 1861 Its two volumes contain biographical sketches of the 1351 fellows and licentiates admitted to the college from its foundation in 1518 to the end of the 18th century A third volume published in 1878 added 372 lives to the total, and carried the record forward to 1825, the year of the college's removal from Warwick Lane to its present site in Pall Mall East The fourth volume, which was largely inspired and launched by Sir Henry Bashford, extends the *Roll* (of fellows only) over a further century It contains short biographies of the 874 fellows who were elected between 1826 and 1925 and who died before Jan 1, 1954 They have been written to a certain standard of detail and a rough (not a rigid) uniformity of presentation, the aim being to ensure that the same detail, when available, is provided in each biography, rather than that they should follow the same exact pattern. No attempt has been made to include complete bibliographies of fellows' writings, but their more important works are named in the text, and there is usually some indication of the branches of medicine in which they were particularly interested

These biographies cover a century of unprecedented change in the practice and organisation of medicine in the British Isles, and in every development fellows of the college played a significant part Marshall Hall, William Gull, William Jenner, Samuel Wilks, Andrew Clark, John Hughlings Jackson, Clifford Allbutt, William Osler, Patrick Manson, Bertrand Dawson, David Bruce, Charles Sherrington, and Frederick Gowland Hopkins were among them Their influence and interests were not confined to medicine, and these biographies relate, too, something of their many activities in other spheres of life The aim has been to convey in small bulk a picture of the man

The four volumes of *Munk's Roll* are a most useful source of information not only about the college in the four centuries of its existence but about the practice of British medicine generally during the same period

An Atlas of Regional Dermatology

G H PERCIVAL, M D, PH D, F R C P E, professor of dermatology, University of Edinburgh, T C DODDS, F I M L T, F I B P Edinburgh E & S Livingstone 1955 Pp 264 *£5*

To produce a book containing 475 colour photographs at a net cost of about 2½*d* per picture is in itself something of an achievement On the whole the colours are adequate and comparable The choice of material is largely representative of the commoner diseases the authors set out to illustrate, but "lupus erythematosus profunda" is a strange choice for two pictures in an elementary text Two other illustrations appear to be colour prints of photographic transparencies of drawings of moulages of patients and it is not surprising that the final effect is unlifelike

The size of the pictures does not permit the demonstration of the finer details of morphology upon which dermatological diagnosis must at times depend, but this book should help those students and practitioners who discover too late that the place to learn dermatology is in the outpatient department of a busy hospital

Die Tests in der klinischen Psychologie

Zweites Halband Editor *Prof Dr* ERICH STERN Zurich Rascher 1955 Pp 450 Sw fr 31 50

IN this volume a number of tests are described which have been used in France, Germany, and Switzerland but are little known in the English-speaking countries

Thus the colour test devised by Max Luscher, of Basle, the pyramid test which Robert Heiss developed on the basis of a method used by Max Pfister, the Wartegg test (here expounded, not very plainly, by its author), and the Sceno test developed by Gerdhild von Staabs are reported in sufficient detail to enable the reader to judge whether he wants to inquire more closely into their theory and clinical or experimental use In most instances he may well conclude that ingenious and potentially useful though they are, the humdrum processes of standardisation and validation should have been applied to them before they were put out as clinically valuable The chapters dealing with familiar tests, such as the Rorschach, do not bespeak an effort at critical appraisal, but rather the attachment which people have to loyal servants and long used tools

Neuroglia

Morphology and Function PAUL GLEES, D PHIL, M D, demonstrator and lecturer in physiology, University of Oxford Oxford *Blackwell Scientific Publications* 1955 Pp 111 *25s*

MUCH of the classical work on the morphology of the glia has been written in German and Spanish This review is therefore useful in that the widely scattered literature has been brought together in concise form The subject is treated historically the anatomy and physiology of the astrocyte, the oligodendrocyte, and the cerebral histiocyte are discussed in turn, and Dr Glees gives his own views which are founded on his morphological studies, largely with silver techniques He justly pays tribute to the important work, so often overlooked, of Ford Robertson in this country At the end of the book there is a short account of the contributions made by the few workers who have so far made use of tissue culture, and the hope is expressed that before long more precise knowledge of the metabolic function of these cells will materialise with the aid of this essential technique

As the concept of glial structure and function is by no means easy, the subject calls for rather more emphasis on the living rather than the fixed cell, but in the present imperfect state of physiological knowledge this is no easy task for an author

Ionography

Electrophoresis in Stabilised Media HUGH J MCDONALD, D SC, professor of biochemistry, Stritch School of Medicine of Loyola University, Chicago Chicago Year Book Publishers *London Interscience Publishers* 1955 Pp 268 *48s*

ELECTROPHORESIS, and particularly paper-strip electrophoresis, is being used increasingly in clinical chemistry, although there are some who believe that it is a technique better kept for the research laboratory This useful book is a comprehensive survey of the vast literature devoted to the technique of electrophoresis on paper and in starch columns and other stabilised media

There is an historical introduction, and a chapter on types of apparatus with an admirably objective viewpoint Methods of scanning are described and criticised, and there is a long section on the determination of electrophoretic mobilities using paper strips The last five chapters deal excellently with the application of electrophoresis in medicine, biochemistry, and chemistry

Arctic Doctor

Dr JOSEPH P MOODY, with W DE GROOT VAN EMBDEN London Odhams Press 1955 Pp 256 *15s*

THE subtitle—an account of strange adventures among the Eskimoes—hardly does full justice to the merits of this book, for Dr Moody has managed to tell in relatively few pages a thrilling tale of his life and work in the Canadian East Arctic The adversities of the climate and the handicaps of single-handed work in this outpost, with a population scattered over 600,000 square miles, necessitated travelling by dog-sledge, canoe, and small aircraft, and sleeping in igloos It entailed the risks of treatment by radio telephone when travelling was impossible, and the control of an epidemic of poliomyelitis To face this task, Dr Moody was well equipped with a mind receptive to the beauty of wild life and Nature (there is a fine description of the aurora borealis), and he was fortified by a strong sense of humour which helped him in his approach to the Eskimoes and the study of their lore, and eventually rewarded him with their confidence

THE LANCET
LONDON SATURDAY, JAN 14, 1956

Food-poisoning

When illness is caused by staphylococcal enterotoxin, symptoms appear so rapidly that the sufferer may make a reasonable guess at their origin and the investigator may be able to save some of the suspected food for examination Salmonella infections, on the other hand, have an incubation period of up to forty-eight hours, and by this time memories are dim and the dustman has called Nevertheless, medical officers of health and bacteriologists must admit that 39% is too large a proportion of all "incidents" to be written off as "cause unknown" this is the figure given in the report[1] of the Public Health Laboratory Service on food-poisoning in England and Wales in 1954—a report which, like its forerunners, is a clear and objective study that makes the best use of information much of which is for many reasons incomplete Clostridial food-poisoning won its first mention in the report for 1951–52, and it may be that imagination and careful bacteriology will reveal other bacterial causes in due time As in many other diseases of doubtful origin, an unrecognised virus has been suggested as a cause of some outbreaks of food-poisoning In the absence of much evidence it would be wise to take a firm grip of Occam's razor Perhaps the chemical examination of food is pursued upon a too-stereotyped plan there are other irritants than the heavy metals, and few doctors or chemists know all the secrets of food-processing But probably the lack of any animals (other than the long-suffering laboratory staff) which may be used to detect bacterial terotoxins is the greatest handicap to increasing knowledge of the origin of food-poisoning

As in previous years, salmonellæ were responsible for more than half the incidents whose cause was known in 1954 Staphylococci and clostridia made up no more than 2% and 1% respectively of the total But these figures are misleading in that a large number of incidents due to salmonellæ were isolated infections while the other genera were associated with outbreaks involving many people The origin of these single infections with salmonellæ remains a mystery The infectious dose of most strains for man is large[2], the organisms may not be evenly distributed through infected food, and symptomless "infections" are not uncommon among the other members of the family of one with overt disease Perhaps the natural history of salmonella infection is not so straightforward as we used to think it may be that sometimes "food-poisoning" is a misnomer Among the vehicles of infection, "made-up" meat maintained its evil reputation, being responsible for 170 out of 250 outbreaks of known cause Re-heated meat is the source *par excellence* of enterotoxic food-poisoning, but sausages, brawn, and meat pies have all had their victims Six outbreaks (of which five were staphylococcal) were traced to tinned meat It took eputable canners a long time to live down their clumsy eginnings in the trade and it is regrettable that food which should in theory be sterile should once again be open to suspicion

The provisions of the new Food Hygiene Regulations[3] are beneficial, and in spite of some objections by representatives of the trade, they do not make any outrageous demands upon caterers Nevertheless the Food and Drugs Amendment Act, 1954, as a whole is a pointed example of the difficulty of regulating the trivialities of daily life by the written word It creates new offences but offers little hope of greater rewards here or hereafter No one can imagine that to punish the malefactor who smokes a cigarette while he wraps a pound of cod in newspaper will make much difference to the figures in future annual reports on the incidence of food-poisoning This Act will do some good but is unlikely to alter those figures very much Vaccination succeeded because smallpox was a horrid disease of which every one had some experience The same to a lesser extent (and helped by brilliant publicity) was true of the campaign against diphtheria If food-poisoning were disfiguring or produced lasting disablement it would not be difficult to whip up some strong feeling on the subject among the public at large As it is, food-poisoning is of little account to most of us because it is far more dangerous to cross Oxford Street on foot than to sup off a hotted-up dish of delicious stew No-one seems to have persuaded the man in the street that he eats his black pudding or saveloy at his peril, and, in truth, he who tries will not have an easy job Legislation which runs too far ahead of public opinion seldom has its designed effect

Medical officers of health have devoted much energy to local campaigns to improve the cleanliness of food and the way in which it is sold and served Some catering firms have seconded these efforts with commendable zeal If the results have been disappointing they have at least served as a warning of this Act and its consequences Before he begins another campaign to the same purpose, the medical officer of health might give some thought to adding to our knowledge of the essential causes of food-poisoning Few have experience wide enough to make that alone the basis for policy and action, and it is only by pooling knowledge (as the Public Health Laboratory Service reports do) that our understanding will increase No outbreak of food-poisoning is too small to deserve full inquiry Not long ago Sir **William Savage**[4] once again advised his colleagues of the advantages of investigating public health problems in person and on the spot It may be convenient to employ sanitary inspectors and health visitors as investigators, but no-one except the medical officer of health has the training and knowledge needed to make the best use of the evidence at hand

The Reluctant Patient

The problem of patients who leave hospital in defiance of medical advice has never received so much attention in this country as it has elsewhere, especially in France and America In France the question has recently been given added emphasis by new legal measures put forward for the treatment of alcoholism, of which the increase is causing much concern, and in the United States, by all accounts, the irregular

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Ion Bull Minist Hlth Lab Serv 1955 14 203

McCullough, N B Eisele, C W *J infect Dis* 1951, 88, 278, *Ibid*, 1951 89 259

[3] The Food Hygiene Regulations 1955 S I 1955 no 1906 H M Stationery Office see *Lancet* 1955 ii 1388

[4] Savage, W *Publ Hlth, Lond*. 1955 68, 71

discharge of tuberculous patients is widespread These difficulties in the *treatment of tuberculosis* are much rarer in this country, but it would be unwise to dismiss as insignificant the irregular departure of patients from our sanatoria, because these people are often *infectious* and *may* be psychotic, and they usually come from and return to the poorer strata of society SNELL[1] found that during the period 1938–51 the over-all irregular-discharge rate for an English sanatorium was 16%, but it had fallen to 5% by 1954 The late Dr LORENZ and his team[2] at the Veterans Administration Hospital at Madison, Wisconsin, have made an extensive and systematic inquiry into irregular discharges and they have classified the patients involved into three groups leaving against medical advice (A M A), absent without official leave (A W O L), and disciplinary discharge (D D)

What leads these patients to take a drastic step which many of them know may lead to permanent ill health and even early death, quite apart from endangering their family? CALDEN[3] devised the Madison sentence completion form, containing 80 items which could be grouped for analysis, to give the patient's reaction to the diagnosis, rest in bed, hospital routine, his family and friends, and many other facets of his life before and during his stay in hospital Using these records, LORENZ et al were able to compare the background and character of 100 irregularly discharged patients with a similar number who stayed and were discharged only when they had received maximum benefit from treatment Of the irregular discharges, 81 were A M A, 10 were A W O L, and 9 were D D Factors which were not statistically significant between the two groups were age, race, marital status, distance of hospital from home, and activity of the disease, but occupation was of importance, and of the 100 who left irregularly 12 had no known occupation and 38 were semi-skilled Fewer irregularly discharged patients had had surgical operations, but this might well be because they had more extensive disease which in itself might have precluded surgical treatment at the time of their discharge, although perhaps not ultimately The average period in hospital for these patients was 148 days, compared with 260 for those discharged normally 40% of irregular discharges took place within the first 3 months, and only 8% after 300 days BEACHAM,[4] studying the records from Baltimore City Hospitals where the irregular-discharge rate among tuberculous patients fell from 51% in 1946 to 20% in 1951, concluded that the rate would fall even further if particular attention was paid to the patients' difficulties before their admission to hospital Women were often worried about the welfare of their children, and men about money matters If these worries could be eased before or soon after admission, the fretful patient would accept his lot much more readily And TEDESCO[5] declared that the physician first making the diagnosis of tuberculosis had a big responsibility, especially in indicating how long treatment might take In this country patients are often more fortunately placed the benefits of National Insurance include special financial provision for the tuberculous, and as the majority of patients are sent to sanatoria through chest clinics or hospitals they have an opportunity to discuss their disabilities and worries with the almoners and, through them, with representatives of the National Assistance Board Health-visitors can also play an important part in calming the family disturbance, especially by taking an interest in the welfare of the children TOLLEN,[6] in considering that the chief reasons why the American patient leaves against advice, wrote of pressure from outside the hospital (usually personal, social, and economic) and influences acting within the hospital, such as the patient's failure to adapt himself to the new life and his dislike of the environment TOLLEN also referred to the ill effects sometimes produced by the attitude of the hospital staff, from porters to physicians, by too strict regulations, and often by the treatment itself SANDS et al[7] came to similar conclusions, and they suggested that isolation, if necessary enforcible by law, was the solution to irregular discharge NORTHROP et al[8] have tried such a scheme for some years They had a reasonably attractive sanatorium with sufficient beds, in not too isolated a spot and staffed by a competent and sympathetic staff, with all the ancillary services of occupational therapy, recreation, vocational guidance, and a medical social service But the irregular-discharge rate was 44% in 1950, and some way of improving matters was sought For difficult patients who were judged unlikely to stay, 27 beds were reserved in a locked ward After two weeks' detention, the patients were allowed in the regular ward, but at the least sign of insubordination they went back to the locked ward It is not surprising to learn that the fire services had to be called in to advise on the safety of the hospital after two attempts had been made to burn down the ward A less severe method, more likely to find favour in this country, was devised by LORENZ et al[9] They noted that many patients left hurriedly in a tantrum, so they devised a slowing-down technique, again involving a special ward with a special doctor The patient who had rashly decided to go was put here while his clothes and money were brought and final investigations were completed, all the people in hospital who might have had a favourable impression on him called to discuss his problems and to say goodbye In the first six months after this ward was open, 24 patients were admitted to it at least once and 16 were dissuaded from leaving as a result the irregular-discharge rate of the hospital fell from 36% to 15% LORENZ *et al* conclude that the ward had this rather unexpected effect because patients did not like to have to explain why they wanted to leave hospital

What happens to the patients who cannot be dissuaded from leaving? BREWSTER and FLETCHER[10] concluded from follow-up surveys that the mortality rate among irregularly discharged patients is two or three times greater than in more amenable patients ALLISON[11] made the interesting point that as many as 47% of those *irregularly* discharged received further hospital treatment, but only 13 7% of those who left normally had to be admitted again

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[10] Brewster, A W, Fletcher, R C *Publ Hlth Rep*, *Wash* 1949 64 687
[11] Allison, S T *Amer Rev Tuberc* 1955 72, 552

As we have said, these matters are of much less concern to chest physicians in this country than in the United States SNELL believes one reason is that here, where hospital beds are at a premium, patients do not willingly give them up , and they often stay longer than American patients, so that new patients can see the ultimate rather than the less impressive intermediate results of chemotherapy and surgery Moreover, it may be that in this country we are prepared to place ourselves more confidently in the hands of the doctors on the assumption that they know best Recent correspondence in our columns indicates that there are in fact a number of patients with active disease, usually among the poorer classes, who discharge themselves , like their American counterparts they may stay in a sanatorium longer if they are readmitted, but they may never be readmitted or not until they have infected a lot of people A recent case [12] serves as a reminder that for those who refuse to go to hospital, the law can be invoked and there are many people who say that it is not invoked often enough We have lately argued [13] that bold moves are now needed if the incomplete victory over tuberculosis is to be turned into a rout , and many chest physicians feel that one way of hastening the defeat of the disease would be to use sterner measures for controlling the intractable patient Among gentler means, the exchange of information about patients (chiefly financial and social) between sanatoria and chest clinics might be increased—for example, by weekly staff conferences at which potential irregular-discharge patients could be discussed Some sanatoria have earned bad reputations among patients, and an analysis of their irregular discharges might be illuminating and chastening The number of tuberculous patients who could thus be restrained from infecting their fellows would not be great , but now that the cooperative patient can almost always be made non-infectious quite quickly, the stubborn few have a new importance

Origin of Antibodies

THERE has been much speculation about the site of origin of antibodies and the mechanism of their formation , and the debate continues, though the field of the controversy is much narrower than it was, and it may even be possible to draw one or two conclusions without setting off the argument afresh No single organ in the body can be identified as the sole producer of antibodies On the other hand, antibodies are not produced at the local site of infection by the antigen, but they *are* formed in the lymph-glands draining the area The type of cell responsible for antibody synthesis is not known At one time lymphocytes were commonly believed to produce antibody, but emphasis has now shifted to the plasma-cell or its precursors Cytology, however, may have to advance a great deal further before we can be certain about the identification of many cellular elements and their life-histories Recently [14] the presence of antibodies in cells has been detected and localised by treating frozen tissue sections with the specific antigens, followed by antibodies which have been labelled by coupling with fluorescent dyes The distribution of antibodies after injection of antigen supports the view that the main site of antibody formation is the plasma-cells or their precursors , in comparison, the contribution of the lymphocytes is small For example, after intravenous injection of antigen into hyperimmune rabbits, little antibody was detected in lymphocytes, but much was found in colonies of plasma-cells present in the red pulp of the spleen, the medullary area of lymph-glands, the submucosa of the ileum, and the portal connective tissue of the liver For technical reasons the bone-marrow could not be studied After injection of antigen into the foot pads of rabbits, antibody was found in the popliteal lymph-glands Antibody was first seen in large immature cells in medullary areas of the glands As the cells differentiated and multiplied, colonies of typical plasma-cells developed and large amounts of antibody were detected in their cytoplasm Few antibody-containing cells were found after primary immunisation but many after a secondary stimulus when, of course, considerable quantities of antibody can be detected in the blood Primary immunisation may result in deposition of antigen in primitive cell types and the secondary antigenic stimulus produces the immediate synthesis of antibody and the development of mature plasma-cells containing the antibody It is suggested that the cell types responsible for antibody synthesis do not exist in the absence of antigenic stimulus The alternative view is that antibodies are formed in cells usually producing normal serum-globulin but the presence of an antigenically active molecular fragment has the effect of a "template" or mould According to this hypothesis, the globulin synthesised is similar to normal serum-proteins, but it is structurally related to the antigen and complementary to it It is now suggested that antibodies have no inactive normal prototypes The same technique has been applied to investigate the enhancement of antibody production by the addition of adjuvants, such as aluminium phosphate, to the antigen Antibody is formed first in the regional lymph-gland and later in the granulation tissue surrounding the nodule which develops at the site of inoculation The adjuvant effects are ascribed partly to delayed absorption of the antigen and prolongation of the antigenic stimulus in the lymph-gland and partly to the production of the local granuloma in which antibody-producing plasma-cells also develop The adjuvant effect of the wax obtained from tubercle bacilli is attributed to a widespread proliferation of plasma-cells in the lymph-glands, spleen, and liver and not to local stimulation of macrophage proliferation

Further light may be thrown on the mechanism of antibody synthesis by the transfer experiments that have been performed with splenic and lymphatic tissue

> Spleens were removed from rabbits which had had an injection of typhoid vaccine four days previously [15] The spleens, minced and suspended in a culture medium, were found to produce agglutinins for several days Antibody production was inhibited by respiratory and tissue poisons and also by cortisone The effect of cortisone may be to inhibit the proliferation of lymphocytes, plasma-cells, or other elements concerned in antibody

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[12] See *Lancet* 1955 ii 819

[13] *Ibid* pp 857 1125

[14] Coons A H Leduc E H Connolly J M *J exp Med* 1955 102 49 Leduc E H, Coons A H , Connolly, J M *Ibid* p 61 White, R G , Coons, A H Connolly, J M *Ibid* pp 73 83

[15] Mountain, I M *J Immunol* 1955, 74, 270 278

synthesis. Antibody-forming activity can be transferred from an injected rabbit into one that has not been immunised by transplanting cells teased from the lymph-glands draining the injected area.

It is now found[16] that if lymph-glands from normal unimmunised rabbits were treated with serum which had been in contact with *Shigella dysenteriae* and if suspensions of these glands were injected into irradiated rabbits, antibodies could be detected three or four days later. The transferred glands had not been exposed to antigenic stimulus in the donor animals but only in vitro, and the antigenic stimulus had not been in the form of bacillary cells but only soluble antigens passing into the serum with which the bacteria had been in contact. Furthermore the recipient animals had been irradiated to destroy their own powers of antibody formation. There is thus good evidence that the cells from the transferred lymph-glands were themselves the antibody-forming elements.

It is interesting to note that cells from mesenteric lymph-glands were effective in these experiments, whilst thymus-gland cells were not. On the other hand, intra-ocular transplants of thymus and Peyer's patch tissue conveyed antibody-forming activity.[17] The donor mice were immunised with tetanus toxoid, and fragments of tissue were transplanted into the anterior chambers of the eyes of mice which had been subjected to whole-body γ-radiation from cobalt-60. Significant but small amounts of tetanus antitoxin appeared in the blood of the recipient mice. When these mice received an intravenous injection of tetanus toxoid there was a specific anamnestic response and the serum-antitoxin rose considerably, although the irradiation had impaired the antigenic response of the recipients' own tissues. The transplants were effective in producing antitoxin in the donor mice only when the donors had been immunised by subcutaneous or intra-abdominal routes and not after intravenous immunisation.

Although the evidence is not conclusive, apparent in-vitro production of diphtheria and tetanus antitoxins has been reported[18] in fragments of lymph-glands and spleen excised from rabbits immunised with diphtheria and tetanus toxoids. The results of the in-vitro experiments seemed to run parallel with passive transfer experiments in which transplantation of lymphatic or splenic cells was followed by antitoxin production in the recipients. Again, passive transfer of cutaneous sensitivity to foreign serum-proteins has been produced by injecting washed leucocytes from the peritoneal exudates of rabbits exhibiting the Arthus phenomenon.[19]

More evidence about the rôle of leucocytes in the body's response to antigenic stimulus comes from work[20] on the fate of intravenous tuberculin in rabbits. Tuberculin protein which had been labelled by radioactive iodine was firmly adsorbed by leucocytes in the blood during the first few hours after injection. Although tuberculin was present in the plasma for some twenty-four hours after injection, no leucocytes containing tuberculin could be detected after the first four hours. Peripheral leucocytes may, therefore be responsible for transporting foreign proteins such as bacillary proteins or toxins to parts of the body remote from the site of their introduction. This would result in the accumulation of such substances in lymph-glands, spleen, and inflammatory foci where leucocytes congregate.

It is impossible to assess the full significance of all the complex results that are accumulating, but some points are clear. There are certainly good reasons for concluding that antibodies are produced in certain cells in lymph-glands, spleen, and elsewhere, and that these cells can continue to produce antibodies when removed from their original host and transplanted into another animal, or even when kept in culture outside the body. We still lack, however, a precise picture of the antibody-producing cells; we understand poorly the relation of antibody synthesis to the production of normal serum proteins; and we do not know how antibodies are produced which are specifically complementary to the antigens administered. The "template" hypothesis, which suggests that antibody is synthesised at the surface of the antigen molecule and thus has a configuration complementary to it, has been subjected to some criticism. This hypothesis requires that antibody be formed only as long as antigen persists in the antibody-forming tissues and cells. There has been no confirmation of in-vitro formation of antibody by the chemical treatment of a mixture of normal serum globulins and antigen. The alternative theory is that antibody synthesis is analogous to adaptive enzyme production. It is suggested that when once adapted to deal with a new type of antigen, cellular enzymes continue to produce antibodies by self-replication of their own structures until re-stimulated by a fresh dose of antigen. Experiments to decide between the two hypotheses of antibody formation have been carried out[21] with the T-agglutinin, an antibody present in normal serum which reacts with specially treated red cells. Treatment of mammalian red cells with cholera-vibrio filtrates removes a surface antigen, thus unmasking the T antigen. Animals immunised with treated red cells develop a high-titre T-agglutinin in the serum. The gradual modification of the T-agglutinin in immunised rabbits resembles the production of adaptive enzymes rather than a process dependent upon antigen "templates," and provides some evidence in favour of the adaptive enzyme hypothesis of antibody formation.

Annotations

POLIOMYELITIS ANTIBODIES IN CHILDREN

Before poliomyelitis vaccine becomes widely available in this country we must decide what is the best age for vaccinating children. And to do this we must know the commonest age at which children are infected in this country, so that they can be vaccinated before they are exposed to the greatest risks. But there is very little published information on the distribution of poliomyelitis antibodies in the sera of British children, and the paper by Dr. Fallon on p. 65 of this issue is therefore particularly welcome.

Dr. Fallon looked for antibody to all three types of virus in sera from 78 children living in Betws-y-Coed, in North Wales; this village was chosen because no case of poliomyelitis has been notified there since 1912, when the disease became notifiable. For comparison, he examined 71 similar sera from Liverpool where poliomyelitis appears each year. The sera were taken from infants and from children up to 14 years old, and the results of serological tests for poliomyelitis antibodies were recorded for different age-groups. The findings indicate clearly that in both Liverpool and Betws-y-Coed infection by poliomyelitis viruses in childhood is extremely common. In Betws-y-Coed, antibodies to type I viruses were found in the youngest children, and in the age-group 0–4 years 8 out of 22 children had antibody to more than one type of virus. The findings also suggest that infection by all three types of virus is quite widespread among Liverpool children, although there is a

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16 Harris T. N., Harris S., Farber M. B. *Ibid* 1955, 75 112.
17 Stoner R. D., Hale W. M. *Ibid* p. 203.
18 Stavitsky A. B. *Ibid*, p. 214.
19 Tremaine M. M., Jeter W. S. *Ibid* 1955, 74, 96.
20 Ritts R. E., Favour, C. B. *Ibid*, 1955, 75, 209.
21 Fraser K. B. *J. Path. Bact.* 1955, 70, 13.

possibility that infection took place later than in the Betws y Coed children Considerable variation in the age of infection can be expected in different parts of the country At a recent meeting of the Society for General Microbiology, Dr A P Goffe reported part of a similar investigation by workers at the Central Public Health Laboratory, Colindale They found that 70% of children under 5 years living in Southend had no poliomyelitis antibodies, whereas 80% of children from Belfast of the same age had antibody to all three types of virus Details of these and of similar investigations from different parts of the country are awaited with interest

Clinical infection in this country is, in general, less widespread than in the United States, but much more serious than it is, for example, in Egypt A comparison of serological findings in this country with those from certain areas in the United States and Egypt suggests that the extent of early infection in this country may also be intermediate between these two areas, but that there may be considerable variations between different parts of this country If we accept the recommendations of the recent World Health Organisation study-group on poliomyelitis vaccines, different areas of Britain may have to be treated differently in the matter of poliomyelitis vaccination for example, it would be hard to justify at the moment widespread vaccination in an area like Betws y Coed where subclinical infections seem to be immunising the population satisfactorily In other areas, the possibility of vaccinating children under 6 years will be raised, but the present evidence of the protection afforded by Salk vaccine extends only to children aged 6–10[1] Research on the protective effect of vaccine in younger children is an important future step

DISABILITIES OF OLD AGE

In many parts of the country the initial efforts of the newly formed geriatric units have been directed towards eliminating or reducing unnecessarily long waiting lists, to shortening the period of illness, to providing adequate treatment for the disabilities of old age, and to placing reabled elderly in suitable acommodation outside hospital Little has yet been done in the preventive medicine of old age, and major preventive advances are unlikely until more is known of the physiology of old age and of the natural history of the common disorders of the elderly Since ageing is a physiological process, it is essential for the clinician to distinguish between slight abnormalities of function due to physiological variation and the early manifestations of disease which will respond to early treatment

There have been few large scale clinical surveys of old people in localised communities, but Maddison et al[2] have recently published the results of a survey of 238 volunteers out of 550 people aged 60 or over who live in two Durham villages A thorough outpatient medical examination, including X-ray examination and laboratory tests, provided a mass of clinical data which was subjected to a factor analysis The determinables were sex, age, hæmoglobin, systolic blood-pressure, diastolic blood-pressure, and diseases found Since any old person may have four or even more diseases at any one time, this determinable can be subdivided into limitless attributes Maddison et al reduced the attributes to 42 by pooling some items with small frequencies, but they wisely point out that this arbitrary choice of attributes may mean that some of great importance are overlooked The factor analysis gave four groups which are thought to be closely related to blood-pressure Thus a systolic blood-pressure of 130 to 159 is associated with health and normal hæmoglobin, but a systolic pressure of 160 to 199 tends to be associated with low hæmoglobin and respiratory, heart and arterial diseases A diastolic pressure of 100 to 109 indicates a tendency to multiple disabilities and obesity whereas a diastolic pressure of 120 to 139 is said to reveal a tendency to malignant hypertension Few will be willing to accept a concept of malignant hypertension wholly based on sphygmomanometer readings made after a journey to an outpatient clinic, and many will doubt whether blood-pressure readings are sufficiently reliable to be used as determinables, except when repeated under basal conditions But the hazard of obesity and the part played by anæmia and malnutrition in predisposing to infection gain statistical significance from Maddison et al 's useful paper

ELECTRON-MICROSCOPY OF THE KIDNEY

The kidney was one of the first organs to be studied with the electron microscope, but reliable observation of its ultramicroscopic structure has been possible only recently, with the use of appropriate methods of fixation and thin section cutting The outstanding contributions have come from anatomists in the University of California and the Karolinska Institute in Stockholm

Pease[1 2] describes the fine structure of the three tissue layers separating the blood in the glomerular capillaries from the " urinary " space—namely, the endothelium, the capillary basement membrane, and the epithelium of Bowman's capsule As he shows clearly in beautiful electron-micrographs, the endothelium is not a continuous layer but has interruptions or pores 0 1 µ in diameter at a separation distance of 0 05 µ, thus forming a fenestrated membrane The capsular epithelium, which with the light microscope appears to be closely applied to the capillary wall, is also incomplete and like the endothelium does not form a continuous physical barrier These epithelial cells lie free in the urinary space They have thick cytoplasmic processes which give off finer branches interdigitating with those from neighbouring cells, and they are finally attached at regular intervals to the capillary basement membrane (on the other side from the endothelial cells) Bowman's capsule is therefore in the form of a cytoplasmic " lattice " with thick and thin cross bars and small channels 0 04 µ in width between the attachments of the thin processes to the capillary wall The basement membrane is a homogeneous layer 0 1 µ wide with a central layer and outer and inner cement layers related to endothelium and epithelium respectively Even with the highest resolution this layer remains a continuous structure with no evidence of a porous system, and thus it forms the sole physical barrier between the circulating blood and the urinary filtrate in the malpighian corpuscle The statement that the membrane is a " non-vital " barrier could however be challenged, because the term " vital " does not necessarily imply " cellular " There is a similar interrupted endothelial lining to the peritubular capillaries, with pores 0 05 µ in diameter—i e , about half the size of those in the glomerular capillary And a similar basement membrane separates the porous endothelium from the basal end of the epithelial cells lining the tubules

Rhodin[3] first described and illustrated the complicated system of double membranes which divides the basal part of the tubule cells into a number of cytoplasmic compartments open towards the apical end of the cell and containing characteristically large mitochondria correspondingly orientated Pease[4] interprets these double membranes as infoldings of the cell plasma membrane, and in his sections they are most noticeable in the

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[1] See *Lancet*, 1955 ii 1279

[2] Maddison, J , Smith, R O F , Olbrich, O *Brit J prev soc Med* 1955 9 113

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[1] Pease D *J Histol* 1955, 3 295

[2] Pease D *Anat Rec* 1955, 121, 701

[3] Rhodin, J Correlation of ultrastructure and function in norma and experimentally changed proximal convoluted cells of the mouse kidney 1955 Department of Anatomy, Karolinska Institute, Stockholm (privately printed)

[4] Pease, D *Anat Rec* 1955, 121 723

distal tubules and the thin segments where they may penetrate right through the cell cytoplasm, *forming* slots sealed off from the lumen of the tubules by cement bars It *is suggested that ionic interchange* between blood and urine occurs through these "slots" This complicated system of folds will increase the basal surface area of the cells *enormously and may be related to* the resorption of water At the apical end of the tubular cells the "brush" borders are finger-like extensions of cell cytoplasm—*short and stubby in the distal tubules* Here and there between the brush processes tiny canals penetrate into the cell substance often *opening into* vacuoles According to this analysis *of the fine structures* of the kidney, the "renal barrier" is in effect a system of pores, canals, and "slots"—a labile ultrafilter whose *varying pattern* will control the molecular interchange between blood and urine

Rhodin has attempted to follow by electron microscopy the cytological changes which accompany the resorption of albumin *He observed that* in the basal *cells of the proximal tubules there* was a fusion of mitochondria with loss of their internal structure as they combined with resorbed protein *to form very large* granules *These large granules eventually re-formed* into typical mitochondria These observations suggest that the *future story* of the pathology of the kidney will be an account of intracellular *changes*—and in *particular* how such changes affect the pattern of the tissue "filter" between blood and urine

HALLUX VALGUS

Harris and Beath[1] found *hallux* valgus in 2 2% of a group of young men, and there can be little doubt that the prevalence increases with age It is certainly more common in the lower social classes,[2] and *also in women* Many observers have noted its close association with an increase in the angle between the first and second metatarsals Truslow[3] suggested *that the primary defect* was one of adduction of the first metatarsal, but Hardy and Clapham[4] have shown that displacement of the metatarsal probably follows displacement of the digit

Studies of the feet of young children have thrown little light on the cause of hallux valgus There is a gradual deviation of the hallux to the outer side as age advances Craigmile[5] found the deviation to be greater in girls than boys at school leaving *age, but* Hardy and Clapham[4] found no such sex difference In normal adults there is apparently no sex difference in the position of the great *toe on radiographic measurement,*[6] but there is clearly a great preponderance of women amongst those who seek treatment for hallux valgus It is hard to reconcile such differing observations

It is commonly held that unshod races are not victims of hallux valgus Engle and Morton,[7] in a study of foot disorders in the natives of the Belgian Congo, do not mention it Wells,[8] however, noted a lateral displacement of *the hallux in the* South African Bantu, and other isolated examples have also been reported These unusual cases may be the result of various forms of arthritis[9] Barnicott and Hardy[10] have now examined the position of the *great* toe in West Africans In these people the hallux normally appears in footprints in line with the medial border of the foot, giving a mean hallux angle of zero In the footprints of the European male and female there is a *deviation to the outer* side of 6 9° and 11° respectively Some Africans, however, show a d*of more than 20° to the outer side* In general, the tion of the great toe of the African increases w and such a change *cannot be associated* with foot

Footwear undoubtedly plays a big part in pr symptoms, and may well increase the defo The importance of good shoes in controlling the of the great toe in children was well shown in the contributory shoe scheme,[5] in which adequate *and frequent shoe changes* were *followed by* a d in the deviation of the toe But, as we have som *said before,*[12] it will need some spectacular ch *fashion to* make people wear shoes that are g their feet, and naturally manufacturers are r to make shoes that are hard to sell

DRUNK IN CHARGE

WHENEVER a person charged with driving or " charge of" a motor vehicle while under the influ drink elects (as is his right) to be tried by jury, he nowadays a fairly good chance of acquittal have, on the whole, been reluctant *to bring in a* of guilty on *this* charge, largely because the o juryman is often not altogether satisfied by the p tion's evidence about the degree to which the was under the influence The alcohol content *blood is rightly recognised as only one point in estab* fitness or otherwise to be in charge *of a car* *tunately all the* other methods adopted by the (and by doctors summoned by the police) are unsystematic, and they may be unsystema applied, especially in parts of the country wh regular police surgeon's services are immediately able Greater uniformity at the first exami *(especially at the medical examination) of the accu* the police station, and greater uniformity in the test based on it, would do much to remove the impr of vagueness which the *jury properly interprets* in of the accused, even when there is no doubt doctor's mind that the driver was in a dan condition

It is therefore interesting to know that efforts for some years been *made by the medical profess* a number of Continental countries, particular Scandinavia, Western Germany, and Switzerlan *settle* in *outline certain guiding* points which invariably be considered by the doctor during examinations The Swiss journal, *Touring*, has pub the text of an unofficial questionary or aide me drawn up by doctors in cooperation with the polic the judiciary, which *has for some months been reg* handed to every doctor in the canton of Geneva as as he is asked to examine drivers suspected of drunk This aide *memoire* (which is filled in on the contains 12 main sections with a number of subs questions For instance, *the* examiner records d about the general aspect of the driver and any di ances of balance or coordination Writing and re tests are performed *After the first contact* has made, the patient is asked about his daily consum of alcohol and his health *Any additional* examin necessary are performed, and if there has been an acc any signs of cerebral damage are recorded If a sa of blood is taken, the exact *time is written down,* a note is made of any alcohol consumed between intervention of the police and the examination Fu *instead of first pronouncing* on the degree of drunken the doctor is advised to answer yes or no to the ques is this person under the influence of alcohol? "I does he appear to be slightly or seriously influen If he is under the influence of alcohol, have you no any fluctuation in his *ability to concentrate?* I you the impression that the patient is accustomed to alcohol or not ? "

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[1] Harris R I, Beath, T Army Foot Survey Ottawa 1947

[2] Hewitt, D, Stewart A M Webb J W *Brit med J* 1953, *ii*, 745

[3] Truslow, W *J Bone Jt Surg* 1925 7 98

[4] Hardy, R H, Clapham, J C R *Lancet* 1952 i 1180

[5] Craigmile, D A *Brit med J* 1953 *ii* 749

[6] Hardy R H, Clapham, J C R *J Bone Jt Surg* 1951, 33B 376

[7] Engle, E T Morton, D J *Ibid* 1931 13 311

[8] Wells, L H *Amer J phys Anthrop* 1931 15, 185

[9] Haines, R W, McDougall, A *Lancet* 1953 i 649

[10] Barnicott, N A, Hardy, R H. *J Anat Lond* 1955, 89 355

[11] *Haines R W, McDougall, A Lancet,* 1954 ii 1305

[12] *Ibid,* 1953, i 1298

This questionary contains no points which are wholly new, its value lies in the cumulative effect of the information assembled and in the anticipation of certain defences likely to be put forward Medical examinations conducted systematically and in close detail on this written basis can obviously give the courts far fuller and more uniform data about the state of the accused at the relevant time than they are now getting Although the document would not itself be admissible under the existing rules of evidence, there is no reason why the court should not allow the doctor in the witness box to refresh his memory by referring to his entries

BY-PASS OPERATION FOR ARTERIAL OCCLUSION

THE excision of diseased or damaged arteries and their restoration by suture or prosthesis is by no means a modern operation, and it can be traced back at least to the end of the nineteenth century, when Murphy, Payr, and Abbe experimented with suture techniques and glass tubes The principles of the eversion suture and endothelial approximation which often bear Carrel's name can be found in an article by Jaboulay and Briau published before the turn of the century In 1897, Murphy successfully excised an aneurysm and reconstructed the femoral artery by a circular invagination suture The widespread application of arterial repair and substitution had, however, to wait until operations could be confidently performed without fear of sepsis and until angiography was sufficiently developed to give the surgeon a clear idea of the problem facing him In the past decade much invention and energy have been directed to the re establishment of blood flow through the main arteries, and three important operations have been used —endarterectomy, excision and grafting, and finally the by-pass operation

Endarterectomy (the shelling out of the clot through a long incision in the arterial wall) has been followed too often by postoperative thrombosis extending proximally and distally, involving collateral vessels, and causing loss of a limb Excision of the thrombosed segment, with re establishment of continuity by means of an arterial graft or prosthesis, such as nylon, 'Orlon,' or 'Vinyon N,' is now a well-established and remarkably successful operation for large vessels such as the aorta and iliac arteries The mortality and morbidity after these operations were performed is surprisingly low, and although all the technical problems have not been entirely solved, the results are much better than those reported with other methods of treatment But the situation is quite different when smaller arteries, such as the femoral or popliteal, are excised and grafted Here the results are disappointing both in the immediate complication of limb gangrene and in the longer follow-up Crawford and De Bakey[1] have lately discussed why this is so They stress that the surgeon must know not only the extent of the occluded segment but also the state of the peripheral arterial bed well beyond the point of occlusion If the artery beyond is much narrowed and rigid, little benefit can be expected by the removal of the occlusion[2] It is even more important that any operation on a limb should be designed to minimise the interference to the collateral circulation The major collateral vessels, on whose preservation the viability of the limb depends, often arise in the patent lumen immediately proximal to the occlusion, and in such cases excision of the thrombosed vessel must include the valuable collateral supply Sometimes the diameter of the inserted graft is less than that of the destroyed collaterals, and if a secondary thrombosis ensues the limb of necessity becomes gangrenous

Crawford and De Bakey therefore use, for the treatment of arteriosclerotic occlusion of the leg arteries, the by-pass operation originally described by Kunlin et al[3] A graft is joined by end to-side anastomosis to the host artery above and below the diseased segment This operation is performed through two small separate incisions which are connected by a tunnel made with a probe or vein stripper As the incisions are well away from the vital branches, the collateral circulation is not in danger, and the host artery is undisturbed except through the two small incisions In fact, the operation simply adds an artificial collateral vessel about the size of the normal artery Crawford and De Bakey use for their anastomosis a freeze dried arterial homograft, the ends of which have been slightly bevelled, this is sutured proximally and distally to the artery by a simple over-and-over stitch using no 5 0 arterial silk Blood-flow through the main artery distal to the occlusion was successfully re established in 37 of the 40 limbs in which this technique was used Success was determined by arteriography or by the return of palpable pulses distal to the block It is particularly significant that none of these patients was made worse by the operation The indications for intervention were severe intermittent claudication and gangrene All the patients with rest-pain and claudication were relieved immediately and have remained well for periods up to eighteen months The results in patients with gangrene were just as impressive In a paper just published Crawford et al[4] confirm that they have found the by-pass operation better than other methods, particularly in patients with relatively long occluded segments If its further trial is equally encouraging, the by-pass operation may indeed prove to be so notable an advance that the indications for operating on occluded arteries may become much wider

UNEXPLAINED OSTEOLYSIS

THE mysterious gradual absorption of a single bone, or of a group of bones, is a rare condition found chiefly in young adults, often after a fracture The ultimate result may be the complete disappearance of part of the skeleton Krikler[5] has recently recorded a case of this kind · a coloured man of 35 said that five years before attending hospital several of his toes shrivelled up and disappeared Such a condition, as Engle and Morton[6] have pointed out, is common in the unshod native, but is usually related to local infection or trauma In Krikler's patient full investigation failed to show an underlying cause, and it seems likely that this is an example of this " idiopathic osteolysis " Gorham et al[7] were able to find only 16 examples of disappearing bones reported in the literature, and they added 2 examples from their own experience. In the recorded cases, trauma seemed largely incidental, although sometimes a pathological fracture was the first indication of bone resorption When a number of bones were affected, they were usually in the same limb Progress of the condition was slow and variable, sometimes it stopped, but occasionally it ended fatally Biopsies suggest that a common feature is an overgrowth of thin-walled blood-vessels, and the osteolysis may be directly related to this angiomatous change The picture of complete and very localised destruction of bone accords well with this view, and seems to distinguish the condition sharply from the post traumatic atrophy first described by Sudek[8] There are good grounds for accepting massive osteolysis as a distinct clinical entity, although its cause and its relation to other forms of osteolysis are obscure

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[1] Crawford E S De Bakey, M. E *Surg Gynec Obstet* 1955, 101 529
[2] Lindbom, A *Acta radiol*, *Stockh*, 1950, suppl 80
[3] Kunlin J Bitory Boely, C, Beaudry E, et al *Rev Chir Paris* 1951 89 206
[4] Crawford E S Creech O jun Cooley D A, De Bakey, M E *Surgery* 1955, 38 981
[5] Krikler D M *S Afr med J* 1955, 29 1050
[6] Engle E T Morton D J *J Bone Jt Surg* 1931 13, 311
[7] Gorham, L W Wright, A W, Shultz H H, Maxon F C jun *Amer J Med* 1954, 17 674
[8] Sudek P *Arch Klin Chir* 1900 62, 147

Public Health

OLD FOLKS AT HOME

The Kinds of Help They Need *

Sir Selwyn Selwyn-Clarke
K B E, C M G, M C, M D Lond, F R C P,
D T M & H, D P H
A PRINCIPAL MEDICAL OFFICER, MINISTRY OF HEALTH

By far the larger proportion of old people remain in their own homes indeed less than one in ten are accommodated in long-stay hospitals or in welfare hostels This is as it should be . for it is both natural and commendable that, at the end of their lives, old people should want to remain in surroundings familiar to them We must recognise, however, that many can do so only on one condition—namely, that when their powers are failing they receive appropriate help

FAMILY, NEIGHBOURS, AND VOLUNTEERS

In such circumstances we think first, of course, of families and relatives But families are on the average much smaller than they were fifty years ago and the individual responsibility for caring for elderly parents is correspondingly heavier Moreover, sons and daughters often go to live in some other part of the country or go abroad, leaving the old person all alone

A second line of defence is the good neighbour In times of full employment far fewer persons stay at home, and many wives do part time work in factories and thus have less time for the neighbourly turn to the old person living next door Nevertheless an immense amount can still be done by voluntary effort, both individually and through old people's welfare committees and Darby and Joan clubs which provide means whereby the aged can enjoy social intercourse and be helped by and help each other

In Swindon the different streets have been assigned to volunteers who make themselves responsible for visiting —once, twice, or more often, every week—all the old people in those streets who have expressed a wish to be visited This ensures at the very least that no old person, living by himself and falling suddenly ill, will lie helpless for days till death brings release Needless to say, not everyone wants to be visited by a stranger, however well-wishing , but most old people welcome visitors who are obviously out to do their best to bring a ray of sunshine into a drab and lonely place and who are not snoopers or busybodies A visit “ after hours ” is especially appreciated, and many an old person is thankful for the kindly gesture involved in the visitor making an evening cup of tea, helping grannie to get to bed, filling the hot-water bottle, putting the commode handy, lighting the safety night-light, and so on Similar visits in the earlier part of the day enable old people with a tendency to become bed-bound to get washed and dressed and into a comfortable chair or even on to a sunny porch Help with the week's shopping, with change of linen and laundry, or in getting to the old people's club, the church, the chapel, or the cinema, can do much to brighten an old person's existence

In some places that I have visited, the Women's Voluntary Services, Women's Institutes, British Red Cross Society, St John Ambulance Association, and various religious and other bodies have joined together to help to bring comfort to the aged Some voluntary bodies and local authorities arrange holidays for old people in the country or by the sea , for example, in Devonshire there is a system whereby some hotels at seaside places are willing to take old people at reduced rates out of season

In some circumstances, despite all the help that can be mustered, it is no longer possible for the old person to remain at home by himself Sometimes, if the house is big enough, the old person can take in a family, who, in return for free lodging, attend to his needs In other cases—as has been done so successfully in Exeter and in a few other towns, often with help from the National Corporation for the Care of the Aged—families are persuaded to “ adopt ” an elderly person and provide board and lodging and care in their spare room at a cost which can be met by the old person, assisted, perhaps, where necessary by the National Assistance Board

I have purposely started with examples of what can be achieved by voluntary effort, because I am convinced that there is a vast reservoir of this still waiting to be tapped After all, even as things stand, more than nine out of every ten persons of pensionable age reach the end of their lives without having to go to live in hospitals and welfare hostels , and, if their needs were better known, a great many younger people would want to help them to avoid a painful transplantation to unfamiliar surroundings at a period of life when it is difficult, if not impossible, to strike fresh roots

HEALTH VISITOR, HOME HELP, AND DISTRICT NURSE

There comes a time, however, when the old need rather more help in their homes than can be supplied from voluntary sources It is at this stage that the health visitor does such valuable work, although the earlier she is on the scene the better She can give friendly advice and encouragement which will prevent an old person from becoming house-bound and cut off from contact with his fellow men She can put him in touch with the various voluntary and local-authority bodies who are in a position to help him in one way or another Sometimes all he needs is the services of a chiropodist, and these can often be provided through an old people's club The health visitor can make sure that the old person does not take to living only on tea and bread and margarine and develop malnutrition She can see whether he needs assistance in keeping his house and himself sweet and clean, and she can arrange for a home help if necessary An efficient but warm-hearted home help can be a wonderful comfort to the old, especially those living alone

The health visitor will do her best to keep the old person up and about, so that he does not become bed bound and is less likely to suffer from chronic constipation, mental deterioration, and incontinence Should he fall ill, she can keep his family doctor advised and, at the doctor's request, call on her nursing colleague for her skilled assistance The district nurse may need to arrange for the loan of bedding, sickroom equipment, and so on, all the time cooperating closely with the patient's doctor Often, too, a patient who returns from hospital will need for a time help from a district nurse and/or a home help Here, the hospital almoner comes into the picture, making sure that the necessary arrangements are in train before the patient is discharged

In providing special accommodation for the old, the emphasis should always be on enabling them to remain active members of the community and on preventing their segregation from children and the young and middle aged In some county boroughs I have seen housing schemes where, in the midst of family houses, there and bungalows for old people, or ground floor flats, the upper floors being allocated to young families who can give a helping hand to the old person in an emergency In others I have seen, in the middle of a housing scheme, a group of single storey bed sitting-rooms (with individual kitchenettes and bathrooms) for single and married old folk, with a warden's house

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* From an address at the annual meeting of the Exeter Maternity and District Nursing Association on June 9, 1955

adjoining so that the old person has someone on the spot to help him, if need be. Yet again I have seen this bungalow arrangement with a sick bay to which an old person can go temporarily when it is unwise to leave him alone in his house and where he can receive nursing care at night if the occasion demands. I believe certain housing authorities have worked on a basis of reserving one tenth of their housing for old people.

There comes a time, however, when despite all manner of domiciliary help an elderly person of slender means can no longer stay the course and needs to go to a welfare home. Wherever possible, this home should not be far away from where he lived so that he can visit or be visited by his family or friends and will not feel cut off from familiar sights and sounds.

In determining when this stage is reached the health visitor plays a particularly important part. She contacts the welfare officer directly or through the medical officer of health, taking special pains to keep the aged person's doctor informed and to consult his wishes.

ILLNESS AND DISABILITY

Where an old person is ill the district nurse, with the help of relatives, neighbours, voluntary workers, and a home help, is often able to tide over the period of illness and to nurse him in his home. Similarly, some welfare homes have sick-bays where a patient can be looked after by the district nurse if he requires more elaborate nursing than the staff of the welfare home are themselves able to give. But when the nature of the illness or the social conditions necessitate hospital care and the family doctor thinks this the only satisfactory means of dealing with the situation, the patient will be removed, with his consent, to a hospital.

Nowadays, happily, old people do not go to these hospitals to die. Quite a large proportion receive active geriatric treatment, with physiotherapy and occupational therapy, and are restored to health and home once more. A remarkable change is taking place in many if not all of the old poor-law infirmaries now used for elderly chronic sick patients, and the dread of entering them is rapidly disappearing.

Some of these hospitals—e.g., the Cowley Road Hospital at Oxford—have a department called a day hospital to which frail ambulants and mentally and physically sick persons of pensionable age go for the day to receive physiotherapy, occupational therapy, and a nourishing midday meal, returning to their homes in the late afternoon. A day hospital of this nature affords great relief to relatives, especially when the old person suffers from mental confusion and cannot safely be left alone in an ordinary house. Once more, if an elderly sick person has to be admitted to a long stay hospital, it is important that this should be as near as possible to his own home if he has any relatives or friends who might visit him.

Where the patient has been in hospital for a considerable time, he may, of course, no longer have a home to which he can return; and then a place has to be found for him in part III dormitories of a joint-user institution, or in one of the welfare homes which are increasingly being built in the vicinity of hospitals, thus reducing the patient's fear of the unknown and increasing the chance of his keeping in touch with friends and family.

Many old people show mental changes, for mental confusion may be just as much an affliction of old age as hardening of the arteries; but it is well to remember that admission of an elderly person to a mental hospital no longer means that he will spend his remaining days there. At least half the patients over 65 years of age admitted to mental hospitals suffer from straightforward depressive illness that can be treated, and it is an encouraging fact that 9% of patients over 65 are discharged within six weeks, 31% within six months and 38% within twelve months.

Incidentally a diet rich in protein and vitamins has sometimes worked wonders in the first few days in the treatment of senile, confused patients who have had to enter a hospital, pointing the way to one of the preventive measures that can be taken to forestall, or at least postpone, the onset of senile degenerative changes. Keeping the elderly person ambulant (ensuring chiropody services) and in contact with human interests through clubs and outings are additional means of retaining mental alertness and a joy in living.

CONCLUSION

In this address I have tried to emphasise three things.

The first is the need for more voluntary effort on behalf of the elderly sick and the aged requiring care. I am certain that many more people would give such help if they knew how much good they could do.

The second, related to it, is the need to develop domiciliary aid of all kinds, both voluntary and statutory.

Thirdly, in planning living conditions, we must do all we can to keep the old people of our community integrated with the younger ones, and not to segregate them in institutions and hospitals unless or until this is unavoidable.

To these points I would add a fourth—namely, the need to coordinate in each area all the different ways in which we are trying to help the aged—so that whatever we do shall be done intelligently and as well as we can do it.

Fog

There has been no evidence that the fog which covered many parts of the country last week has had an appreciable effect on mortality or morbidity. Certainly nothing comparable to the 1952 experiences has been reported. In London calls on the Emergency Bed Service were about the usual for the time of year. Special measures for the care and investigation of fog victims in London had been prepared by the Medical Research Council but only a few patients were admitted to the beds set apart for fog casualties at St. Bartholomew's Hospital, the Brompton Hospital, Hammersmith Hospital, and the London Chest Hospital. At Barts bottles of ammonia were left open in some of the wards; we referred earlier[1] to the plans for investigating the use of ammonia as a possible means of preventing damage to the lungs by acid vapours.

Epidemic Respiratory Illness in Children

On Christmas Eve there was a sudden demand for beds in the children's hospitals in Liverpool, and special wards had to be opened at Fazakerley Infectious Diseases Hospital to deal with the infants requiring admission. We are indebted to Dr. Andrew Semple, medical officer of health for Liverpool, for the following account of the outbreak so far.

General practitioners and pædiatricians in the area began to see many cases of acute respiratory infection over the Christmas holiday. The condition was described as an acute bronchitis, bronchiolitis, or pneumonia, almost entirely confined to children under eighteen months. In Alder Hey Hospital alone, up to Jan. 3, 57 cases were admitted, 42 with a diagnosis of bronchopneumonia and 15 with a diagnosis of acute bronchitis. Most of the children were not very ill by the time they settled down in hospital, but practitioners reported that in the early stages there was striking evidence of acute respiratory infection. The number of notifications of acute primary pneumonia for the week ending Jan. 7 was 36, compared with 17 for the corresponding week last year. Up to Jan. 3 about 130 cases had been traced and by Jan. 9 the Liverpool public-health department knew of about 230 cases.

Although many children have been admitted to hospital, there are indications that a considerable number more are being adequately treated at home. 1 of the children involved died, and post-mortem specimens have been sent to the M R C Virus Reference Laboratory, together with throat-washings, stools, and blood from acute cases It is generally felt this is probably a virus infection It has appeared in all parts of the city The acute infection seems to be mainly confined to babies although there are some indications that preschool-children over the age of 2 are also affected, and the public-health department is following up the contacts of children admitted to hospital

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[1] *Lancet*, 1955, ii, 975.

In Sunderland about 100 children have been treated at the Children's Hospital in the past month for an epidemic respiratory infection [1] 40 of them were still in hospital on Jan 9 There was a similar epidemic in Sunderland two years ago

Statistical Review of England and Wales

The medical tables of the Registrar-General's Statistical Review of England and Wales 1954 [2] were published last month Some of the main figures had already been published in earlier returns [3] and in the annual report of the Ministry of Health [4] The new volume gives details of deaths from all causes and notifications of infectious diseases in 1954, by age, sex, area of residence, and time of year

Of the total infant mortality in 1954, the loss in the first week after birth accounted for nearly 60%, and the loss in the first three months of life for over 80% The death rate of children aged 1–4 years in 1954 was 0 94 per 1000 population In 1953 it was 1 18 and in 1920 it was 12 08—a decline of over 90% in thirty four years

Deaths resulting from accidents in the home and residential institutions continued to increase, and numbered 6617 Of this total 4790 (72%) were deaths of old people aged 65 or over 4188 of all such accidental deaths were due to falls Deaths in the home and residential institutions due to accidental poisoning by domestic gases continued to increase —from 461 in 1952 and 554 in 1953 to 614 in 1954 There were 597 deaths due to accidents caused by fire and explosion of combustible material 687 children under 5 died in accidents in the home and residential institutions—compared with 731 in 1953 Of these, 250 were certified as due to inhalation and ingestion of food and 182 to accidental suffocation in bed or cradle

Also published recently was the text volume of the Registrar General's Statistical Review for 1952 [5] This is the official commentary on the civil and medical statistics for 1952, already published

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1 *Manchester Guardian* Jan 10, 1955
2 The Registrar General's Statistical Review, 1954, part I Tables *Medical* H M Stationery Office Pp 375 12s 6d
3 See *Lancet*, 1955 i, 248, 813
4 *Ibid*, 1955, ii 1289
5 The Registrar General's Statistical Review of England and Wales 1952 Text H M Stationery Office Pp 256 8s

Infectious Diseases in England and Wales

Disease	Week ended December				
	3	10	17	24	31*
Diphtheria	25	14	17	13	11
Dysentery	615	680	837	857	559
Encephalitis					
Infective	6	4	3	1	3
Postinfectious	2	2		2	3
Food poisoning	451	188	210	120	146
Measles excluding rubella	2757	2819	2982	2482	3759
Meningococcal infection	41	23	30	17	15
Ophthalmia neonatorum	24	27	18	23	14
Paratyphoid fever	0	10	9	6	9
Pneumonia primary or influenzal	462	517	551	535	652
Poliomyelitis					
Paralytic	73	87	58	44	43
Non paralytic	42	43	31	20	19
Puerperal pyrexia	215	221	204	176	204
Scarlet fever	1127	1226	1039	955	856
Smallpox					
Tuberculosis					
Respiratory	627	655	539	454	476
Meninges and C N S	4	16	11	7	7
Other	75	67	62	63	52
Typhoid fever	6	1	4	3	
Whooping-cough	1112	1177	1068	941	878

* Not including late returns

Special Articles

SKIING INJURIES IN NOVICES

J A Williams
M B Birm, F R C S
LATE CAPTAIN, R A M C

I describe here skiing injuries, particularly those to the knee, among 2000 British troops and their families in Austria during the season of 1952–53, and refer to a follow-up of knee injuries sustained in the previous season

Most of the patients were troops learning to ski, the injuries were sustained from one day to twelve weeks after they had first worn skis

The majority of the injuries were strains of the knee or ankle, or both (see accompanying table) There were 100 such injuries, whereas there were only 5 cases of fractured tibia and fibula and 6 cases of undisplaced fracture of the ankle Austrian practitioners at ski centres agreed that this was a typical distribution of injuries in novices, experienced skiers tend to sustain fewer and more severe injuries

TYPES OF SKIING INJURY

Type of injury	Cases	
	No	Percentage of population at risk
Strain of knee	54	2 7
Strain of ankle	46	2 3
Fractured tibia and fibula	5	0 25
1st deg Pott's fracture	6	0 3
Dislocated shoulder	2	0 1

Knee Injuries

Of the 54 patients with knee injuries, I examined and treated 44 All but 1 were followed up for from three to six months after injury The injuries, which differed from one another only in the degrees of severity, were strains of the internal lateral ligaments of the knee joint No patient had a tear of his internal semilunar cartilage

Mechanism of Injury

There were two common causes of injury, both of which are more likely to operate in the inexpert than in the expert skier (1) crossing the skis when attempting a Stem-Christiania or a "snow-plough" turn (20 patients), and (2) divergence of skis when running into deeper snow (15 patients) In both groups there was a combination of rotation and abduction strains, the rotation being internal in the first group and external in the second, in all cases the abduction strain was apparently the greater force Injury usually did not take place with the patient at speed, but was a gradual strain caused by the falling body-weight abducting and rotating the knee, the foot being firmly fixed in the snow by the ski No patient had knee strain while attempting a Telemark turn, which was not used in skiing instruction

Many patients in the first group who suffered internal rotation of the knee had strains of the lateral ligament of the ankle, but no patient in the second group had any associated ankle injury

Diagnosis

In all cases pain was referred to the medial side of the joint, and there was tenderness in the joint line over, or anterior to, the internal lateral ligament Patients examined some days after the injury were tender in front of the lower attachment of the ligament, and in severe cases bruises were visible at this point The mastia). He had a typical eunuchoid facies, no facial hair, scanty pubic hair, and very fine brittle, and scanty scalp hair. His voice was high pitched and tended to squeak when he became excited. His skin was dry and scaly, with local infection on his face. His blood pressure in the sitting posture was 160/105 mm Hg, and his penis was very small and retracted into the pubic fat, his right testis was undescended, and his left testis was small. At a life assurance examination a short time before he had been graded as a second class life and accepted only on a greatly increased premium.

Treatment and Progress.—Treatment was started early in 1952 with intramuscular testosterone propionate 50 mg twice weekly. His blood pressure was again checked before the start of treatment and found to be still 160/105 mm Hg in the sitting posture. This produced an immediate and very dramatic improvement in all his symptoms. He became energetic, cheerful, keen on his work and hobbies, and very active, and evinced an interest in women for the first time. This treatment was continued for a month and then reduced to 50 mg weekly supplemented by 10 mg of methyl testosterone by mouth daily. After five months of this treatment a striking change had taken place. Facial hair had begun to grow, his voice had deepened and lost its squeakiness, and he had lost over $1^{1}/_{2}$ st in weight, the fat all having disappeared from his breasts, hips, thighs, and lower abdomen. His penis was larger and had emerged from the pubic fat, and he was having erections weekly. His right testis had descended into the scrotum and increased in size. His scalp hair had changed completely, being thicker, stronger, and more profuse. His skin rash had disappeared, and his skin was less coarse. His personality had changed, and he was more ambitious, had more drive and energy, and was cheerful and no longer felt shy and inferior. His blood pressure in the sitting posture was 155/100 mm Hg. The treatment was then changed to testosterone phenyl propionate 50 mg by subcutaneous injection, which the patient gave himself at intervals of four to eight weeks over the next three years.

Follow up.—All the changes have been maintained except the loss of weight (he weighs nearly 13 st again), but the distribution of the fat is now typically of the obese masculine type. His penis is now $4^{1}/_{2}$ inches long on erection and not retracted when flaccid. He has occasional nocturnal emissions, usually six or seven days after his injection. His blood pressure has fallen to 140/90 mm Hg in the sitting posture, and at a recent life assurance examination he was classified as a first class life and accepted at normal rates. He has been promoted to managing director of his firm and is going to marry. No ill effect has so far been detected after four years' treatment.

Discussion

This case shows several rather unusual features: the presence of a congenital abnormality of the genito-urinary tract; the late age at which the treatment was started, the very dramatic changes, especially psychological, the effect on the scalp hair (its changed character may have been due to hormonal therapy or to the psychological changes), and the lowering of the blood pressure. This last change is the most difficult to explain. There seem to be three possibilities: (1) it was purely coincidental and would have occurred in any event, (2) it was due to relief of the psychological tension, and (3) the hormonal therapy exerted a direct effect on it through the pituitary gland or through the adrenal glands.

New Inventions

A PLASTER OVERBOOT

A WALKING-PLASTER requires some form of protective cover or attachment. There are many different types available, these include metal or wooden rockers, 'Sorbo' rubber heels, Bohler irons, sections of rubber tyres, canvas overboots, and the Ludun boot. Most of these, however, have one or more disadvantages:

(1) The appliance may cause an abnormal gait, which often persists after the plaster cast has been removed.

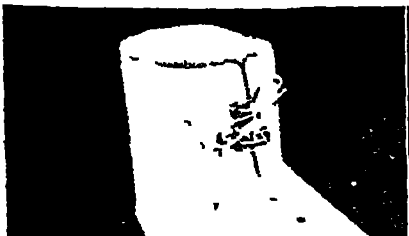

Fig 1—P V C boot and sponge-rubber insole

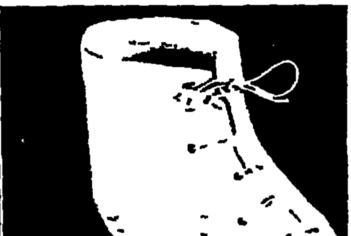

Fig 2—Latex boot and insole of felt covered cork

(2) The appliance offers no protection and the plaster gets soft in wet weather.

(3) The appliance may tear the bed clothes.

(4) The appliance may be difficult to put on correctly.

(5) The appliance may be intrinsically expensive or difficult to manufacture, and further expense is incurred by the use of plaster bandages to attach the appliance firmly to the cast.

To obviate these disadvantages a plaster overboot was designed and made from polyvinyl chloride (P.V.C.).

This boot (fig. 1) is cheap, light, waterproof, easy to slip on and off, and æsthetically not unpleasing to the eye. It enables the patient to simulate a heel-and-toe gait, and additional springiness is gained by the use of a sorbo rubber insole. The material is durable, as is shown by the fact that the boot has been in continuous use for eighteen months with very little sign of wear on the sole. If it does wear thin, the base of the boot can be redipped into liquid P.V.C.

The process used in making the boot is as follows:

(1) Preheat mould to 160°C. Dip the canvas webbing in the P.V.C. and fit to the mould, and then pregel for two minutes in an oven at 110°C.

(2) Dip again for 45 seconds and pregel in the oven for 5 minutes at 110°C.

(3) Redip the base only for 2 minutes and stove in oven for 25–30 minutes at 160°C.

After the P.V.C. prototypes were put on trial, a simpler boot was developed (based on the same principles), this boot can be made quite easily in any hospital workshop. Instead of P.V.C. latex is used. The plaster cast, covered with stockinet, is dipped into latex and then dried at 120°C for 10 minutes, this is repeated once for a small boot and twice for a large boot. After drying, an ordinary crepe sole is stuck on to the base because the latex does not grip as well as the P.V.C. This boot (fig. 2) is slightly more bulky in appearance and slightly heavier but costs a little less. The price of one boot is about 5s., and the total working-time required to manufacture one latex boot is 15 minutes. It has been found by experience that only four sizes of over-boot are necessary, and from this small range an overboot can be selected to fit any plaster.

I am grateful to Messrs Pryor & Howard for making the P.V.C. prototype, Mr W. Tuck, workshop manager at the Royal National Orthopædic Hospital, for making the latex boot, and Mr Robert J. Whitley, F.R.P.S., for the photographs.

Royal National Orthopædic Hospital London

MARTIN SINGER
M.B. Cape Town, F.R.C.S.

Special Articles

HAZARDS OF NUCLEAR AND ALLIED RADIATIONS

The report[1] was published on Tuesday of the committee appointed by the Medical Research Council to consider the medical aspects of nuclear radiation, including the genetic aspects The committee was set up under the chairmanship of Sir Harold Himsworth, F R S because of the widespread concern about the possible long-term effects of test explosions of nuclear weapons This is however only one aspect of the hazards to man of ionising radiations, and the committee's report deals with present knowledge of the whole subject

An attempt is made to assess the contribution from each source of radiation to which the inhabitants of this country are at present, or might in future, be exposed The most outstanding finding is that by far the largest contribution is made by diagnostic X-ray examinations, and that examinations of a relatively few sites of the body account for most of the population dose, examination of the chest is relatively unimportant The results of an investigation which is still in progress (a preliminary report by Mr Osborn and Mr Smith appears on this page) suggest that this source provides a gonad dose of 22% additional to that received from natural sources, and that this figure may well be an underestimate It is concluded that present practice in diagnostic radiology should be reviewed to clarify the indications for the different special examinations now being carried out

The estimated population doses of radiation to the gonads are as follows -

Source of radiation	*Approximate dose to gonads as a percentage of natural background*
Natural background	100
Diagnostic radiology	at least 22
Radiotherapy	?
Shoe-fitting	0 1
Luminous watches and clocks	1
Television sets	much less than 1
High altitude flying	insignificant
Occupational exposure	
Radiology and industry	at least 1 6
Atomic Energy Authority	0 1
Fall-out from test explosions	less than 1

The inhabitants of this country may receive in the next 50 years, from nuclear weapons already exploded, about 0 02% to 0 04% of the radiation that they will receive during the same period from natural sources If the firing of bombs were to continue indefinitely at the same rate as over the past few years, there would be a build-up of activity, gradually reaching a plateau in about a hundred years, which would give the average individual a dose over a period of 30 years of about 1% of what he would receive in the same period from natural sources The individual and genetic effects of such a dose of external radiation would be insignificant

The most important constituent of fall-out from bombs is strontium 90 which, if ingested, is concentrated in bone where it may give rise to destructive changes including cancer In relation to strontium 90, the committee concludes that " . at its present level, no detectable increase in the incidence of ill-effects is to be expected " The maximum permissible concentration in bone allowed for those who might have to deal with this substance is 1000 micromicrocuries per g of calcium in the skeleton For the general population, however, the committee believes that the figure should not exceed 100 and that immediate consideration would be required if the level showed signs of rising greatly beyond 10 At present, measurements in this country show that the highest concentration in bone is about 1 micromicrocurie and if the present rate of firing continues, this level may be increased tenfold in the course of several decades

The committee sponsored a detailed study of the incidence of leukæmia among over 13,000 patients treated with X rays during the past 20 years for ankylosing spondylitis The results suggest that there is an increase in the small chance of developing leukæmia after exposure to a total dose of radiation which might, in exceptional circumstances, be met with in civilian life It is not certain, however whether any increase would occur if the same dose were spread over many years

The committee concludes that, with proper safeguards, exposure in peacetime can be maintained at levels which can be accepted by the individual without undue concern either for himself or his offspring But since genetic effects are eventually distributed throughout the whole population, a relatively high dose to a fraction of the community can only be offset by a correspondingly low dose to the remainder, and it is therefore important for those not occupied in work involving radiation to receive as little as possible The committee declares ' Our present knowledge does not justify us in naming any specific figure as a limit for the average dose of radiation which might be received by the population as a whole It is highly desirable that such a figure should be named as soon as possible, and we understand that the International Commission on Radiological Protection has this matter under consideration "

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[1] Hazards to Man of Nuclear and Allied Radiations H M Stationery Office Pp 128 *5s 6d*

THE GENETICALLY SIGNIFICANT RADIATION DOSE FROM THE DIAGNOSTIC USE OF X RAYS IN ENGLAND AND WALES

A PRELIMINARY SURVEY

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E E Smith
B Sc Lond, A Inst P
DEPUTY DIRECTOR, RADIOLOGICAL PROTECTION SERVICE
DOWNS HOSPITAL, SUTTON, SURREY

In recent years, increasing attention has been paid to the genetic consequences of exposure to ionising radiations, and various attempts have been made to estimate the maximum accumulated dose, in excess of natural background, that can safely be received by human beings Such estimates have been based largely on experiments on fruit-flies (*Drosophila*) and mice, and considerable speculation has attended the extrapolation to man

At present, because of uncertainty about the proportion of observed spontaneous gene mutations which are induced by radiations, the permitted exposure is often expressed as a percentage of the background dose rather than in a definite number of röntgens rems, or rads

The most recent pronouncement on this subject by the International Commission on Radiological Protection (1956) states

> " Hitherto, the Commission has occupied itself with workers in hospitals the new atomic industries and research institutions, but has now assumed responsibilities in relation to much larger groups of persons, or whole populations, which might be exposed to radiation by radioactive materials, either natural *or* artificial, in very small quantities in water or food, as well as irradiation from radioactive materials in the atmosphere and contamination of the earth's surface Its recommendations have therefore been extended to a consideration of these larger populations
>
> " Unfortunately information on the genetic and other effects on populations is extremely scanty and the Commission has not, *therefore, felt* it possible to lay down precise doses but has indicated that for the whole population it would be prudent to limit the dose of radiation received by gametes from all

Reviews of Books

Control of Disease in the Tropics

T H DAVEY, O B E , M D , D T M , and W P H LIGHTBODY, C B E , L R C P , School of Tropical Medicine, Liverpool London H K Lewis Pp 408 47s 6d

THE appearance of a new textbook on the preventive aspects of tropical disease is an event of great importance to thousands of doctors who work in the tropics, and to the many students who take courses of tropical medicine and hygiene each year The authors have set out the principles of control and prevention, disease by disease, systematically, succinctly, and clearly

Helpful diagrams illustrate transmission cycles There are sections on housing, water supplies, disposal of human and animal wastes, nutrition and vital statistics An appendix gives detailed information on practical procedures The book is well produced, on good paper and well bound, at a reasonable price (we note, without regret, the omission of the customary statement that an insecticide has been applied in the binding)

A book like this must necessarily be condensed and didactic, and it might have been an advantage to include references on important subjects, for more detailed reading, at the end of each chapter When referring to the only standard text book on a subject (even by authors whose opinions are so highly respected), the reader may expect at least a mention of views which, if not yet universally accepted, are widely discussed and acted on A conspicuous omission is the assessment of malarial endemicity by calculation of the daily rate of infected bites—a method in increasing use, and about which any tropical practitioner might need help

In the control of insect borne diseases, one or two recommendations err on the side of idealism For example, few villagers will cooperate in bi weekly "dry pot" days, whereas a weekly day is comparatively easy to achieve Again, the nuisance value to European women of thigh length mosquito boots and their suspensory apparatus is an item seriously to be weighed against the extra protection afforded over and above that of the efficient modern antimalarial prophylactics Neurosis is commoner than malaria as a reason for European women leaving the tropics, and taking their husbands with them

In the control of simulium, dicophane (D D T) is not necessarily best applied as an emulsion The most remarkable results so far, in Saskatchewan, were achieved with a solution The implications of this experiment, in results, economy of dicophane, and sparing of fish life, are important

We welcome and commend this book, which fills a gap in the ranks of medical textbooks

Doctor's Offices and Clinics

Medical and Dental PAUL HAYDEN KIRK and EUGENE D STERNBERG New York Reinhold London Chapman & Hall 1955 Pp 218 96s

THE post-Danckwerts interest-free loans for group-practice premises are likely to have, over the years, a profound effect on British general practice The move towards group practice will be intensified, and general practitioners, secure in good buildings of their own, will be able to face the future with increasing confidence But the emphasis must be on *good* buildings hence, the growing importance of the design of group-practice centres

It might be supposed that the ideas of American doctors and architects would be far removed from the prospects confronting their English counterparts in Bow or Bromley yet, strangely enough, similar problems have produced similar answers Most American cities are now undergoing decentralisation People are moving out from up-town apartments to low-density suburban residencies So the doctors leave their 'offices" in commercial blocks in the centre and build for themselves special-purpose buildings in the new residential suburbs As in the English country towns in the past twenty or thirty years, the economics of the situation encourage group practice The American general practitioner is as concerned as the English one to keep down costs The result is that the architectural solutions have a direct relevance to British needs It is more than fortuitous that the buildings illustrated in this book are very similar to the group-practice centres provided by the Nuffield Provincial Hospitals Trust at Harlow New Town Economy, efficiency, and a homely friendly atmosphere are combined in one-storey buildings which yet manage to look purposeful and distinguished This is a book to be studied carefully by those contemplating the construction of their own group-practice centre It could usefully be read in conjunction with the Nuffield survey of *Good General Practice*,[1] as a necessary occasional corrective But it is surprising how seldom such correction is necessary

Genetics in the Atomic Age

CHARLOTTE AUERBACH, PH D , D SC , Institute of Animal Genetics, University of Edinburgh Edinburgh and London Oliver & Boyd 1956 Pp 106 8s 6d

THIS is a readable and amusing little book by a geneticist who has made important discoveries in the chemical induction of mutations Her aim is serious it is to give the reader enough of the background of genetics for him to appreciate the dangers of an increase in the exposure of human germ-plasm to radiation and this is well done There is no unjustified "scare" about the dangers of radiation, and the present uncertainty and ignorance of the size of the effects in man is made clear But Dr Auerbach also emphasises that there is no "safe dose," that every increase in radiation will bring some increase in mutations, and that the very great majority of these will be harmful She is pessimistic about the possibility of men and women taking control of their own evolution by speeding the elimination of harmful mutations from the population, and encouraging the spread through the population of the very occasional useful mutation

The Dynamic Equilibrium of Body Proteins

Hæmoglobin, Plasma Proteins, Organ and Tissue Proteins GEORGE H WHIPPLE, M D , professor of pathology emeritus, University of Rochester, New York Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1956 Pp 68 23s 0d

THIS book sets out in the barest possible terms the facts that show that the body-proteins, all of them, exist in a dynamic equilibrium with each other The plasma proteins and tissue-proteins are constantly interchanging, and Professor Whipple thinks that, for this to proceed breakdown only to polypeptide level is needed The earlier work with injection and withdrawal of plasma proteins, and the later work with material labelled with C^{14}, are briefly mentioned The effect of inflammation on the synthesis of hæmoglobin, and the fact that the placenta will allow proteins to pass from mother to fœtus, are among other topics He emphasises the key position of the liver

It is interesting to see from this book the topics and results that Whipple considers most important in his experimental work on protein metabolism that began thirty years ago But it is hard to know to whom such an outline is addressed, it is much too brief for physicians or medical students, and investigators in this field will surely be familiar with all the points

Blood Group Substances

Their Chemistry and Immunochemistry ELVIN A KABAT departments of microbiology and neurology, College of Physicians and Surgeons, Columbia University New York Academic Press London Academic Books 1956 Pp 330 64s

THIS volume collects together and comments upon an immense amount of information on the quantitative immunochemistry of the blood-group substances, and it gives a remarkably extensive bibliography The information is technical in the extreme and no concessions are made to the man who knows only a little about the immunology of blood groups, still less to general readers The latter can only turn over the pages in wonder that so much is known about the immunochemistry of the blood groups, and that it has had so little application to everyday work with the blood groups To the small band of initiates, this book will undoubtedly be useful sources additional to the natural background, to an amount of the order of magnitude of the natural background."

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[1] Taylor, S Good General Practice London 1954

In these circumstances it is necessary to know the average background exposure and the average dose now being received from all the additional sources of ionising radiation to which people are exposed. Here we are concerned only with the radiation received by the "genetically alive" fraction of the population—i.e., predominantly young people, from their conception to the age at which their last child is conceived. This requires a knowledge of vital statistics, some aspects of which are at present incomplete.

Spiers (1956) has assessed the annual dose received by the gonads from all sources of natural radiation, the most important of which are cosmic rays, gamma rays due to the radioactivity of the environment, and beta and gamma rays from the naturally radioactive isotope of potassium in the body. This dose varies in different localities (Spiers and Griffiths 1956) and countries (Sievert 1956). The average values for Leeds (0·090 rad per annum for females and 0·100 rad per annum for males) are used here. If the high radon concentration reported for London by Anderson et al. (1954) is found to be fairly general, these values will have to be increased.

The sources of additional exposure to ionising radiation are numerous, and all have been introduced in the last fifty to sixty years. They include diagnostic and therapeutic radiology, luminised articles (such as clocks and watches), television and other high-voltage cathode-ray tubes, high-voltage rectifying valves, shoe-fitting fluoroscopes, industrial radiology in all its aspects, research equipment of many kinds, and nuclear weapons and power. Of all these sources there is no doubt that, in this country at least, diagnostic radiology has been by far the most important up to now.

We describe here an attempt to estimate the genetically significant dose received by the population of England and Wales from this cause. This has been done previously for Australia (Martin 1955), for the U.S.A. (Billings et al. 1955, Clark 1956), and for the United Kingdom (Stanford et al. 1952, Farmer 1955). Our data, although still far from complete, are thought to be more comprehensive than those hitherto available.

Methods

In order to make this estimate, we must know how many X-ray diagnostic examinations are made each year and the distribution of the various types of examination in terms of age and sex. We must also know the average technique for each type of examination in so far as it affects the dose delivered to the gonads. Finally, we must know the vital statistics of the community as regards the conception of children.

Vital Statistics

Previous published work has estimated the radiation dose received by the gonads up to the age of 30, the approximate mean age of reproduction. We prefer the method of Farmer (1955), in which the dose received by any person from conception up to a given age is weighted according to the probability that he or she will conceive a child at that age.

Fundamentally, the work described here is an attempt to ascertain whether the number of genetic mutations induced by the radiation used in diagnostic radiology is significant or not. For this we have assumed that the number of radiation-induced mutations added to the population at the birth of a child is proportional to the total radiation dose received by the gonads of both parents from the time at which each of them was conceived up to the time at which their child was conceived. Though such a calculation can be made simply for a single individual, when a whole population is concerned it can only be done statistically. We have accordingly weighted the dose accumulated by the gonads of a person from conception up to a given age according to the probable number of children to be born to a person of that sex at that age (the "risk of parenthood") taken from general population statistics. A dose so weighted becomes a new unit, which we call the "röntgen equivalent genetic" or "reg," and radiation doses weighted in this way we call "genetically significant radiation doses." The accumulated dose received by the gonads from natural radiation has been calculated similarly to enable a direct comparison to be made.

TABLE I—STATISTICS OF PARENTHOOD

Age (yr.)	Risk of parenthood *		Risk of subsequent parenthood †	
	Male	Female	Male	Female
0–14	0	0	2·177	2·216
15–19	0·016	0·110	2·169	2·161
20–24	0·320	0·673	1·996	1·769
25–29	0·654	0·607	1·505	1·054
30–34	0·507	0·445	0·895	0·514
35–39	0·315	0·222	0·439	0·180
40–44	0·182	0·065	0·176	0·036
45–49	0·065	0·004	0·052	0·002
50–54	0·020	0	0·010	0
55 or more	0	0	0	0

* Risk of parenthood is the average number of children to be born to a member of the community during the period specified.

† Risk of subsequent parenthood is the average number of children expected to be born to a member of the community after the mid-point of the period specified.

When the genetically significant radiation dose is summated for the whole of a person's life, or is summated over a given period for a group of people or a whole population, it is numerically equal to the dose received by a person at the given age multiplied by the probable number of children to be conceived by that person subsequently (the "risk of subsequent parenthood"). Since this method of calculation is arithmetically easier, it has been used.

The "risk of parenthood" for females is assessed from statistics published by the Registrar General (1955) for 1953 by using only the figures for live births, whether legitimate or illegitimate. For males the required information is available only for 1938 (Royal Commission on Population 1950). Women certainly tended to have children at an earlier age in 1953 than in 1938, and, since the relative age of women and men at marriage has not changed appreciably, it is assumed that the tendency is present to the same extent in men, and the 1938 figures have been corrected accordingly. The data used are given in table I.

It is implicitly assumed that all hospital X-ray patients (except those undergoing salpingography) are normally fertile people whose "risk of parenthood" is the same at any given age as that for the population at large. This may not be wholly true, but any deviation is likely to be small, and in any case we have no information on which to base a correction. Salpingography, being normally undertaken to assist in the diagnosis of infertility, must be treated differently because all the women thus examined are married and anxious to have children. It is assumed that, on the average, each woman so examined subsequently bears one child.

Annual Number of Examinations

The number of diagnostic X-ray examinations made each year at present is given in table II, which shows that the great majority of them are made in National Health Service hospitals. The source of the figure is the annual reports of the Ministry of Health. For 1951 and 1952 these give the "number of examinations," and for 1953 and 1954 the "units of work done." The known increase for 1952 over 1951 is 13%, and that for 1954 over 1953 is 11%. The figure given in table II is obtained by assuming that the increase for 1953 over 1952 and the increase for 1955 over 1954 are both 12%, and from this we also

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obtain the conversion factor 1 8566 "units of work" per examination That this factor is substantially accurate has been confirmed by the data we have obtained from several of the hospitals included in our analysis

The number of mass miniature radiography examinations is obtained from the Ministry of Health statistics branch Some of the remaining figures in table II have been obtained from official sources, and some are unofficial estimates by people in a position to make them As will be shown, however, their contribution to the genetically significant radiation dose is small

The total of more than 17,000,000 represents an average of one examination per person in the country every two and a half years On the basis of our samples, it appears that 7,720,000 of these annual examinations are made on the 18,500,000 people aged less than 30 This is much greater than earlier estimates, which assumed an average of only one examination per person up to the age of 30

The age and sex distributions of the hospital examinations have been determined by analysing the work of five typical hospitals—two teaching, two non-teaching, and one children's The number of examinations analysed, however, is less than 1 in 800 of the annual number of examinations for the country as a whole, and it is clear that a more complete and representative analysis is desirable This is especially true because, as will be shown later, the greater part of the dose is received during a small minority of examinations Where there was a substantial difference between the figures for the teaching and the non-teaching hospitals, the figures were weighted in favour of the non teaching hospitals On the whole, however, differences were small, as is shown in table III, which lists as percentages of all X ray diagnostic patients the numbers of all the patients (irrespective of age and sex) undergoing certain types of examination in which the doses may be high Agreement is even better when the numbers of patients under 45 years of age are extracted, as can be done for some of these hospitals

The age and sex distributions of the examinations for the N H S and non-N H S hospitals and private medical radiology have therefore been taken as the same as the mean of the figures from the five hospitals marked in table III with an asterisk, multiplied up to a total of 12,670,000 examinations The totals for all ages, but divided between the sexes and between the different types of examination, are given as percentages in table VI The distributions of the examinations for the other sources detailed in table II have been obtained and treated similarly

TABLE II—NUMBER OF DIAGNOSTIC X RAY EXAMINATIONS PER ANNUM IN ENGLAND AND WALES (1954 EXCEPT WHERE OTHERWISE STATED)

Source of examination		Number	Percentage of total	
Ministry of Health				
N H S hospitals		12 200 000*	69 1	91 1
Mass miniature radiography		3 358 000†	19 0	
Dental services		528 000†	3 0	
Non N H S hospitals (say 3% of N H S hospitals)‡		370 000*	2 1	
Private dental radiography		330 000‡	1 9	
Private medical radiology		100 000‡	0 6	
The Services				
Royal Army Medical Corps	216 000‡			
Royal Navy	228 000§			
Royal Air Force	180,000‡			
		624 000	3 5	
National Coal Board		40 000‖	0 2	
Medical Research Council pneumoconiosis research unit		37 000§	0 2	
Others		73 000¶	0 4	
Total		17 660,000		

* Estimate for 1955 (see text)
† Figures for 1954 supplied by the Ministry of Health statistics branch
‡ Estimate
§ Official figure
‖ Estimate of annual number from Jan 1 1957 onwards
¶ Total for 7 smaller units which are not considered further in this paper

All figures refer to England and Wales only except the Services (which include units stationed abroad) and the National Coal Board

TABLE III—PERCENTAGE OF ALL X RAY DEPARTMENT PATIENTS SUBJECTED TO CERTAIN EXAMINATIONS

Hospital	No in sample	Lumbar spine	Abdomen	Pyelography	Pelvis	Hip and femur	Barium enema	Salpingography
Teaching								
A	78 319		4 58	1 97			1 19	0 028
B*	7110	3 38	2 38	2 27	2 24	2 53	1 57	0 026
C*	4018	3 78	3 32	2 48	1 56	2 78	1 50	0 348
D	45 037		2 42	3 25	2 63		1 69	
E	8226		1 70	2 28			0 46	
F	65 503		4 14	2 71	3 32			0 171
G	63 869	4 71	9 95	2 74	3 75		1 11	0
Non teaching								
H*	1931	3 89	1 50	1 99	1 02	1 54	2 69	0
I	5019	12 10	3 13	3 67			1 56	0 080
J*	6269	5 29	2 25	2 29	1 64	7 75	1 52	0
Children's								
K*	1277	1 57	2 58	0 94	0 70	2 27	0 25	

* Detailed statistics for these hospitals giving the age and sex distribution for all types of examination were used for the main calculations
No figures available

In view of the special circumstances, the numbers of salpingographies, radiological pelvimetries, and obstetric abdominal examinations have been obtained differently It will be seen from table III that the average percentage of salpingograms from eight hospitals is 0 082% and from this it has been assumed that the value for the country as a whole is not less than 0 05% On this basis 6330 examinations of this type are undertaken annually The information obtained about radiological pelvimetry and obstetric abdominal examinations is summarised in table IV The arithmetic means of the figures for pelvimetry and obstetric abdominal examinations are 93 and 250 per 1000 live births respectively In view of the uncertainty attaching to these figures, we assume that for the country as a whole there are not less than 60 pelvimetries and 200 obstetric abdominal examinations per 1000 live births in hospital Of the 673,651 live births in 1954, 64 1% (i e , 431,810) took place in hospital (Ministry of Health 1954) We have therefore assumed that at least 26,000 X ray pelvimetries and 86,000 obstetric abdominal X-ray examinations are made annually

Except for pelvimetries, the number of fœtal gonads irradiated has been based on the number of women in each five year age group subjected to each type of exami-

TABLE IV—PROPORTION OF PREGNANCIES SUBJECTED TO PELVIMETRY AND OBSTETRIC ABDOMINAL X RAY EXAMINATIONS

Hospital	No of pelvimetries	No of films per examination	No of obstetric abdomens	No of live births in hospital	No per 1000 live births	
					Pelvimetry	Obstetric abdomen
A	83	3	213	~1877	44	116
C	159	3–4	209	1456	109	144
F	103		381	928	111	410
G	57		322	1960	29	164
I	21		6	162	130	37
L	273	4–5	ca 1500	3388	81	445
M	150	3	285	913	~165	313
N	23	3	280	919	25	307
O	137	3	357	941	146	380
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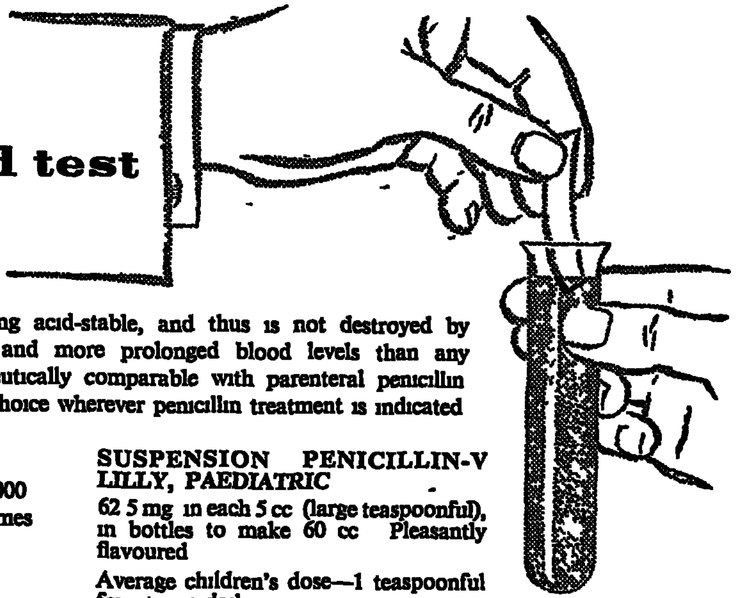

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nation and on the risk of parenthood for that group. The numbers so obtained were reduced by 6% to allow for fœtal and neonatal mortality, and by 20% to allow for the well-known reluctance to radiograph a pregnant woman if the matter can wait until after the birth of the child. The number thus obtained in the case of abdominal examinations is supplemented by the number of obstetric abdominal examinations as determined above.

Doses Received by Gonads

The most comprehensive survey of radiation doses received by the gonads in diagnostic radiology is that by Stanford and Vance (1955). They emphasise the variations to be expected from case to case and also the variations between different techniques. Their figures, however, are based on the very careful techniques in use at Guy's Hospital. A smaller number of measurements made at another teaching hospital gave results on the whole similar but differing in particular examinations by a factor of more than 10. Those reported by Martin (1955) are on the whole substantially higher than those of Stanford and Vance. The Stanford and Vance dose values have been used as the basis of this work (with one or two exceptions detailed below) partly because they are conservative and partly because they are comprehensive. They do, however, only represent the technique in use at one hospital, where all reasonable steps are taken to reduce to the minimum the doses received by the gonads. Perhaps the most important of these steps are accurate coning of the X-ray beam, reducing to the minimum the number of films and screening time of each examination, and using fast films and screens where practicable. In many hospitals less care is taken over these matters. It is therefore likely that the average doses for the country are substantially higher than those of Stanford and Vance.

The doses received in pelvimetry and salpingography have been assessed separately using the minimum estimates given in the literature, by Stanford (1951) and Barnett and Bewley (1955) respectively. In calculating the dose for pelvimetry a three-film technique is assumed, although many hospitals take more than three films.

Except for X-ray pelvimetry, we have not found any published report of doses of radiation received by the fœtal gonads. We have therefore assumed that, if the fœtal gonads are exposed only to scatter, the dose is the same as that to the maternal ovaries, but if they are exposed to the direct beam, the dose is the geometric mean between the dose to the maternal ovaries and the dose to the maternal skin (Stanford and Vance 1955) except in pelvimetry, where figures based on Stanford (1951) have been used.

The doses per examination that have been used are listed in table v.

TABLE V—DOSES IN MR RECEIVED BY GONADS PER EXAMINATION

Examination	Male	Female	Fœtal
Head	0.8	0.2	0.2
Teeth	4.75	0.8	0.8
Shoulder	0.22	0.03	0.03
Arm, hand	0.26	0.05	0.05
Rib, sternum	0.48	0.16	0.16
Chest, large film	0.36	0.07	0.07
,, M M R	0.25	0.15	0.15
,, special*	37	5.4	5.4
Barium swallow and meal	20	9	9
Barium enema	40	20	20
Abdomen	69	200	580
Cholecystogram	1.8	15.6	15.6
Pyelography	486	1290	3210
Bladder	279	690	2610
Pelvis	1100	210	800
Hip femur	710	210	800
Leg foot	3.5	0.6	0.6
Spine, cervical	1.74	0.18	0.18
,, thoracic	33	15	15
,, lumbar	129	713	713
Lumbosacral joint	22	220	1540
Sacroiliac joint	129	713	2700
Salpingogram	0	1700	0
Pelvimetry	0	1280	2680

* An average value for bronchography, tomography &c.

Results

The results were calculated from the available data as detailed above. The genetically significant dose of radiation received annually from all X-ray diagnostic sources in England and Wales is presented in table vi together with the percentage of each specific type of examination in terms of all the examinations undertaken. The annual totals are 496,355 r eg for males and 484,644 r eg for females. To compare these with the doses received from natural radiations it is necessary to convert the units from röntgens to rads. Spiers (1946), who calculated the absorption of energy in different types of tissue for X rays of different wave-lengths, gave 87 ergs per g per röntgen for muscle subjected to X rays of diagnostic quality. If this figure applies to gonad tissue, the two totals given above become 432,000 and 422,000 respectively when expressed in terms of rads, the total for both sexes being 854,000 rad equivalent-genetic (rad eg).

The annual doses of natural radiation calculated from the same vital statistics amount to 2,186,800 and 1,722,150 rad-eg for males and females respectively, the total for both sexes being 3,908,950 rad eg. Thus the contribution from X-ray diagnostic radiology represents an increase of 22% over the dose due to natural radiation. The data, however, were selected with a view to estimating the minimum contribution from diagnostic radiology; therefore the actual value may be several times greater than this.

Discussion

Previous estimates of the genetically significant dose of X rays from diagnostic radiology have been based on a number of examinations per annum considerably below the actual number. Stanford et al. (1952) and Stanford and Vance (1955) assume that each person undergoes one such examination up to the age of 30. Farmer (1955) calculates from two hospitals to the whole country by the ratio of beds. The figures given in table II are regarded as being considerably more accurate than either, although they are subject to a possible uncertainty of a small percentage.

The doses received (table v) are inevitably known with much less accuracy. Many other workers have observed higher doses than those used here (Osborn 1951, 1952, and unpublished observations, Macgregor and Oliver 1952, Bercy et al. 1955, Martin and Williams 1946). The doses cited by Martin (1955) are the only other comprehensive data. If these are used throughout, the genetically significant radiation due to diagnostic radiology rises from 22% to 36% of natural radiation. Further, as Stanford and Vance (1955) point out, small inaccuracies of setting up can cause great differences in the dose received by the gonads. They cite that, if for a male patient undergoing intravenous pyelography the alignment of the bladder film is incorrect and the testes are exposed to the direct beam, the dose received in the examination is increased by a factor of 25. Table vi shows that, if such an error were general, this single alteration would increase the figure of 22% to 30%.

No allowance has been made for cases where films are unsatisfactory and are repeated, or where trial or additional films are taken in addition to the normal ones for the particular examination.

The results presented here are not intended to be an accurate estimate of the genetically significant radiation dose being received from X-ray diagnostic radiology at present; insufficient data are available for this. They are intended to indicate a probable lower limit to this quantity. The actual amount being received annually at present is likely to be greater, but whether by a factor of 2, or 5, or even 10, we cannot yet say. *It is not a constant value*, for the number of diagnostic examinations in N.H.S. hospitals is apparently increasing by about

THE LANCET

LONDON SATURDAY, JUNE 16, 1956

Pain in Peptic Ulcer

THE cause of pain in peptic ulcer is probably complex. Two possible factors have received particular attention—namely acidity and motility. There is evidence to support both the "acidity" and "motility" schools of thought, just as there is evidence contrary to both. In favour of acid as the cause of pain, PALMER,[1] using a fairly high concentration of HCl found a correlation between the introduction of acid into the stomach and the onset of pain. The results of BONNEY and PICKERING[2] and others led them to the same conclusion. Against this hypothesis are the many observations showing a complete dissociation between pain and the acidity of the gastric contents.[3–5] Among the supporters of the motility school were HURST[6] and HARDT,[7] who noted pain associated with gastric contractions in the absence of free acid, and some recent work is in agreement with this conclusion.[8] When a large number of admirable observers are sharply divided into two camps, it is certainly necessary to reconsider the whole question and this has been done by SMITH[9] in a series of careful observations. He finds that there is much to be said for both sides—as well as much against them. He introduced acid and alkali into the stomach of patients with peptic ulcer, and simultaneously recorded gastric motility by means of a balloon-kymograph technique. His results make it clear that the pain of peptic ulceration cannot be satisfactorily explained solely by changes in acidity of the gastric contents, nor by varying degrees of movement of the stomach or duodenum. Some patients reacted to acid by feeling pain, others did not, but felt pain when there was no free acid or when acidity was low. SMITH records that one patient felt a spasm of pain after the gastric contents had been rendered alkaline with sodium bicarbonate. Pain and gastric motility were similarly unrelated, though occasionally movement was accompanied by pain. The only possible conclusion to be drawn from this work, as from the earlier observations, is that acidity and motility sometimes trigger pain, but they are not inevitably and causally related to it.

A third consideration is the abnormal tissue at the site of the ulcer where dead and dying cells, together with living ones, lie in inflamed and œdematous tissue. Since pain is more easily produced in an inflamed area than in a normal one, inflammation must clearly be taken into account. KINSELLA[5] held that, in logical order, inflammation was the primary cause of pain, the motor disturbance the secondary cause, and the acid the tertiary cause. Histamine was one of the first inflammation-producing substances whose action was analysed by LEWIS in his celebrated work on the triple response in skin. It is perhaps less well known that viscera also give a triple response—i.e., local œdema and wealing and, at a short distance from the site of injury, vasodilatation of arterioles via an axon reflex. The triple response follows local tissue injury and the liberation of histamine from the injured cells; it also follows the local appearance of endogenous histamine liberators, or the injection of exogenous ones, such as the lecithinase of bee-stings. But histamine is not the only substance causing inflammation and œdema. Hyaluronic acid is produced by connective tissue, and the enzyme hyaluronidase is also present in tissues in a bound form.[10] Hyaluronidase is in all probability liberated as the result of injury, and it can then convert the hyaluronic acid from its normal gel-like consistence to a more fluid sol-like state which permits the easy spread of substances in solution. This action may be demonstrated by the use of dyes.[11] Thus, where there is tissue injury there will be vasodilatation and a breakdown of tissue barriers. The resulting increase in the permeability of blood-vessel walls enables dissolved substances to spread and affect a wider area. Certain polypeptides also induce vasodilatation and probably do so in the normal organism[12] being formed from plasma-proteins by the action of enzymes released in the course of cellular activity. One such polypeptide is bradykinin. Inflammation does not of itself cause pain as was demonstrated in the stomach of Tom by WOLF and WOLFF,[13] and in skin by EMMELIN and FELDBERG,[14] who showed that nettle-stings contain histamine and acetylcholine. Injected into the skin histamine by itself causes itching and inflammation but no pain but a combination of histamine and acetylcholine causes the itching and pain characteristic of nettle-stings. In this connection, bradykinin is of particular interest because it may be a mediator of pathological pain, thus it, or a substance with similar chemical and physical properties, can be shown to have parallel effects in producing pain and vasodilatation when applied to the exposed base of a cantharidin blister in man.[15] Bradykinin is by no means the only polypeptide with such properties, in fact there is good ground for believing that in this category there are a large number of polypeptides formed by the proteolytic digestion of tissue or plasma-proteins.

In the stomach at the site of an ulcer cells have been disrupted and have liberated their enzymes and cell proteins, and exuded blood-serum is also present. These are the conditions necessary for the formation of a variety of polypeptides and for the release of histamine—all of which are liable to cause inflammation, œdema, and pain. In normal circumstances the small amounts of these substances formed would be confined in their proper channels, but where normal tissue barriers have broken down, as by the action of hyaluronidase, they may spread irregularly. Further, any stimulus causing vagal activity (in the absence of diluting food) will result in gastric movements which

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[2] Bonney G L W Pickering G W *Clin Sci* 1946–48 6 63
[3] Ginsburg, H Tumpowsky I Hamburger W W *J Amer med Ass* 1916 67 990
[4] Ryle J A *Lancet* i 1925 583
[5] Kinsella V J *Ibid* i 1929 1130 *Ibid* 1953, ii 353
[6] Hurst A F The Sensibility of the Alimentary Canal London 1911
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[9] Smith A W M *Quart J Med* 1955 24 393
[10] Feldberg W *Int Arch Allergy N Y* 1955 8 15
[11] Zweifach B W *Rev canad Biol* 53 12 179
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[13] Wolf S Wolff H G Human Gastric Function New York 1947
[14] Emmelin N Feldberg W *J Physiol* 1947 106 440
[15] Armstrong D Keele C A Jepson J B, Stewart J W *Nature Lond* 1954 174, 791

12% each year. Some very fragmentary available evidence suggests, however, that the genetically significant radiation dose has not been increasing at such a high rate very long. The great improvement in film and screen speeds in the last twenty-five years has reduced the doses necessary to produce an acceptable result and has tended to compensate for the greatly increased number of examinations. In fact, it appears that thirty years ago the genetically significant radiation dose from diagnostic radiology was not very different from what it is today, within a factor of about 2. The consumption of films was then at about 20% of the present level, but the introduction of intensifying screens and the increase in film speed have reduced the average exposure to 20% or less. It is to be hoped that technical developments, such as image intensification, will bring about a further reduction in dose, thus enabling the increasing number of examinations to be made without adding to the genetically significant dose.

Table VI shows that many of the common types of examination (e.g., of limbs, teeth, and chest) contribute altogether a very small proportion of the total genetically significant radiation dose. A few other examinations (e.g., of hip and lumbar spine pyelograms, and pelvimetry) amount to only about 7% of the total number of examinations yet contribute nearly three-quarters of the total radiation. It is clear that, if it is desirable to reduce the genetically significant radiation dose from diagnostic radiology, it is this latter group of examinations that should receive first consideration. The proportion of the total dose received by fœtal gonads is particularly noteworthy.

TABLE VI—GENETICALLY SIGNIFICANT RADIATION DOSE FROM X RAY DIAGNOSTIC RADIOLOGY

—	Males			Females			Fœtal gonads	
	% of all examinations†	Reg per annum	% of all dose‡	% of all examinations†	Reg per annum	% of all dose‡	Reg per annum	% of all dose‡
Hospitals								
Head	3.9	820	0.1	3.4	174		5	
Teeth	0.2	137		0.3	40		2	
Shoulder	0.8	26		0.6	2			
Arm and hand	4.8	319		4.3	39		1	
Rib and sternum	0.4	24		0.1	1			
Chest—								
Large film	11.8	919	0.1	12.5	192		8	
Special	0.4	2109	0.2	0.8	365		129	
Barium swallow and meal	2.6	3680	0.4	1.6	960	0.1	94	
Barium enema	0.5	1943	0.2	0.7	514	0.1	39	
Abdomen (with obstetric)	0.6	10 657	1.1	1.1	39 630	4.0	62 691	6.4
Cholecystogram	0.2	17		0.4	171		35	
Pyelography	0.7	29 878	3.0	0.6	104 941	10.7	22 390	2.3
Bladder	0.1	1084	0.1	0.1	3544	0.4	3773	0.4
Pelvis	0.7	72 657	7.4	0.7	23 000	2.3	6766	0.7
Hip and femur	1.4	187 909	19.2	1.4	36 939	3.8	2285	0.2
Leg and foot	5.0	3580	0.4	3.9	383		10	
Spine—								
Cervical	0.4	128		0.7	11			
Thoracic	0.5	1467	0.1	0.6	1004	0.1	65	
Lumbar	1.4	25 128	2.6	1.4	105 889	10.8	7319	0.7
Salpingogram	0	0	0	0.1	10 761	1.1	0	0
Pelvimetry	0	0	0	0.1	29 574	3.0	153 087	15.6
	36.4	342 482	34.9	35.4	358 134	36.4	258 699	26.3
Reallocation of fœtal dose*		133 056	13.5		125 643	12.8		
	36.4	475 538	48.4	35.4	483 777	49.2		
General dental service	1.8	537	0.1	3.0	211			
Armed Services	3.4	19 833	2.2	0.1	403	0.1		
Mass miniature radiography	11.5	424		7.6	251			
National Coal Board	0.2	20		0	0	0		
Others	0.5	3		0.1	2			
Totals	53.8	496 355	50.7	46.2	484 644	49.3		

* In the sex ratio at birth 1.059 : 1.

† Percentage of all diagnostic X ray examinations in England and Wales.

‡ Percentage of all genetically significant radiation arising from diagnostic radiology in England and Wales.

Negligible dose.

It is to be hoped that a fuller investigation of techniques, doses delivered to the gonads, and radiology department statistics will enable a reasonably accurate estimate of the genetically significant radiation dose from diagnostic radiology to be made.

Conclusion

The amount of genetically significant radiation dose from diagnostic radiology is not negligible, amounting to at least 22% of that from natural radiation sources, and possibly much more than this. Whether this constitutes an appreciable genetic hazard to the population as a whole is not for us to say, but the wording of the latest recommendation by the International Commission on Radiological Protection suggests that this is not impossible.

Summary

An analysis has been made of the number of X ray diagnostic examinations performed per annum in England and Wales, and a subdivision obtained from five selected hospitals into type of examination and into age and sex of the patients examined.

In addition, an assessment has been made of the minimum dose received by the gonads in each type of examination, and the probability of reproduction as a function of age.

The results show that it is unlikely that the genetically significant radiation dose received by the population of England and Wales from X-ray diagnostic radiology amounts to less than 22% of that received from natural sources, and it may well be several times greater than this figure.

Most of this radiation is received in a few types of examination undergone by relatively few patients, and by fœtal gonads in examinations during pregnancy.

The work described here was originally undertaken for the Medical Research Council's Committee on the Medical Aspects of Nuclear Radiation, under the chairmanship of Sir Harold Himsworth. We are greatly indebted to Dr T. C. Carter for guidance on its genetic aspects and to Prof. A. Bradford Hill for helpful comment on its statistical aspects. Many other people, far too numerous to name, have provided invaluable data, especially the radiologists, radiographers, physicists, and records officers of the hospitals studied and the appropriate medical and statistical officers of various Ministries and other organisations, and we are most grateful for all the trouble they have taken.

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may stir and distribute the locally accumulated breakdown products till enough sensory nerve-endings are stimulated to give a sensation of pain The gastric acid, produced by vagal activity, may reach sensitive areas and add to the pain Pepsin may attack the acellular protective coating of the ulcer base Histamine will certainly be present where there is injured tissue, and whether vagal activity will add more histamine is a moot point Acetylcholine will also be liberated at the vagal nerve-endings Whether any or all of these factors do give rise to a sensation of pain will depend on the temperament of the individual, on the conformation of the ulcer, and on other variables such as blood-pressure and blood-flow at a given moment The elimination of any one pain factor may tip the balance in the patient's favour Anticholinergic drugs, for instance, are useful because they reduce gastric movements and secretions, but they have to be given in doses which produce some general effects

The intermittency of pain in peptic ulcer is no more or less mysterious than its intermittency in any inflamed raw area, or in toothache Nor is it a peculiarity of peptic-ulcer pain that it is relieved by rest and relaxation, which reduce to a minimum the reflex stimulation of motor and secretory nerves Whether pain is or is not felt must, surely, depend on whether the many factors involved do, at a given moment, sum to a stimulus great enough to induce a sensation of pain

Cancer of the Colon

Black et al [1] have lately criticised the grounds for the assumption that five, ten, or even fifteen years' survival after treatment for cancer is in fact the result of treatment Their arguments concerning cancer of the breast add weight to this view [2], and McKinnon [3] has also pointed to the apparent failure of earlier treatment to reduce mortality from breast cancer Fortunately the doubts which these observations raise need not affect surgical judgment so far as cancer of the colon is concerned, since a lesion at this site must be removed if only to relieve diarrhœa, anæmia, and obstruction—though the surgeon naturally hopes that he is also improving the patient's chances of avoiding a recurrence Shallow et al,[4] in following 750 patients after excision of growth from the large bowel, discovered a significant decline in the incidence of recurrence or metastasis after the third year It cannot, however, be concluded that those who survive longer have surgery to thank for this, they may have had a tumour with that type of life-history

Nevertheless, surgeons continue to remove what they can when they can, and in the colon endeavour turns to dealing with recurrences The large bowel must be considered in its entirety when treating cancer discovered at one particular site, for the colon seems liable to malignant change in more than one place in the same patient Of the patients studied by Shallow et al, 42 had two separate primary lesions, and in 2 the second lesion arose after resection Ginzburg and Dreiling [5] describe 25 such patients, in 1 of whom there were three and in another four primary lesions Most of the additional lesions developed after the first one had been discovered the interval varying from one to twenty-three years Ginzburg and Dreiling pertinently observe that when another growth appears within a year it may well have been present but not noticed at the first operation Beal and Cornell [6] found 10 patients, with two simultaneous lesions in a series of 140 resections, recurrence developed at the suture line in 21 and was commonest after sigmoid resection—but this was also the commonest primary site (81 cases)

There is cogency in Cole's contention that exfoliated malignant cells may provide seedlings which grow in the suture line and thus give rise to these recurrences, and it is proper to follow his technique of occluding the bowel with tapes above and below the growth in order to avoid contamination of the proximal and distal areas destined for anastomosis [7] But it is important not to lose sight of the fact that the development of a growth in the colon may indicate a precancerous state throughout the large bowel Over thirty years ago, Dukes [8] gave evidence of this by drawing attention to adenomas Swinton and Warren [9] have found that, in 14% of 827 patients with large-bowel-growth, the lesion was proved histologically to have started in an adenomatous polyp, and 35% of their patients had multiple polyps 22% of Beal and Cornell's series were thus affected In 100 patients treated for polyps, van Buskirk [10] found adenomas to be multiple in 35 Fortunately they are usually within range of the sigmoidoscope, and this was so with 78% of van Buskirk's patients and with 70% of the polyps seen by Swinton and Warren 71 of van Buskirk's patients were examined after their original treatment and 12 were found to have new or recurrent polyps Ravdin [11] believes that nearly all multiple primary lesions are grafted on adenomatous polyps, and the incidence he cites of 75% of large-bowel cancer lying within 26 cm of the anus coincides with the distribution of adenomas But he also indicts inflammatory polyps arising in ulcerative colitis this overlooks the fact that polyps in this disease are rarely *adenomatous* indeed there is no proof yet that this condition, more properly termed pseudopolyposis to avoid confusion leads to carcinoma in ulcerative colitis, though the adenomatous polyp, when it occurs, doubtless can

These facts must be weighed in treatment Careful examination of the large gut is essential when a colonic or rectal cancer is excised, since another growth may lurk elsewhere unsuspected After resection, patients should be seen at regular intervals and the whole bowel must be investigated when suspicious symptoms start anew Ginzburg and Dreiling [5] were able to undertake further resection for 23 of their patients with subsequent primary lesions For adenomas alone the position is difficult, beyond the sigmoidoscope they are not easy to

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ANTENATAL CARE

A Subject for Discussion

A CONCERTED effort against toxæmia of pregnancy is proposed by the Ministry of Health As a first step the Ministry has invited the chairmen of boards of governors, and of hospital management committees which control a substantial number of maternity beds, to convene local conferences At these, it is hoped, representatives of all the groups concerned with midwifery under the National Health Service will discuss a memorandum produced by the Standing Maternity and Midwifery Advisory Committee

This memorandum points out that, besides being the principal cause of avoidable maternal death in this country, toxæmia of pregnancy is also a major cause of stillbirth and neonatal death—nowadays often grouped together as "perinatal mortality" In the past six years the perinatal mortality for the whole country has remained stationary Many deaths could be prevented by early detection and treatment of toxæmia

> "In Aberdeen, Baird and his co workers, in Australia, the practice of the *Women's Hospital, Crown Street, Sydney*, described by Hamlin, and in New Zealand, Dawson, have shown that by more strict attention to antenatal care a significant lowering of the incidence of eclampsia and over 50% reduction in perinatal mortality rate can be obtained All attribute their success to prompt detection of toxæmia through strict attention to antenatal care followed by early admission to *hospital* and good sedation in severe pre eclampsia This early recognition of toxæmia depends upon a routine designed to detect the smallest deviation from the normal, for example, a rising blood pressure (usually a diastolic pressure of over 90 mm of mercury) slight œdema or unduly rapid gain in weight Albuminuria is considered a late sign indicating a serious risk of antepartum hæmorrhage The danger of intra uterine death of the fœtus is said to be in direct proportion to the height of the blood-pressure and it is especially great when the systolic pressure remains at 160 mm of mercury or more"

Under the maternity medical services the doctor must provide all necessary antenatal care including an examination on booking and at 36 weeks But in cases of toxæmia causing stillbirth or neonatal death, pregnancy is usually concluded before 36 weeks The reference to the 36th week may well have *obscured the importance* of a medical examination at 30–32 weeks and careful intermediate examination thereafter

The *supervision a mother* is to receive should be mapped out when the primary booking is made, and, if more than one agency is involved, it should be clear how responsibility is to be shared

> "Any evidence of malnutrition, renal disease, heart disease, pulmonary tuberculosis, or other serious illness in the past or any complications in a previous pregnancy are reasons for seeking a hospital booking It is desirable where practical that all primiparæ over the age of 30, all multiparæ over the age of 40, mothers having their fourth or more confinement and those with multiple pregnancies as well as all cases of social need should have their babies in hospital"

An X-ray examination of the chest is always advisable, and arrangements should be made for a thorough dental examination and early treatment The patient's basal blood pressure should be established during the early months of pregnancy and *her weight noted* The urine should be tested, including a catheter specimen if there is a suspicion of albuminuria Blood should be taken for examination

> "At 30–32 weeks multiple pregnancies and some obstetric abnormalities will be detectable Special attention should be paid at this stage to *the blood pressure* and any slight rise, abnormal weight gain or other sign of toxæmia should lead to frequent and regular observations in order that treatment may be provided more promptly than has been customary in the past The urine should of course be tested and albuminuria if it occurs and is not related to other known disease, should be regarded as a late sign of toxæmia to be promptly and seriously treated"

The midwife should see her patient monthly until the 28th week, fortnightly until the 34th and 36th week, and then weekly Free interchange of information between midwife and doctor should always be arranged as part of the plan for antenatal care made at the time of booking

Blood examination is needed to estimate the mother's hæmoglobin (or even for a full blood count) at booking and again at *30–32* weeks, to establish the mother's blood-group, and to establish whether or not she is rhesus negative "Tests for antibodies will be necessary later in pregnancy in rhesus negative women, and all women with antibodies should be confined in special centres with facilities for prompt exchange transfusions i e, *within eight hours of birth, if the baby requires it*" Blood tests for venereal disease are also required

Once early toxæmia and other abnormalities have been *recognised, there are* three essentials for a good service (1) a constant watch on all patients, especially non attenders, (2) an adequate number of antenatal beds *so that treatment may be started* as early as possible, and (3) for the multipara a good home help service

Medicine and the Law

Continued Detention in Institution Questioned

AT Leicester Assizes recently a man aged 26 was charged with carnal knowledge of a girl of 19 stated to be a mental defective [1] With another girl she had absconded from the institution to which she had been committed The man had found the two girls in a state of distress in the middle of the night, and had taken them to his room, where the one girl had remained for a week At first the man pleaded not *guilty to the charge of carnal knowledge*, but later he changed his plea and was given an absolute discharge Mr Justice Stable expressed concern at the *detention of the girl, and said that he would write to the* Home Secretary

It appears that in 1953 the girl was charged with *stealing 13s, was dealt with under the* Mental Deficiency Acts, and was committed to an institution At one stage she seems to have been certified as feeble minded—i e, *as a person whose mental deficiency*, though it did not amount to idiocy or imbecility, made her need care, supervision, and control From the press reports it is not clear whether she was so certified before the charge of theft or as a result of it at all events, she was later certified as a moral defective—i e, as a person whose mental deficiency is coupled with strongly vicious or criminal propensities In 1955 the order for her detention was extended for another five years, which is the normal period of extension when an order is renewed after being in force for two successive years

At the recent trial Mr Justice Stable questioned the girl about the circumstances in which this extension was ordered She told the judge that she was not interviewed at the time, nor consulted about staying another five years The judge then questioned the medical superintendent, who said that *the girl's account* was incorrect When an order was about to lapse, he said, the patient was interviewed by two special visiting magistrates accompanied by an *independent* adviser, the patient had every opportunity to make representations, and her parents or guardians could be present

Mr Justice Stable said that, having seen the girl and having had an opportunity to form an opinion about her intellectual capacity, he thought it a case which required careful revision "If she had been sentenced to borstal demonstrate, even using evacuation barium studies and air contrast 49% of those seen by van Buskirk[10] were impalpable, and at laparotomy only a large polyp can be felt with ease through the bowel wall Coloscopy, using a sigmoidoscope passed into a well-prepared bowel opened at laparotomy, has been suggested, but few would care to undertake it Since most adenomas lie, however, within the rectum or close by, sigmoidoscopy is perhaps the most valuable investigation and one which Castro et al[12] feel should be a routine whenever possible, in practical terms, the sigmoidoscope can be passed at all anal or rectal examinations Because there may be adenomas at a higher level in association with a colonic growth, Ravdin[11] recommends that colectomy should be as wide as possible compatible with preserving the major blood-supply to the remaining colon, and Lillehei and Wangensteen[13] advise total or subtotal colectomy, having operated thus for polyps or carcinoma on 73 patients with a mortality of 5 5%

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[1] *Times* May 21 and 25 1956 *Leicester Mercury* May 24 1956

Exploring Leucocyte Reserves

When a patient has a pyogenic infection or sustains an injury, there is a prompt and considerable increase in the number of granulocytes in the circulating blood Where do these granulocytes come from, how quickly can they be replaced, how big is the reserve and where is it, what is the life span of the granulocytes ? These questions are not easy to answer Yoffey[14] calculated for guineapigs that the reserve of myeloid cells in the bone-marrow was about 100 times the number of cells in the circulating blood, and he noted that 75% of the cells were segmented or band forms, ready or almost ready for discharge into the circulation Kline and Cliffton[15] estimated the average life-span of the human leucocyte at 13 2 days, a much longer life-span than had been thought likely from the results of animal experiments Osgood et al[16] labelled leucocytes with radioactive ^{32}P incorporated in the desoxyribonucleic acid (D N A) of the nuclei, and they found the life-span of granulocytes in chronic myeloid leukæmia was about 3 days, and of lymphocytes in chronic lymphatic leukæmia about 30 days Bierman et al,[17] in cross-circulation experiments in man, calculated that about 30,000 leucocytes per c mm per day left the circulation, which works out to the huge total of about 1 5 × 10^{11} daily Lawrence and his colleagues in California have approached these problems by using the technique of leucopheresis and by combining it with the marking of leucocytes with radioactive phosphorus In leucopheresis blood is withdrawn from the femoral artery of an animal the blood is centrifuged, the layer of white cells and platelets is removed, and the blood is returned to the circulation by the femoral vein, in this way it is possible to clear the leucocytes from large volumes of blood in a short time Preliminary results with leucopheresis in dogs were reported last year[18] If three blood-volumes per hour are cleared of leucocytes, the white-cell count in the peripheral blood falls to just under 20% of base level in about $1^{1}/_{2}$ hours, and this level is maintained even if the leucopheresis is continued When the removal of leucocytes is stopped, there is a pause before any new white cells appear, but after 1–2 hours the count rises rapidly for 6–8 hours until a count perhaps twice as high as the original basal count is reached, then the rate of increase slows and after 24–36 hours the count steadies at a level $2^{1}/_{2}$ to $3^{1}/_{2}$ times the original level If leucopheresis is carried out at a slower rate (say, one blood-volume cleared per hour), the white count falls to only 40–60% of the initial level and recovers quickly when the withdrawal ceases These experiments indicate that the circulating blood-volume must be cleared of leucocytes in somewhat less than one hour to exceed the rate of entry of these cells from the reserve areas, and Lawrence calculates that, for the dog, the entry of leucocytes into the blood must have been rather less than 0 8 × 10^{10} cells per hour The rate is accelerated by repeated leucopheresis, for example, in one experiment the rate of recovery after a first leucopheresis was 0 25 × 10^{10} cells entering the circulation per hour, but after a second experiment the rate was 1 7 × 10^{10} cells per hour The leucocytes that enter the blood after leucopheresis are mature types and immature cells do not appear until the 3rd or 4th day Similarly, hyperplasia of the granulocyte-forming tissue in the marrow does not show for at least 24 hours and then it increases so that many myelocytes, promyelocytes, and myeloblasts appear

This work has now been extended by Craddock et al[19] They consider that these results show that the *initial* response to loss of granulocytes is the release of mature cells from the storage areas, and the response does not depend upon growth in the marrow They found that, even in dogs who had received enough total body irradiation to cause aplasia of the marrow, the response to leucopheresis was at first similar to that of the normal animal, though the height of the leucocyte-count reached in the recovery stage is relatively low It is this reserve of mature or nearly mature granulocytes that is the source of cells for any body reaction that calls forth a leucocytosis, such as, presumably, a pyogenic infection It is therefore very important, and Craddock et al have attempted to define its site and estimate its size There are three possible sites of the "ready reserve" of leucocytes those in the blood-stream, including those sequestered in relatively stagnant parts of the vascular system, those that have migrated out into the tissues and those in the bone marrow throughout the body Craddock and his co-workers consider that replacements after leucopheresis come almost exclusively from the bone-marrow Experiments aimed at mobilising the cells in the vascular bed suggest that this source is unimportant, and leucopheresis in heavily irradiated dogs shows that a fixed agranulocytosis can occur while there are still large collections of leucocytes in the lungs and other tissues For tracing the entry into the circulation of newly formed leucocytes from the marrow, Craddock et al used the method of incorporating ^{32}P into the D N A of the leucocytes and, in view of unsatisfactory features in existing methods, they used a new technique of D N A extraction developed for them by Simmons she would have had three years' training Because she was sentenced in 1953 as a moral defective for stealing 13s, it seems amazing that she should be kept in an institution until 1960 "

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[12] Castro A F Ault G W Smith, R S *Ibid*, 1951 92 164

[13] Lillehei R C Wangensteen O H *J Amer med Ass* 1955 159 163

[14] Yoffey J M *Ann N Y Acad Sci* 1955 59 928

[15] Kline D L Cliffton E E *J appl Physiol* 1952 5 79

[16] Osgood E E Li J G Tivey H Duerst M L Seaman A J *Science* 1951 114 95

[17] Bierman H R Byron L, Lanman, J T *Bull Univ Calif med Center* 1949 1, 89

[18] Lawrence, J S *J Amer med Ass* 1955 157 1212

[19] Craddock C G jun, Perry, S Lawrence, J S *J clin Invest* 1956 35, 285

The case is a further reminder of the concern which the courts show for the liberty of the individual, particularly in this type of case [2]

[2] See *Lancet*, April 7 1956, pp 371, 378

The Casualty Department*

I THE WORK AND THE STAFF

T G LOWDEN

B M Oxfd, F R C S

CONSULTING SURGEON, SUNDERLAND GROUP HOSPITALS

OVER 11½ million attendances were made at casualty departments in England and Wales in 1952, and about 80% of these attendances were made at non-teaching hospitals [1] By its magnitude, the work of these departments merits far more attention than it generally gets

Whereas most parts of the hospital have had their functions developed on a clinical basis, with a tendency to more and more specialisation, the casualty department has pursued an opposite course Because the limits of its clinical work are difficult to define, it has developed on a functional basis, and it carries out minor procedures belonging to many specialties It is often a coordinating mechanism on the medical side, just as the secretary's office is a coordinating mechanism on the administrative side, and it often does work which might properly be regarded as part of the administrative machine Moreover, it is the part of the hospital most closely in contact with the public, because access to it is the most informal it is the hospital's shop window, where deficiencies are noticed by a large number of people

Unquestionably many casualty departments could be very much better than they are, and it may be useful to consider possible means of improvement and how they could be applied to the majority rather than to the few

The Work

The Patients

The patients come from many sources

1 Those with complaints which in the ordinary course of events would take them to their family doctor may come on their own initiative, because their own doctor is unavailable, because the hospital is nearer, because they think the hospital doctor is better, because they have no family doctor, or because they are away from home This type of case covers a wide field of medicine and surgery and can easily produce an unwieldy clinic

2 Patients are sent to hospital by non-medical agents, such as works foremen or the police, because it is thought that their condition needs urgent attention These cases include most minor accidents occurring in industry, in the home, and in the streets, and, in most areas, all accidents, whether major or minor

3 Patients are referred to the casualty department by general practitioners for a variety of reasons

(*a*) Because it has facilities which they believe to be better than their own, such as serum which has not become outdated, antibiotics which may not be available to them, or sterile dressings

(*b*) Because it has facilities which are not available in general practice, especially for cases requiring surgery under anæsthesia

(*c*) Because they want a second opinion, but do not regard the case as important enough to go through the formality of a consultant's outpatient clinic

(*d*) Because they think that the case needs hospital treatment urgently

(*e*) Because they require an X ray report 5–10% of all cases coming to certain casualty departments are sent for X ray examination to confirm, as a medicolegal precaution, the *absence* of bony injury

4 Other departments in the same hospital, or other hospitals may refer cases, mainly for minor surgery, or for postoperative outpatient dressings

5 Many casualty departments, because they deal with the admission and disposal of casual or urgent cases, are used also as the reception department for waiting-list and outpatient cases Some do this only outside normal office hours, but others do it at all times of the day

The Responsibilities

The department's responsibilities may be divided into those of treatment and those of disposal In highly organised and departmentalised areas disposal duties increase at the expense of treatment, because an increase in the number of special clinics increases the indications to refer casualty cases elsewhere

This particularly affects the treatment of fractures When accident services are inadequate to cope with all fractures, casualty departments may have to reduce fractures and refer them only for further reduction (if that is necessary) and rehabilitation Some are required to treat ambulant fractures and refer the rest to fracture services In a few places, where a well-organised and entirely adequate fracture service operates, the casualty department's responsibility is confined to diagnosis, except for the occasional fracture or fracture-dislocation which needs urgent release of pressure upon vessels or nerves

Some casualty departments control beds in a short-stay ward, undertake resuscitation and preoperative preparation, and hold cases for twenty-four or forty eight hours for clinical observation or for postoperative care

A highly departmentalised area tends to split up the work still further Children's hospitals, accident hospitals, " mainly general " hospitals (which are usually ex-municipal hospitals), and sometimes as many as three general hospitals in the same area, all maintain facilities for treating the same type of case Works first aid posts, pithead clinics, and clinics run by industrial and school medical officers contribute to the dissemination of effort

Up to one-fifth of all casualty cases may be suffering from acute superficial sepsis Where the department deals with fractures, the tendency is for acute sepsis to come among the responsibilities of the orthopædic or accident service Tendon injuries also, because they are often associated with fractures or injuries to the joints, are being included in the orthopædic surgeon's sphere On the other hand, many accident services are at present far from comprehensive The capacity or the situation of an accident hospital may limit its influence to less than half the community concerned It may accept only bone and joint cases, whereas burns, soft tissue, visceral, and head injuries are accommodated elsewhere

The segregation of accident cases from other types of surgical case has many disadvantages, and as strong an argument can be produced for the development of the accident service in close association with a general surgical as with an orthopædic unit Furthermore, it is possible that an accident hospital is less desirable than an accident service within a general hospital A " complete " hospital offers a better opportunity to mobilise various specialties for the treatment of multiple injuries, and an accident hospital may have to duplicate ancillary services, such as bacteriology, pathology, and blood transfusion units, which are better centralised

The Staff

The care of the casualty patients is in the hands of people with widely varying abilities, and, although nowadays there is a tendency for the department to

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* First of three articles dealing with some of the difficulties facing casualty departments of non teaching hospitals, and outlining a scheme for a more comprehensive accident service

[1] Hospital and Specialist Services England and Wales Statistics for the Year ended Dec 31 1952 H M Stationery Office 1954

Since the response to leucopheresis comes almost exclusively from the myeloid cells, no separation of granulocytes and lymphocytes was made The results show that it is about 3 days before cells containing ^{32}P appear in the circulation, leucopheresis carried out 24 hours after the administration of ^{32}P yields cells that are unlabelled It is therefore possible to choose a time, about the 3rd day after the dose of ^{32}P, when the peripheral leucocytes still contain only negligible amounts of labelled D N A, but when the almost mature cells in the marrow have a very high activity Leucopheresis experiments at such a time show that the activity of the cells removed from the circulating blood at the first clearance is only low But when, after the lag period of 1–2 hours, the leucocyte-count begins to rise, the cells have a high specific activity and clearly most of them come from the marrow pool of labelled granulocytes

CRADDOCK et al consider that their data show that the release of leucocytes from the marrow is " geared to the utilization rate of leukocytes in the periphery ", the cells may be migrating into the tissues or being destroyed in the circulation But the marrow tissue takes time to respond by hyperplasia to demands for more leucocytes, and sudden calls are met initially from this reserve of relatively mature cells in the marrow This reserve appears to be large, " the marrow reserve," they say, " affords a huge buffer between supply by growth, which is fixed within certain limits, and demand, which may vary very widely The rate and degree of replenishment of the peripheral blood with leukocytes under conditions of increased need is initially geared to the marrow reserves and not to the rate of growth of myeloid tissue " These results are of much interest The type of response described by the Californian workers applies to loss of leucocytes only and it remains to be confirmed that the response to inflammation or infection is indeed similar But in the meantime the idea of a large marrow reserve of mature neutrophil granulocytes, mentioned by YOFFEY, must be taken into account when explaining leucocyte reactions The idea may explain, for instance, why in acute agranulocytosis the bone-marrow is found so often to be almost entirely denuded of myeloid cells at the time of clinical onset, the answer may well be that the marrow was damaged some time before and the clinical agranulocytosis appears when the reserve pool is exhausted Compared with what we know about the erythrocyte, our knowledge of the quantitative physiology of leucocytes is indeed small, but researches like those we have described are now yielding results

Annotations

THE E E G AND THE CLASSIFICATION OF EPILEPSY

IN the past decade or so the electroencephalographic findings in epilepsy have illustrated how advances in diagnostic technique may raise problems in clinical classification For instance, a characteristic E E G pattern —bilaterally synchronous 3 per second wave and spike —is so common in petit mal that the terms " petit mal " and " wave and-spike dysrhythmia " are at times used interchangeably There are difficulties in such a usage The correlation between cases diagnosed clinically as petit mal and the occurrence of wave and-spike patterns is as high as 80% in some large series But when the position is viewed from the other direction, and all wave and spike records are screened for the type of clinical attack they show, the figures are much less convincing. Moreover, the 3-per-second wave and-spike may show slow or fast variants, though the general pattern is maintained If only " classical 3 per second wave and spike " is accepted in E E G diagnosis, then some cases which would be generally regarded clinically as petit mal will be excluded, on the other hand, if variants are included, then many cases clinically quite unlike petit mal will be found, especially in the group of akinetic and myoclonic epilepsies Indeed, in these two groups, the E E G findings, and often the response to the newer petit-mal anticonvulsants, have suggested that they are linked with petit mal, and the term " petit mal triad " has been coined to cover the three Even with a broader equation of petit mal triad and wave and spike pattern, however, a difficulty may still arise clinically in distinguishing true petit mal from psychomotor or temporal-lobe epilepsy, when the latter consists only in momentary clouding of consciousness with vasomotor change and brief automatism

There are thus arguments from both the clinical and E E G aspect against equating petit mal and wave and-spike dysrhythmia, while recognising a close link which is valuable in diagnosis The difficulty is partly one of nomenclature and may be largely overcome, as Symonds[1] suggests, by the introduction of new terms which are based on recent E E G knowledge and are untrammelled by past clinical associations

The problem has recently been considered by Clark and Knott,[2] who found that of 178 patients with wave and spike patterns only 16% had attacks which were entirely of the petit mal triad, and though 70% had these in addition to other types of attack, 30% had no attacks which could be so classified These findings illustrate clearly both the diagnostically useful correlation between the clinical and the electrical evidence, and the difficulties of considering the two as synonymous Clark and Knott also found, as have others, that classical 3 per second wave and-spike, though not its variants, is closely associated with idiopathic epilepsy, and this is in some ways the most reliable implication of the E E G evidence

The logical development in the classification of epilepsies is to group them according to the site of origin of the epileptic discharge This was envisaged by Hughlings Jackson in his conception of the aura, or " local sign," of an attack as demonstrating its site of origin The E E G, and its extension to electrocorticography and recording from the depth of the brain, is an important aid in this development, since it may localise accurately the site of electrical discharge Already, evidence suggests that the initial disturbance in petit mal may be in the thalamus, and in this sense we may soon be able to recognise with some confidence cortical, thalamic, and even hypothalamic epilepsies But the growing knowledge of the complexity and profusion of connections between cortex and subcortical structures certainly does not suggest that the initial discharge or its clinical manifestations will remain so conveniently localised

SPLENECTOMY FOR BACTERIAL ENDOCARDITIS

TEN years of antibiotics have so improved the outlook in bacterial endocarditis that two thirds of those affected may now be expected to recover In a disease which in the past was almost always fatal, this is a great advance, but there is still a challenge in the fact that 1 patient in 3 will not survive In many ultimately fatal cases, the enlist the help of increasingly senior people, there are many patients who do not see a doctor on first attendance, and some who do not see a doctor at all.

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[1] Symonds, C P *Brit med J* 1955, i 1235

[2] Clark E C Knott J R *EEG clin Neurophysiol* 1955, 7 161

Local Practitioners

In some clinics local practitioners attend at prearranged times, and see cases which are referred to them by the nursing staff, and some small towns staff the local casualty department with a rota of the local practitioners. The system has evolved in response to local demands, and often works very well.

The General Medical Services Committee of the B.M.A.[2] has recommended that help for the casualty department from local practitioners should be encouraged, because of the shortage of junior hospital officers, and according to a report of the Ministry of Health[1] general practitioners already attend to approximately 8% of casualty patients. I think that this figure includes many who do not see a doctor at all.

Residents' Rota

A second common method of supervision in small hospitals is for house-surgeons and other residents to submit to a rota of duty in the casualty department, each taking his turn to deal with the daily clinic and to attend to new patients as they arrive. The work is frequently put upon that house surgeon who is on inpatient emergency duty, and this means that calls to casualty fall on the busiest resident who is least able to attend to them promptly. This is sometimes only a nominal arrangement, and the department is actually covered by extemporisations made amongst the residents themselves—residents of all specialties "rallying round" a young colleague who is under heavy pressure of work. I believe that many administrators are quite unaware of the extent to which this system depends on the spirit of fellowship which inspires residents to help one another out of difficulties.

Casualty Officers

Most general hospitals of 200 beds or over have an establishment for a casualty officer, but frequently the appointment is shared with another department, such as orthopædics, E.N.T., eyes, skins, or anæsthetics. This is seldom attractive to the young medical graduate, and is often the last vacancy to be filled from a batch of applicants.

It should also be admitted, in spite of what has been said about the cooperation between the residents, that in some hospitals relief duties in the casualty department are irksome to residents busy with inpatient work, and are a cause of friction where the morale of the staff is low.

A few larger non-teaching hospitals have more than one casualty officer, usually a registrar or senior house officer, and a recently qualified junior house-surgeon. Here again, as in many features of this department, custom plays a greater part than reason. Some hospitals with an establishment for two casualty officers do no more work than others with one. Some have more than two, allowing generous off-duty periods for study.

Senior Casualty Officers

A recently established grade is the senior casualty officer, with the same pay and status as a senior hospital medical officer. His appointment does not exceed four years. The grade is designed to establish a more responsible and experienced type of doctor in the department, and to give the opportunity for an improvement in the standard of clinical work. It is being filled at present mainly by senior registrars who have exhausted their inpatient appointments without an early prospect of promotion, and who, for the most part, have their eyes turned elsewhere. Anyone intending to specialise in major surgery is unlikely to regard four years in a casualty department as other than a period of marking time, unless opportunities are created in the future for him to utilise the experience he has gained. With the exception of two or three teaching hospitals, where full-time consultants have been appointed, opportunities for advancement within the casualty departments do not exist.

Consultants

The day-to-day participation of consultants in the activities of the casualty department is uncommon. In some hospitals a regular weekly or twice-weekly clinic is held by a consultant surgeon in or close to the department, but the type of case he sees may be selected according to his particular interests—in septic hands perhaps, or fractures—rather than according to the severity or length of the illness.

A casualty patient may therefore receive attention at the hands of any grade in the hospital service, from senior nurse to consultant surgeon. The clinical severity of the condition is not the only consideration which determines the quality of attention. The status of the medical attendant tends to rise with the amount of work at the clinic, but even this is not always the governing factor, and established custom plays a great part.

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2. Brit. med. J. 1953, i, 103.

Parliament

The Laissez-faire Loaf

IN the House of Lords, on June 7, Lord HANKEY, who rose to ask the Government for information about the bread of the nation, pointed out that in approving the report of the Cohen Panel the Government had overruled their own experts. The result, he said, was not a health loaf, but a whitewashed political loaf, denatured, shorn of its bran, with its store of Nature's best replaced by three synthetic products of a chemical factory. It was a loaf that could not be produced without improvers and bleachers. Since the agene fiasco he believed that Parliament should not sanction a bread that could not be made without an improver. Four improvers were now permitted—chlorine dioxide, potassium bromate, ascorbic acid, and an aeration process. The last was less suspect than the three chemical improvers. For the most part the millers had adopted chlorine dioxide. This choice made Lord Hankey uneasy, for chlorine dioxide was twice as powerful as agene and might therefore be twice as dangerous. In his view it was not free from suspicion. It was known to destroy vitamins E and B_1 and the essential fatty acids, and it had lately been suggested that lack of this beneficial trinity, due partly to low extraction of flour and partly to the use of improvers, was influencing the growing prevalence of diseases such as coronary thrombosis, lung cancer, and leukæmia. The protection against ill health which Nature provided in the grain was being whittled away to meet a carefully fostered craving for white bread. The synthetic substances that it was proposed to add to the 70% bread would not make good the loss, even if the industries concerned could be relied on to supply them. He urged the Government to accept the advice of their own experts and stand firm on 80%-extraction bread, but this time without chemical improvers.

"Bread and flour of high extraction without added oxidising agents, and margarine and shortening made with less hardening of fats, would be important factors in decreasing some very serious diseases of civilisation."

Lord DOUGLAS of BARLOCH said that a persistent endeavour was being made to pretend that starchy flour was equal to or better than wholemeal. The last experiment used in support of this thesis was conducted in two German orphanages. Yet in fact it proved nothing except that if you took a number of undernourished children and fed them with anything they would make infection is subdued but death follows from the mechanical effects of the damaged valve , in others, the infection is never controlled in spite of appropriate antibiotic therapy In such cases it has been suggested that the infection is maintained by the presence of septic infarcts in the spleen, and from time to time splenectomy has been advocated

In pre-antibiotic days, Polowe[1] reviewed 15 cases in which splenectomy failed to prevent a fatal outcome More recently, Fellinger and Weissel[2] in Germany and Giraud and his colleagues[3] in France have tried the operation with antibiotic cover, but their results have been equivocal In America Lingeman et al,[4] from Indianapolis, report 3 cases in which operation appeared to be the deciding move that achieved a cure All 3 patients had had episodes of splenic pain, and infected infarcts were found, although the spleens had not been palpable before operation

There is no evidence from the few cases that have been reported to suggest that splenectomy should be widely undertaken in the treatment of bacterial endocarditis , but the possibility that splenectomy may help should not be dismissed out of hand

PELVIC ARTERIOGRAPHY

ALTHOUGH cerebral arteriography is now a well-established means of localising intracranial lesions only recently has the use of angiography been extended to other sites in the body , and there is now much interest in its possible value in the diagnosis of pelvic disease The first accounts were of pelvic arteriograms after translumbar puncture of the aorta,[5 6] and though Hartnett[7] *described the operation as* a "*simple procedure*," no British workers seem to have accepted his reassurance In 1952 Sutton,[8] in this country, and Borell et al ,[9] in Sweden, showed that pelvic angiograms could be obtained by percutaneous retrograde injection of the femoral and iliac arteries , the Swedish workers have continued to use this method, and an excellent monograph by Fernstrom[10] is now available, from which the value of the technique may be assessed

The femoral artery is punctured just below the groin and a 'Polythene' catheter is introduced up the external iliac artery to a point near the aortic bifurcation (Bilateral filling is important to get the greatest diagnostic help) A pressure syringe is used to inject 40 to 50 *ml of opaque* solution within three seconds Using this technique, 700 injections have been given to 448 patients There have been no complications worse than urticaria, nausea and vomiting From the many beautiful illustrations in Fernstrom's monograph, it is easy to appreciate the disturbances of the normal vascular pattern typical of uterine fibroids, as distinct from ovarian cysts, to pick out tubal pregnancies, and often to define the site of the placenta Yet it is doubtful whether this technique, which has yielded much valuable experimental evidence has a place in everyday practice Except in placental localisation, the information it gives will not commonly be required and in the definition of the placental site soft tissue radiography, as developed by Reid[11] and Whitehead[12] gives comparable results and avoids what must sometimes be a trying experience for the patient

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[1] Polowe, D *Arch Surg* 1939 38 139
[2] Fellinger, K Weissel W *Dtsch med Wschr* 1952 77 499
[3] Giraud, G Cazal P Zatour H Levy A Puech P *Arch Mal Cœur* 1954 47 410
[4] Lingeman C J Smith E B Battersby J S Behnke R H *Arch intern Med* 1956 97 309
[5] Dos Santos R Lamas A C Caldas J P Arteriographie des membres et de l aorte abdominale Paris 1931
[6] Coutts W E Opazo L Banderas Bianchi T Sanhueza O *Amer J Obstet Gynec* 1935 29 566
[7] Hartnett L J *Ibid* 1948 55 940
[8] Sutton D *Brit J Radiol* 1952 25 320
[9] Borell U Fernstrom I Lindblom K , Westman A *Acta radiol Stockh* 1952 38 247
[10] Fernstrom I *Ibid* 1955 suppl 122
[11] Reid F *Brit J Radiol* 1953 26 406
[12] Whitehead A S *Ibid* p 401

SALIVARY CYLINDROMA

THE term "cylindroma" was first used by Billroth in 1859 to describe a tumour of peculiar histological pattern, in which alternating cylinders of cells and hyaline material are arranged round a central cavity which may contain mucus Gradually the term has come to be applied to salivary, and sometimes to bronchial, adenomas of this pattern In salivary tumours the name has been extended to apply also to adenomas composed of small dark cells resembling basal cells, with few mitoses, arranged round cystic cavities, sometimes in one or two layers The hyaline material and mucus are usually Schiff-positive

The present-day emergence of "cylindroma" from the welter of names describing salivary tumours has been explained by Harrison[1] in a recent Hunterian lecture on ectopic mixed salivary tumours In a study of 82 of these growths treated over sixteen years, he found that whereas two-thirds of the 29 patients with "mixed" adenomas were alive and well up to fourteen years after treatment of the primary growth, those with a cylindromatous tumour showed a disturbingly high rate of recurrences and mortality 50% of 46 patients were dead within eight years, and another 25% had frank local recurrence Only 8 patients were alive and well and only 4 of these for five years or more In 9 cases there was metastasis to cervical lymph-nodes and in 6 metastasis to viscera and skeleton

The grave prognosis of the cylindromatous type of tumour prompted a detailed study Harrison found this type was more common in ectopic sites 66% of cylindromas were outside the major salivary glands the commonest site being the hard palate , all the tumours found at the base of the tongue were cylindromas Two thirds of the tumours were in females, usually between 30 and 70 years of age Lemaître et al[2] found cylindroma most commonly in the parotid and submaxillary glands but Berdal and Mylius[3] agree with Harrison that ectopic sites are more usual The tumour can occur in any part of the anterior-foregut region and respiratory tract down to the lower bronchi It presents clinically as a slowly growing swelling, most commonly of the hard palate It may be small or involve the whole palate Ulceration is common, but it is often symptomless unless it invades the maxillary sinus, when there is pain, or the nasal cavity, when obstruction results The course is one of relentless recurrent growth, with a tendency to invasion of the skull[4] Metastases occur late and are found in the lymph-nodes, lungs,[1] bones,[3 4] brain,[1] liver,[1 5] and kidney[5]

The results of treatment are uniformly poor, whether by radium, X rays, or surgery, either singly or combined Harrison observed recurrence after treatment in two thirds of his cases up to twelve years after treatment of the primary tumour The best treatment seems to be wide radical excision of the surgically accessible tumours[1 3] Biopsy before the histological pattern is destroyed by irradiation is important,[4] so that the surgeon may be aware beforehand of the need for wide excision Radiosensitivity is low, particularly when bone is invaded.[3]

The behaviour and results of treatment of cylindroma prompt the question whether it is not in fact a histological variant of salivary carcinoma Bauer and Bauer[5] classify it as adenocarcinoma, noting the tendency to invade capsular tissues, nerve-sheaths, and lymphatics Willis,[6] emphasising the malignant potentialities of salivary adenomas, illustrates a cylindromatous *tumour* which recurred as frankly undifferentiated carcinoma after excision Both Lemaître et al[2] and Berdal and Mylius[3] point out, however that pure cylindroma should be dis-fairly rapid progress in weight and height The fundamental question to be answered was what was the effect of eating bleached and denatured bread and other flour products, not over a year, but over a life-time

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[1] Harrison K *Ann R Coll Surg Engl* 1956 18 99
[2] Lemaître F et al *Acta otolaryng Stockh* 1936 24 112
[3] Berdal P Mylius E *Ibid*, 1954 suppl 118, p 32
[4] Russell H *Brit J Surg* 1955 43 248
[5] Bauer W H Bauer J H *Arch Path* 1953 55 328
[6] Willis, R A Pathology of Tumours London 1953 p 340

Lord Douglas took exception to the use of such words as “ enrichment ” and “ fortification ” when applied to a flour that was really impoverished Nor did he agree with the Cohen Panel's view that people would necessarily get what was needed for nutrition from the rest of their diet The rest of their diet was also steadily being impoverished by processing and chemical treatments He was against compulsion, but he believed that people should be told the truth If it was desired to go on producing flour which has been bleached, it should be labelled “ Bleached with chlorine dioxide ” When people knew how their food was being impoverished they would make up their minds about what was best for them

Lord TEVIOT pointed out that large combine bakeries were buying up the smaller bakeries, where most of the wholemeal bread was made Those who stood up for the health of the people had a tremendous vested interest against them in the millers, and on top of that there was the vested interest of those who made the medicines to cure the evil which the other people had created Lord BALFOUR of BURLEIGH, as a former chairman of the Medical Research Council, regretted that the Government should disregard the opinion of their scientific advisers

Lord STAMP, returning to the effects of improvers, said that chlorine dioxide had no harmful effect on animals, and extensive experiments at the Cereals Research Station showed that of the substances important for nutrition it destroyed only vitamin E No other change was noted except some oxidation of the unsaturated fatty acids These facts were known to the M R C committee when the use of chlorine dioxide was sanctioned Prolonged storage would have much the same effect Nor was bread our only source of these substances It had been calculated that in an average mixed diet bread made from untreated flour would supply only about 20% of our intake of vitamin E Sterility, muscular dystrophy, and coronary disease had all been attributed to lack of vitamin E, but treatment of these conditions by vitamin-E medication had been disappointing Deficiency of vitamin E and unsaturated fatty acids had yet to be associated definitely with impaired health in human beings There seemed, therefore, to be no case for condemning the use of chlorine dioxide as a flour-improver on these grounds But that was not to say that it could be regarded as completely satisfactory The search must continue for a method which was above all criticism and which was acceptable to all sides

Lord SEMPILL wanted to see the establishment, under the Ministry of Health, of a counterpart of the Food and Drug Administration of the United States No new chemicals should be allowed in food processing and production before they had been adequately tested for their toxic effects

Lord HADEN-GUEST thought that previous speakers had exaggerated the effects of bread on the general health situation The physical condition of the population was better now than it had ever been He was certain that a large proportion of the people of this country would refuse to eat wholemeal bread, because they did not like it.

Earl ST ALDWYN, parliamentary secretary to the Ministry of Agriculture, said that the Government did not require the use of improvers, they did not even advise that improvers should be used, they merely refrained from preventing their use It would have been wrong to use statutory powers to rush the millers into giving up the agene process without allowing them time to make other arrangements It remained true that no-one had yet succeeded in demonstrating that flour treated with agene did any harm to human beings. Admittedly agene had been found to cause hysteria in dogs, but no such evidence had been found against any of the improvers now used Experts were not yet clear about the part which vitamin E played in the human diet But bread was by no means the only source of vitamin E, and, though flour treated with improvers had been eaten in large quantities for many years, there was plenty of evidence to show that vitamin E was present in large amounts in the blood of the inhabitants of this country No-one had yet succeeded in demonstrating that lack of this vitamin caused any known illness Fatty acids were also present in other foods Calculations made by the Ministry of Agriculture, Fisheries, and Food suggested that the amount of fatty acids in the British diet was 40% more than before the 1914–18 war There was no evidence which would justify the Government in prohibiting the use of improvers, but they would be kept under close scrutiny In reply to a question from Lord HANKEY, he said that the aeration process was in use but needed expensive machinery

Turning to the composition of flour, he pointed out that here again the Government were not requiring people to eat the whiter bread, the Government were merely refraining from denying it to them The Government were now proposing to take the subsidy off bread, and in the future bakers would be free to produce whatever bread they liked—or the consumers liked—at a free market price Regulations would be laid before Parliament under the Food and Drugs Act, 1955, requiring that all flour should contain not less vitamin B_1, nicotinic acid, and iron than was at present required to be restored to the whiter flour For technical reasons the minimum extraction-rate of 80% for subsidised flour was difficult to enforce The keen demand for the whitest available National bread had led traders to take advantage of the difficulties of enforcement The result was that in practice the flour being used for subsidised National bread contained less of the token nutrients than the flour used for unsubsidised bread

The Government had been chided for not accepting the advice of their own experts They were not so much rejecting the advice as being confronted with conflicting advice Into the balance between the two scientific points of view the responsible Ministers had thrown two other considerations which were not the concern of scientists as such First, there was the political view that by and large it was undesirable to require people to eat one thing when they obviously preferred another Secondly, there was the administrative view of the difficulty of enforcing regulations prescribing a minimum extraction-rate for flour The Government would await the advice of the Food Standards Committee, who would be asked to consider whether, in addition to the requirements about the token nutrients, more extensive regulations governing the composition of flour and bread were needed to protect consumers

Crown Privilege for Documents

In the House of Lords on June 6, Viscount KILMUIR, the Lord Chancellor, made a statement on the Government's policy on Crown privilege for documents and oral evidence The problem, he said, was not a new one but had come into prominence of recent years, because, since the Crown Proceedings Act, 1947, the Crown had been liable to be sued in the same way as private persons This change had thrown into relief its privileged position with regard to the production of documents and other evidence In the course of his statement Lord Kilmuir dealt specially with medical reports and records

In the recent case of Ellis *v* the Home Office, he recalled, judicial criticism was directed at a claim for privilege for reports made by a prison doctor which might have been relevant to the claim for negligence against the Crown Here the Government had two proposals to make The first was that ordinary medical records kept by departments in respect of the health of civilian employees should not be the subject of Crown privilege In the case of medical reports and records in the Fighting Services the Government considered that privilege should still be claimed, so far as proceedings between private litigants—usually matrimonial proceedings—were concerned Service doctors owed a special duty to the commanding officer, and frank reports were essential. It was also important in the Services that a man should report readily to the medical officer, who was a doctor tinguished from "mixed" adenomas with areas of cylindromatous pattern Russell[4] considers that cylindroma merits separation as a clinical and pathological entity from salivary adenocarcinoma because of its relatively slow growth, uniform histological pattern, and the rarity and late appearance of metastases, the converse features are usual in salivary adenocarcinoma Whatever the truth about the classification or nomenclature of the cylindroma, it seems that recognition of the microscopic pattern by the pathologist is the first step in the attack on this rare but serious disease

DIFFUSING CAPACITY IN EMPHYSEMA

BECAUSE of the many difficulties involved, there have been few lengthy studies of the course of emphysema, and the one by Bates and his colleagues[5] is therefore all the more welcome They observed 59 patients with clinical evidence of emphysema for as long as five years in some cases and for three years on the average In addition to other criteria, patients were admitted to the series only if dyspnœa was present at all seasons of the year and if no cause other than respiratory disease could be found for it Patients in whom pulmonary heart disease had developed were not included Pulmonary function tests—vital capacity, functional residual capacity, mixing efficiency, maximum ventilatory volume, and diffusing capacity—were carried out initially and at intervals thereafter, so that the results could be compared with clinical progress There were 17 deaths during the observation period, 4 from non-respiratory causes and the other 13 (76% of the deaths) from pulmonary heart disease According to life tables, the expected number of deaths for the period was 4 Clinical deterioration in individual cases was reflected in the results of all the function tests with one important exception the approaching onset of pulmonary heart disease was heralded only by a fall in the diffusing capacity of the lungs

The patients were also divided into groups according to the degree of dyspnœa present, and the results of pulmonary function tests in each group were compared with those in the other groups and with the results of the same tests in a group of patients with seasonal dyspnœa and evidence only of chronic bronchitis The mean values of the function tests declined progressively from the chronic bronchitic group to the most dyspnœic emphysema group—a "poor prognosis" group—which comprised patients who died within six months of their last function test There was a considerable overlap, however, in the findings in the different groups, and the only test which clearly separated the ones at opposite ends of the scale of clinical severity (the chronic-bronchitic and the "poor prognosis" groups) was the test of diffusing capacity

The diffusing capacity of the lung may be defined as the quantity of reference gas (Bates et al used carbon monoxide) which passes per minute from the alveoli into the blood at a pressure gradient of 1 mm Hg The lack of correlation between the results of this test and those of the determinations of vital capacity, functional residual capacity, mixing efficiency, and maximum ventilatory volume is in accordance with the observations of Shepard et al[6] in patients with chronic obstructive disease of the respiratory passages To explain the discrepancy, they postulated that a fall in diffusing capacity is related mainly to impairment of the blood gas exchange surface of the lungs, whereas the results of the other tests reflect principally the degree of obstruction of the airway Diffusing capacity in emphysema can therefore be reduced by actual loss of alveoli, by diminution of the blood-supply to the alveoli which remain, or by thickening due to œdema from right ventricular failure Bronchial obstruction, however, by producing irregularity of gas distribution and thus limiting the effective area of blood gas exchange, may also reduce the diffusing capacity,[5 6] and a lessening of bronchospasm may therefore account for an improvement in the figures which was noted in one of Bates et al 's cases It has also been shown that the validity of the test is increased if it is carried out when the patient is doing sufficient exercise to ensure that the whole of the available vascular bed is brought into use[7] Bates et al are convinced that tests of diffusing capacity are an indispensable aid in the prognosis of emphysema, because, although tests of ventilatory function correlate well with the degree of dyspnœa, the reduction of the pulmonary capillary bed which precedes the onset of right ventricular failure may not be accompanied by an appreciable increase in breathlessness and can be detected only by a fall in the diffusing capacity

Further work on the value of estimating the diffusing capacity in chronic obstructive disease of the respiratory passages is clearly desirable, for if it is found that current tests, or refinements of them, are capable of detecting the onset and indicating the extent of pulmonary damage, clinical analysis of this condition will gain greatly in precision Moreover, if effective remedies for chronic bronchitis are discovered, it should be possible to predict how far they will relieve disability in the individual case

RUPTURE OF THE SPLEEN

THE spleen not uncommonly ruptures after injury to the upper abdomen, such as a motor accident in which the driver is forced against the steering wheel Spontaneous rupture is a well-known complication of diseases in which the spleen is greatly enlarged, particularly malaria, and it has been reported after infarction It is usually all too plain that some intra-abdominal catastrophe has befallen, and the diagnosis may not be difficult But delayed rupture, with signs appearing some time after the injury, is a well known diagnostic trap, and X-ray examination may help

In straight films of the normal abdomen, the spleen is visible in whole or in part, especially when the stomach and splenic flexure contain gas When the spleen is small and clearly seen on the radiograph, rupture is a very unlikely diagnosis When the spleen has ruptured its outline is either partly or wholly obliterated The fundus of the stomach may be displaced medially and the splenic flexure downwards There may be slight elevation of the left side of the diaphragm, and any associated retroperitoneal hæmorrhage or œdema may obscure the upper part of the psoas shadow on the left and the outline of the left kidney

Deaver,[8] Frimmen Dahl,[9] and O'Neil and Rousseau[10] have placed the radiological signs on record In a recent paper, Wang and Robbins[11] analysed 33 cases to determine the frequency with which these signs are found 25 showed complete and 6 partial obliteration of the splenic outline The 2 patients in which the organ looked normal had small intracapsular hæmorrhages 18 showed complete and 7 partial loss of the left renal outline, and in 6 the kidneys were displaced downwards In roughly half, the left psoas shadow was more or less obliterated, and there was displacement of the stomach or colon Rather less than a third showed fracture of the ribs, and in 3 there was widening of the dorsal paravertebral space by upward extension of retroperitoneal hæmorrhage or œdema

Prof W H WYNN, of Birmingham, died on June 11.

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[5] Bates D V Knott, J M S Christie, R V Quart J Med 1956 25 137

[6] Shepard R H Cohn J F Cohen, G Armstrong B W Carroll D G Donoso, H Riley R L Amer Rev Tuberc 1955 71 249

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[8] Deaver J M Ann Surg 1911 113 477

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[10] O Neil J J Rousseau J P Ann Surg 1945 121 111

[11] Wang C C Robbins L L New Engl J Med 1956 254, 445

not of his choice but in whom he must have confidence this was especially so in the case of venereal disease Some of these considerations applied to prison doctors, who owed a special duty to the prison governor, and their reports and records should still be privileged in proceedings between private litigants

Where, however, the Crown or the doctor employed by the Crown was being sued for negligence, the Government proposed that privilege should not be claimed With regard to both proposals he added, there might be reports of a specially confidential character which ought still to be privileged The Government also proposed that, if medical documents or indeed other documents, were relevant to the defence in criminal proceedings, Crown privilege should not be claimed At present many of these documents were made available only on the more serious crimes, such as murder, manslaughter, and rape

Milk Tablets for School-children

In the House of Commons on June 6, Mr **Michael Stewart** prayed against the regulations permitting local authorities to supply milk tablets in schools if milk of the proper quality is not available at a reasonable price[1] He asked for an assurance that children who were supplied with milk tablets were not likely to suffer in nutrition, health, or in any way, and that in every important respect these milk tablets were as good as milk Had the emergence of the milk tablet over the horizon, particularly in the great cities, caused suppliers to modify their view as to the price they should charge[2] Last year about a quarter of the milk supplied to schools was supplied at a discount If we could get all milk supplied at the same discount we could save £270,000 a year—more than the Government's proposed economies in milk for nursery-school children

Mr **Horace King** agreed that by supplying milk tablets we might bring the suppliers to heel but we also faced the possibility of a dangerous setback in milk consumption by our children Sir **Charles Taylor**, who declared his interest in the milk industry, pointed out that the supply of school milk in $^1/_3$-pint bottles required a special bottling machine, the bottle probably cost as much as, if not more than, its contents

Mr **Dennis Vosper**, parliamentary secretary to the Ministry of Education, said that the regulations were necessary to ensure the continuance of school milk He gave an assurance that the milk tablets were nutritionally equal to liquid milk and that they had the approval of the Ministry of Food They were more attractive to school-children than dried milk and the cost was no greater, but little less, than that of liquid or dried milk There had been criticism of milk tablets in certain schools, but the Ministry had no positive evidence that they had been much abused

When the Minister of Education took over the supply of milk, he recalled, it was thought reasonable to expect a discount on bulk supply, as in hospitals and other institutions Local education authorities were therefore expected through normal tendering procedure to secure reasonable terms for the supply of milk Their original efforts met with organised resistance, and the Public Accounts Committee in their third report in 1955–56 recommended that all possible steps should be taken to secure that milk was supplied to schools at genuinely competitive prices That report was sent to local authorities towards the end of last year together with a letter saying that the Minister would give the authorities support in any action they thought fit to take, even to the extent of stopping the supplies of school milk He was glad to say that had not been necessary It would be wrong to think that the milk tablet was the only method employed to secure reductions in price In May, 1955, of 83 county boroughs 55 were paying the maximum retail price for milk In May, 1956 only 2 county boroughs were doing so He hoped that it might not be necessary for the local authorities to use the regulations and that the desire of the Minister and the House that supplies of liquid milk should be available to all school-children at a reasonable cost would be achieved If that did not happen it might be necessary from time to time to appeal for the use of tablets of dried milk, not in preference to liquid milk but as an adequate alternative to paying an unreasonable price The motion was by leave withdrawn

Medical Bill

In the House of Lords on June 6 Viscount **Kilmuir**, the Lord Chancellor, introduced the Medical Bill, a measure to consolidate enactments relating to medical practitioners with corrections and improvements made under the Consolidation of Enactments (Procedure) Act, 1949

QUESTION TIME

Health Visitors in Scotland

Replying to a question, Mr **James Stuart**, Secretary of State for Scotland said that staff employed on health visiting duties in Scotland at the end of 1955 were equivalent to 1160 whole time visitors, about a third not being fully qualified The Working Party on Health Visitors, in their recent report, proposed a target of 1 visitor to 4300 population, which for Scotland as a whole would be met by just under 1200 visitor

R A F Medical Officers and Flying Experience

Replying to a question, Mr **Nigel Birch**, Secretary of State for Air, said that a number of medical officers were trained to fly modern operational aircraft and served for a time as pilots They were subsequently employed in special posts at the Institute of Aviation Medicine, at certain flying stations and Command headquarters, and at the Air Ministry where their flying experience was of particular value From time to time they were replaced by younger men with similar training, so that the most up to date experience was always available Medical officers not trained as pilots were encouraged to fly as passengers whenever this could be arranged

Vacancies for Geriatric Physicians

Replying to a question, Mr **R H Turton**, Minister of Health, said that 7 posts of assistant physician (geriatrics) were vacant throughout England and Wales There was 1 vacancy in the Newcastle, Leeds, Sheffield, South East Metropolitan, and South Western regional hospital board areas and 2 in the Manchester area

Appointments for Registrars of Non-teaching Hospitals

Replying to a question, Mr **Turton** said that 52 consultant posts in general surgery had been filled in the last two years Of those appointed at least 13 had held appointments as senior registrars in non teaching hospitals

Mr **S J McAdden** Is the Minister aware that there is considerable frustration among registrars in hospitals other than teaching hospitals, in that they feel they are not getting a fair crack of the whip in respect of these appointments? Has the Minister in mind some method of improving the position of such men, who, in other than teaching hospitals are doing a considerable amount of surgical work, and whose salary in some cases is considerably less than £1000 a year? Mr **Turton** The selection of senior registrars is made on the advice of statutory appointments advisory committees, on which the majority of members are medical men

Proposed Closure of a London Hospital

Replying to a question Mr **Turton** said that he was considering the views which had been expressed regarding the proposal of the North East Regional Hospital Board to close the St George in the East Hospital London, E 1, at the end of July, 1956 He hoped to reach a decision shortly

Retirement Pensions

Mr **S T Swingler** asked the Minister how many doctors and dentists in the National Health Service would be eligible for pensions on retirement in 1958, and what proportions they were of the doctors and dentists in the scheme—Mr **Turton** replied About 3500 doctors and 1500 dentists representing approximately 14% and 17% respectively These figures do not include doctors and dentists employed full time in hospitals

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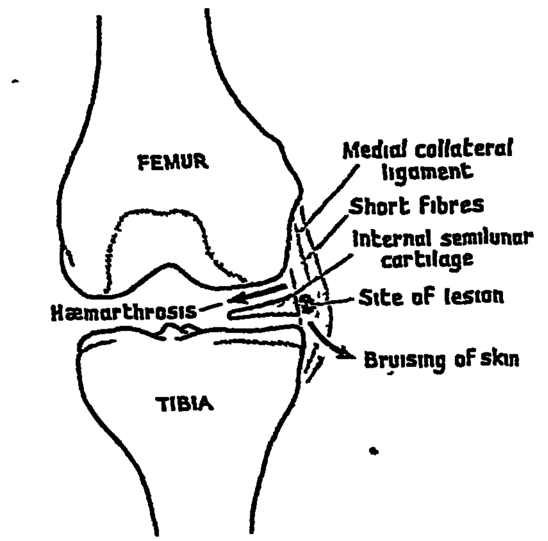
1 See *Lancet* Feb 25 1956 302 *Ibid* Mar 3, 1956 p 610



Suggested site of the lesion in skiing strains of the knee, showing directions of extravasation of blood

hæmatoma caused at the time of injury probably tracked downwards along the line of the ligament

Abduction of the knee caused pain in all patients If the pain was severe, preventing relaxation of the internal lateral ligament, an examination under anæsthesia was made No complete tear of this ligament was found

Effusion into the knee joint was present in all cases, and was first detected between one and six hours after injury The accompanying figure shows the suggested site of the hæmatoma, its probable entry into the joint, and its track along the fibres of the ligament

In 2 patients there was a more rapid onset of tense effusion and hæmarthroses were aspirated. 2 other patients had large bloodstained effusions aspirated some days after injury Patients with hæmarthrosis differed from those with severe strain only in the rate of onset and the tension of the effusion.

20 patients with severe injuries were examined radiographically, but in no case was any flake of bone detached from the insertions of the internal lateral ligament Within the period of the follow-up no case of calcification in the ligament (Pellegrini Stieda syndrome) was found

Treatment

Complete rupture of the internal lateral ligament was first excluded and the fluid was aspirated where necessary A firm, well-padded crêpe or flannel bandage was applied and the knee kept on pillows in full extension Early quadriceps exercises were started with particular emphasis on vastus-medialis control, these exercises were supervised by a physiotherapist

When quadriceps tone returned and the effusion had subsided, the patient started walking and the exercises were intensified Skiing was again allowed when quadriceps tone was good and there was no return of effusion after full activity In many cases there was still tenderness in the joint line at this stage

Early in the season 2 patients with severe strains were treated in plaster-of-paris cylinders for four weeks, in accordance with the practice in some Austrian centres Both patients were comfortable until the plaster was removed, when considerable quadriceps wasting was found with instability of the knee-joint Despite physiotherapy for weeks, 1 of these patients had to be physically downgraded

Follow-up

The time the patients were off full duty varied with the nature of their work and the severity of their injuries, the average time for a soldier on heavy duties was one month Patients with minor strains of the knee were often skiing again two weeks after injury, but only a few skied with any enjoyment in a shorter time this may be a useful guide to people sustaining injuries to the knee on short winter holidays 4 patients with moderately severe strains took part in competitive skiing between one and two months after their injuries

43 patients were seen at three to six months after injury All had functionally normal knees and were on full duties The patient who was downgraded was not followed up 20 patients still had slight tenderness in or below the joint line on the medial side 2 of these complained of such tenderness, and manipulation under anæsthesia six months later relieved this symptom 2 other patients had tenderness after eighteen months but functionally normal knees No patient had symptoms suggesting a cartilage tear

Meniscectomy was not carried out on any of my patients

Review of Previous Cases

In the preceding year meniscectomy had been undertaken on account of skiing injuries in 6 cases at the Military Hospital at Klagenfurt

Case 1 had previously had a "soccer" injury with locking of the knee, locking while skiing was precipitated by performing a "kick turn"

Case 2 had a definite "bucket-handle" tear of the internal cartilage, but he had had knee symptoms, particularly after playing "soccer," before starting to ski

Case 3 was operated on two weeks after injury He had pain and effusion Extravasation of blood was found under the capsule of the joint; the internal cartilage was removed, but no tear was found.

Case 4 was operated on a month after injury He had pain and effusion The internal cartilage was removed, but no tear was found

Case 5 was operated on a month after injury The internal cartilage was loose peripherally, but no tear was found.

Case 6 was operated on six weeks after injury, on account of instability of his knee-joint The internal cartilage was loose peripherally, but no tear was found. This patient tended to exaggerate his symptoms and he failed to coöperate in postoperative physiotherapy He was off full duty for six months, but when I examined him nine months after meniscectomy he had a functionally normal knee He skied throughout the next season without his knee troubling him

Discussion

Wiles (1949) states that the semilunar cartilages are seldom damaged in skiing injuries to the knee, although such an injury is often diagnosed. He says that the injured knee is relieved of the weight of the body at the time of injury, and the cartilage is endangered only by a strain during a Telemark turn when the weight is on the leading leg The coronary ligament or the internal lateral ligament is the structure likely to be damaged

Morrison and Coughlin (1950) reviewing 254 injuries in experienced skiers and novices, reported only 47 strains of the internal lateral ligament They note that most of the severe injuries of all types were to experienced skiers travelling at high speed They subsequently found that in 3 cases of knee strain there were cartilage tears, but they do not exclude previous trauma 1 of their patients had a complete rupture of the internal lateral ligament with disruption of the joint Their treatment of strains of the knee was more conservative than mine, and they used plaster-of-paris cylinders in severe cases They do not report any follow-up

Conclusions

The common skiing injury to the knee in a novice is a tear of the short capsular fibres of the internal lateral ligament True tearing of the avascular part of the cartilage is unlikely to result directly from the injury, but dislocation of a previously torn cartilage may be precipitated

The mechanism of the injury, in which abduction is a constant factor, suggests that the internal cartilage is not in danger of being trapped between the tibia and the *rotating* femur as in "soccer" or similar injuries This is substantiated by the fact that in two seasons no case of *cartilage* tear was found that could be directly attributed to a skiing injury I suggest that the site of the lesion is the attachment of the short fibres of the ligament to the cartilage, the bruising and hæmarthrosis show that the site is vascular, and rapid healing can be expected

Where it is certain that there is not a complete tear of the internal lateral ligament, patients are most satisfactorily treated by the restoration of quadriceps tone and early mobility The application of plaster cylinders in incomplete tears causes quadriceps wasting, even if quadriceps drill is practised while the cylinder is on, and the knee is unstable when the plaster is removed

I would like to thank Brigadier J H Huston for permission to study the patients, and Lieut Colonel J M Matheson, R A M C, for his encouragement

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In the Mental Hospital *

THE RISE AND FALL OF MENTAL NURSING

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THIS series of articles, and especially those by Dr Bickford[1] and Dr Cameron and his colleagues,[2] demonstrating the vital rôle of nurses in the recovery of mental hospital patients, has brought a breath of fresh air into this electrically charged field Their nurses achieved much with chronic patients, how much more may be expected from a similar approach to early cases It is therefore the more urgent to ascertain the deeper cause of the present decline of mental nursing as a profession This decline, over the past twenty years coincides with the spectacular rise and spread of "modern physical methods of treatment" Is there perhaps an inverse relation between the two?

1956 is a suitable year in which to appraise the present situation, for one hundred years ago was published the most important over-all contribution to the welfare of mental hospital patients ever made *The Treatment of the Insane without Mechanical Restraints*, by John Conolly

Briefly, before the 1830s, as far as this country is concerned, difficult, violent, delirious, or suicidal patients were automatically clapped into various restraining devices ranging in general from chains to strait waistcoats, and in detail according to the technical ingenuity of the physician Patients were regularly bled, purged, vomited, blistered, and drugged That the popular mind erroneously equates insanity with violent behaviour arose in part from the cruelties practised on patients and their reactions to a punitive, suppressing environment

THE MOVE AGAINST RESTRAINT

The first *attempt to* establish the study of the insane as a specialty was made by William Battie, incidentally one of the very *few* psychiatrists to become President of the Royal College of Physicians of London He wrote that "such unhappy objects ought by no means to be abandoned, much less shut up in loathsome prisons as criminals or nuisances to the society" His kindly spirit led him to proclaim[3] that "the regimen in this is perhaps of more importance than in any distemper" Pargeter,[4] in 1792, wished to "abolish at once recourse to chains and cords," and Arnold,[5] in 1809, felt they "should never be used but in the case of poor *patients*" The Retreat at York, opened by the Society of Friends in 1796, was the first institution in which insane persons were treated as human beings by a "regimen" of "moral treatment," and thus was the birthplace of all subsequent reform culminating in the great movement for "non restraint" Tuke's stirring and challenging account[6] of the practice of the Retreat inspired all subsequent work with the insane and led directly to Conolly's great reform By the 1830s its kindly spirit had spread to the doctors of Lincoln Asylum In 1839 Conolly at Hanwell Asylum made the bold and successful experiment of putting into practice the *principle of non restraint in a large mental* hospital—acknowledged the world over as the major advance in the history of the guardianship of the insane The attitude of attendants changed from that of keepers to that of nurses, violence became exceptional, refractory patients took their place and worked in the hospital community, the recovery-rate rose to more than two thirds of all admissions

"The great principle of the non restraint system is to exclude all hurtful excitement from a brain already disposed to excitement On this principle it abolishes mechanical restraint and *also, on this principle* it regulates every word, look, and action of all who come *in contact with the insane*"[7] The *influence of a healthy* person's mind became the chief therapy in mental disease, and the mental nurse its most important agent

> "The physician who justly understands the non restraint system well knows that the attendants are his most essential instruments They may often be considered, indeed, his best medicines He confides the most confidential duties to them he entrusts them with the happiness, by day and by night, of all the patients under their especial care To control the violent, without anger, to soothe the irritable, without weak and foolish concessions, to cheer and comfort the depressed, to guard the imbecile and the impulsive, and to direct all"[7]

TRAINING OF NURSES AND DOCTORS

Thus the demand arose for mental nurses and their organised training In 1854, Dr W A F Browne, at Crichton Royal Mental Hospital, commenced a course of lectures comprising "a full, if popular, discussion of insanity in the different forms, intelligible by the shrewd and sensible, if somewhat illiterate class of persons employed as attendants and nurses"[8] In 1891 the Royal Medico Psychological Association held the first examinations which "remained for many years the only, uniform national system of training and certification of *any body of nurses in any country*" †[9]

The training of mental nurses was paralleled by the training of *mental hospital doctors*

> "The resort to instruments of mechanical coercion was inconsistent alike with any *medical consideration of the various* forms of mental *disease*, and *their* causes, as it was with attention to the numerous *auxiliary or moral means of cure* which are so greatly relied upon where the ancient methods of

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* A group of articles chiefly concerned with the value of active occupation and work for mental patients and the means whereby it is best provided

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† The first final examinations of the General Nursing Council were not held until 1925

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In England Now

A Running Commentary by Peripatetic Correspondents

Of late years the number of physicians has risen steeply and now it is an impossible task for a national association to arrange meetings for all of them Indeed if pædiatricians neurologists, dermatologists and research-workers are included there must be over 1000 This probably was foreseen by Dr Hugh Barber of Derby when he founded the East Midlands Physicians' Association sixteen years ago For some time it met twice yearly in the county towns of Leicester, Derby Nottingham, and Lincoln These four counties and little Rutland later joined with South Yorkshire to form the Sheffield region, and that city is now included in the rota of meeting-places

The West Midlands Physicians Association was founded six years ago and though it admits to its meetings a limited number of pædiatricians pathologists, radiologists and other specialists its founder members were all physicians Its meetings are held twice a year one in Birmingham and one in a peripheral hospital It has visited Stoke-on-Trent, Wolverhampton, Coventry, Shrewsbury and Leamington This year it has met at the Royal Stafford Infirmary where Fowler of Solution fame Erasmus Darwin, and William Withering were physicians

The meetings are developing a routine We forgather at 10 30 A M for 11 A M for a cup of coffee Papers occupy the rest of the morning Lunch is always eaten standing up so that physicians can move about to talk to friends for with the years many acquaintances have ripened into friendships Further papers are given in the afternoon and after tea in the winter meeting in Birmingham This is also the occasion of the annual dinner, to which we have three times welcomed the president of the Association of Physicians of Great Britain and Ireland

Perhaps the highlight of our social activities was the spring meeting at Leamington last year, when a party of over 70 physicians and their wives, collected for dinner at Stratford on Avon to see *All's Well That Ends Well* ' That title expressed what many felt Even if there cannot be a national association for all regional societies offer an ideal alternative method of advancing medicine and promoting friendship

* * *

On getting home from the maternity hospital, a mother noticed on her baby's back two small red papules These were symmetrically placed one on each side near the angle of the corresponding scapula Somewhat worried and puzzled, she consulted her doctor who thought they were pressure sores and prescribed appropriate treatment This, however failed to arrest the development of the papules which became more prominent Seeking a second opinion, the mother was astonished and alarmed to learn that her infant had been born with two additional nipples The second opinion added that there was nothing much he could do about it and counselled resignation to the Divine Will

There the situation rested till the mother and infant duly attended the B C G clinic and the nipples " were measured and the readings recorded, as required, on form B C G 4 The mother's relief was considerable

Now we make only one mark, and tell everybody everything

* * *

I laid down my pen

' Just tell me what you think of this will you ? *THREE MONTHS' PRACTICAL COURSE for Prospective Brides and Housewives in the Domestic Sciences, including the Cookery and Service of Meals, the Ablution of Crockery, Silver, and Cutlery, the care of Footwear, Furniture, and House Fabrics, Labour saving Bedmaking* and a few more attractive items we must think up *Fees, 30 guineas, inclusive of Full Board and Lodging* That's only 10 guineas a month, and dirt cheap But what have I left out ? "

' Answering the telephone "

Legible transcription of telephone messages What about car cleaning and maintenance ? "

" Not ' replied my wife firmly ' within the terms of reference "

' A pity Then how about whitewashing at weekends ? When I could lend a hand ?

' No ' But you've forgotten the ordinary Monday mornings '

Oh yes, stupid of me Let's say, *Labour saving Bed making and Laundry*

Whose labour are you saving ? '

' Yours of course We must have seminars in something - I know, *Seminars in First-aid and Sick Nursing* We could easily get Aunt Madge to come and stay '

Not a bit of it I'll gladly oblige for a week or two '

" Fair 'do's We'll take it turn and turn about *Vacancies for* two ? three ? how many could you be doing with ? *Vacancies for* (say) *two students on Feb 1st Apply Box Number* '

Where are you going to stick this ? she asked

' *Times* agony column of course

" How much is it going to cost ? '

" Dunno About two or three pounds I suppose '

' You can buy us a really good dinner for two or three pounds You can be getting the car out '

But I wish we had tried it just to see what happened

* * *

Now that we have put away our boots and listened to our wives telling us what fools we are to go on playing at our age we have a chance to ponder philosophically over the lure of the oval ball

For many years I have been convinced that as a sect, we rugby players must be kinder to our wives than the average husband Our incidence of divorces, wife-beating convictions, and bills for post-argument fur coats must be significantly below the average All the frustrations of the week's work are vented to atmosphere on Saturday afternoon Pity the opposing forward who lies on the ball a second too long the wing forward who always seems to be off side (' O K skipper I'll get him next scrum ') and so on When it's all over one returns home in a state of monastic calm framed by a few convivial pints and ready for the problems of next week Will some enterprising statistician please do a controlled study to prove my hypothesis

' What's that, dear ? Of course I ll need them next season, after all, I'm only 35 "

* * *

The patient who knows the answers can be a great help to the peripatetic paperhanger and ours listened unsympathetically to our account of blisters on the wall and the needling technique which we developed for reducing them (see this column May 26) He was unimpressed by the undoubted success of the manœuvre ' Your paper wasn't wet enough," he said, ' unless a thick paper is pretty well soaked through that sort of thing can happen What you should do is measure and cut five or six strips of paper at a time and paste them all By the time the fifth has been pasted the first will be ready to go up after a second coat of paste "

Paperhangers, by the way, vary in status There are the consultants, such as my patient, who do difficult and complicated operations on ceilings, and then Registrars who work on walls but make perfect butt-joins with matching of patterns. Mere practitioners in paperhanging prefer unpatterned paper and allow a good half-inch of overlap In spite of our original contributions to the subject we foresee no upgrading until we have mastered butt-joins

* * *

News from School —After the exams, during the somewhat empty weeks before the end of term, certain of us plan to make *many hundred* pounds of fudge and toffee, sell it, and buy a well for an Indian village Others of us intend making teddy bears to the same end, but I reckon the market for fudge has a more secure bottom A good watery well costs £70 we are told and saves a five mile walk to a cholera ridden water hole —through, as our informant made no bones about telling us (unfortunate phrase ?) man eating tiger territory and prednisone inhibit spontaneous fibrinolytic activity in cirrhosis, they do not significantly reduce the intensification encountered in response to the injection of adrenaline We very much doubt therefore, whether this mode of treatment would be successful in preventing or controlling the hæmorrhage associated with intense fibrinolysis which has been frequently reported by surgeons operating on patients with cirrhosis although the mechanism was unrecognised

H C KWAAN
A J S MCFADZEAN

Department of Medicine
University of Hong Kong

RHESUS(D) FACTOR IN SARCOIDOSIS

SIR,—Through the courtesy of the physicians of the Brompton Hospital I have examined the records of 64 patients with sarcoidosis in whom the blood-groups have been determined Histological evidence had been obtained in 46 (72%) of these Lungs or hilar lymph-nodes were involved in all cases The blood groups were as follows

Rh(D) factor		*A B O group*			
Negative	*Positive*	*O*	*A*	*B*	*AB*
11 (17%)	54 (83%)	38 (59%)	22 (34%)	3 (5%)	1 (2%)

In comparison, the blood-groups of 419 inpatients of this hospital, determined during the past three months, were as follows

Rh(D) factor		*A B O group*			
Negative	*Positive*	*O*	*A*	*B*	*AB*
71 (17%)	348 (83%)	199 (48%)	164 (39%)	39 (9%)	17 (4%)

These figures support those reported by Dr Smellie (June 2) from King's College Hospital, showing a similar prevalence of Rh(D) negative blood in the patients with sarcoidosis to that in the general population, and are additional evidence against the suggestion by Dr Cudkowicz (April 21) that this blood-group might be more frequent in patients with sarcoidosis

Brompton Hospital
London S W 3

K M CITRON

EXTRADURAL HÆMATOMA

SIR,—Mr Whalley (May 26) remarks that unskilled anæsthesia in this condition causes increased cerebral congestion which may lead to tentorial herniation.

We feel that it is so essential in these cases for the airway to be perfectly clear that an experienced anæsthetist should always be present and should pass a cuffed endotracheal tube after clearing the mouth and pharynx of all obstruction In some cases this can be done after spraying the larynx with local anæsthetic solution, but in others the administration of a small amount of muscle relaxant with or without a minimal quantity of thiopentone may also be necessary A suction apparatus should be ready in case the patient vomits at this stage The improvement in the patient's condition after intubation is most gratifying, and troublesome hæmorrhage during operation is minimised The endotracheal tube should be connected to an open-circuit type of anæsthetic apparatus (we employ Ayre's T piece for this purpose) Oxygen and, if necessary nitrous oxide or trichloroethylene is administered It is most important to avoid any positive pressure in the anæsthetic circuit The proposed scalp incision is then thoroughly infiltrated with a local-anæsthetic solution When the cerebral compression has been relieved by the surgeon any tendency of the recovering patient to struggle before completion of the operation can be controlled by the administration of fractional doses of muscle relaxant and/or thiopentone

This procedure has been followed in 13 out of 14 consecutive cases of extradural hæmatoma operated on by one of us, with recovery in all but 1—a child aged 6 years whose compression had been present for thirty hours when first seen

The guiding principles we believe, should be the establishment and maintenance of a clear airway, the administration of a high concentration of oxygen, the avoidance of all struggling and straining, and the use of the absolute minimum of anæsthetic agents In this way cerebral venous congestion is diminished and good operating conditions are obtained

KATHLEEN BELL
PATRICK CLARKE

Newcastle General Hospital

FEMALE CHROMATIN IN MALE EUNUCHOID

SIR,—The implications of the following case seem to us sufficiently far reaching to justify its brief and early publication in the hope that investigation at other centres may yield confirmatory findings

The patient aged 35 is apparently a typical male, obese eunuchoid He has not undergone puberty Both breasts are enlarged, but the tissue composing them is solely fat (confirmed by biopsy) The penis is small and the fully descended testes soft and tiny, but there are no external features whatever of hermaphroditism—no evidence of persistence of mullerian duct structures Laparotomy (Prof J H Louw) revealed no female organs in the pelvis in particular no uterus, and no third gonad even in the renal area The follicle stimulating hormone in the urine was positive at 48 mouse units (Dr A Kipps)

Bilateral testicular biopsy was performed and histological examination showed total absence of spermatogenesis, with a reduced number of tubules composed entirely of Sertoli cells The Leydig cells were massed together in clumps and appeared to contain a good deal of lipoid There was no hyalinisation or fibrosis (unlike the typical appearance in the Klinefelter syndrome) No ovarian tissue was seen

Most unexpectedly in an excellent section of skin some 60% of cells contained the typical female sex chromatin ' This has been confirmed by a second piece of skin from the other side of the body

This patient thus illustrates prepubertal primary hypogonadism in an anatomical male with no trace of hermaphroditism, yet whose cell nuclei are of the type associated with the genetic female

W P U JACKSON
B G SHAPIRO
C J UYS
R HOFFENBERG

Groote Schuur Hospital and
Medical School
University of Cape Town
South Africa

Appointments

BLAIR J D M B Glasg D A part time consultant anæsthetist Sheffield R H B (duties in Grimsby and Louth)

POND MARGARET M M R C S D C H M O London County Council public health department

Colonial Appointments

BEAUBRUN M H M B Edin D P M M O, grade B mental hospital health department Trinidad

BOYD P I M D Lond M O H (grade A) Trinidad

BURY E J B A Camb M R C S D P H D M S Western Region Nigeria

COMMISSIONG L M M B Edin M R C P E D T M & H D D M S (institutions) Trinidad

DUKE B O L M B Camb D T M & H medical research officer (grade I) West African Council for Medical Research Western Region Nigeria

FURNESS J E M B Lond senior M O (clinical) Northern Region Nigeria

GREWAL N N S M B Punjab F R C S E senior surgeon Public Hospital Georgetown British Guiana

HOOD P A M B Edin M O Brunei

LIU S M B Lond D A specialist anæsthetist Mauritius

MOORE G W M R C S L S M senior M O (admin) Northern Region Nigeria

ROGERS H C M D C M Queen's Univ Ont L M C C registrar (surgical) Barbados

SEARSON G J A M B N U I senior M O Barbados

SUTCLIFFE, W M M B Leeds M O Northern Rhodesia

SWAN T T, M CH N U I F R C S I specialist surgeon, Western Region Nigeria

THOMSON I G M B Aberd D T M & H senior M O (admin) Northern Region Nigeria

TUST E M D Warsaw, D T M & H district M O St Lucia Windwards

WILLIS G C M D McGill M O (medical registration) Singapore

Letters to the Editor

BREAD

SIR,—The report of the Panel on Composition and Nutritive Value of Flour is not clear on one point The panel state that they were "impressed by the evidence for the demand for white flour and white bread" Yet they do not give this evidence in their report Were the results of any surveys of consumers' demands available to them? The only quantitative evidence which they give is to be found in Appendix I of their report This shows that in 1953 the sale of unsubsidised white bread was 4 4% of total sales and that by 1955 this figure had fallen to 0 8% According to the report, a $1^3/_4$ lb loaf made from subsidised National flour cost 7½*d*, whereas loaves from flours of lower extraction-rates cost from 10½*d* to 1*s* *For a large family this price differential is* clearly very important But for an individual eating half a loaf a day, it amounts to between 1½*d* and 2*d* a day—*approximately the cost of one cigarette* During the period *to which these figures apply, large sections of* the population were enjoying relative economic prosperity Yet only a very small proportion were prepared to pay the price equivalent of one cigarette to eat white bread *Further, this proportion fell steadily during the* period This quantitative evidence, which the panel give in their report, would appear to indicate that the demand for white bread from the public was very small *Could the panel explain their reasons for neglecting this* evidence, which they give without comment, and could they give us the evidence for the popular demand which so impressed them? At the moment, their report appears *to rest on a basis of surmise, and one foundation stone* of fact seems to have been rejected

Physiology Department,
Edinburgh University

R PASSMORE

RESPIRATORY INVOLVEMENT IN POLIOMYELITIS

SIR,—*Professor* Trueta and *Dr* Agerholm (June 2) state that tracheotomy, by leading to chronic pulmonary infection with further diminution of ventilation, can be a tragic complication in cases of severe residual paralysis *following* poliomyelitis and that, in the absence *of an effective cough, closure of the stoma may be* dangerous It could be added that aspiration may have infected the lungs before tracheotomy is performed and *the stoma then allows the frequent removal of con*taminated bronchial secretions by deep suction which, in the acute phase, is necessary at intervals throughout the 24 hours

The possibility mentioned *by Professor Trueta and* Dr Agerholm of leaving an orally introduced tube in situ seems impracticable, since the period of bulbar paralysis, though limited, may last for weeks, during which *the patient* would *presumably* have to remain anæsthetised, and there is also the likelihood of laryngeal ulceration

In *bulbospinal* poliomyelitis, tracheotomy is not done for the sake of administering artificial respiration by positive pressure but for the sake of a clear airway—of which, when accompanied by efficient bronchial suction, it is the best and sometimes the only guarantee As Professor Trueta and *Dr Agerholm say, the decision* to perform a *tracheotomy must rest* with the man on the spot His first duty is to save the patient's life, if necessary by tracheotomy, which we believe should not be reserved *for situations without* full hospital facilities, but rather the opposite

Whitley Hospital
Coventry

J F GALPINE
H S KANDER

SIR,—May I add a short note to the wise comment on this subject made by Professor Trueta and Dr Agerholm, and incidentally fall in with their prudent suggestion that experience in this field should be pooled?

Certainly some cases of severe respiratory involvement need tracheotomy I think that, apart from urgent *transportation problems, these are relatively few* In the past, I have treated successfully with Dr Harwood Stevenson at the Royal National Orthopædic Hospital a group of cases of considerable severity by means of bronchoscopic suction supplemented by skilled physiotherapy It is possible to do this even when the patient is in a cabinet respirator and I have found that it is, to a surprising degree, a life saving measure It is an axiom of laryngology that tracheostomy or laryngostomy tubes must be removed at the earliest possible moment in order to avoid the well known harmful sequelæ These patients are obviously extremely vulnerable to these sequelæ and the nature of their lesion delays or prevents the closing of the tracheal stoma

It seems to me, therefore, that the adoption of tracheotomy as a prophylactic measure, or as anything approaching *routine,* would *be a serious mistake* The need for it can often be avoided by adequate bronchoscopic suction and judicious physiotherapy

London, W 1

A M ZAMORA

PHENOBARBITONE POISONING TREATED WITH BEMEGRIDE

SIR,—Dr Hurdle and Dr Lane are to be congratulated on their valuable and very interesting contribution to your issue of June 2 May I, however, venture to comment on a few points in their *discussion of the* case, which I feel may be important in treating future cases?

They very *correctly* state that bemegride does not appear to be toxic, and they draw attention to the danger that those *who treat such cases may fail to realise that the drug may have to be given for a long time to prevent regression* But I would not agree with their suggestion that it seems more sensible to mix the bemegride with the intravenous transfusion fluid in the bottle rather than to inject it intermittently Apart from the disadvantage this method would entail of not knowing what the effective concentration of bemegride has to be in the intravenous fluid (a difficulty *the authors themselves* encountered), had the intermittent method of administration[1] been continued (provided spasm *of the vein* had not *occurred), the boy might have recovered consciousness* earlier The criteria *of the* "safe state" have a very safe guide as my *colleagues* and I have always found, further courses of both drugs are given when regression sets in after the safe state had been once restored[2,3] It is important that the safe state be restored as soon as possible, for this minimises both the immediate risk to the patient's life and the remote risk associated with possible complications of prolonged barbiturate *coma*[1-4]—*hence the necessity* of removing the barbiturate effectively from the system as soon as possible

Besides these points, one should not entirely *dismiss* even the remote possibility of toxic signs developing The early signs are vomiting or retching, which may be accompanied by *slight flicker of the fingers*[1] and *twitching of facial and* limb muscles This was noticed in one of our patients successfully treated (a girl $2^1/_2$),[3] to whom the drugs were given in the same course, after the signs of the safe state had appeared If intermittent administration is adopted, one can effectively discontinue the drugs before serious toxic signs develop

It is, I feel, unwise to use amiphenazole (in addition to bemegride) only when the respiration is depressed *It has been established that amiphenazole* besides being a respiratory stimulant is also a barbiturate antagonist

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[1] Shulman A Shaw F H, Cass N M Whyte H M *Brit med J* 1955 i 1238
[2] *Perinpanayagam,* M S *Lancet* 1955 ii 620
[3] Perinpanayagam M S Nicholls G, Osmond, J D *Brit med J* 1955, ii 912
[4] Perlstein Meyer A *In* Advances in Paediatrics, edited by *S Z Levine London* 1955 vol 7 p 222

Obituary

KNUD FABER

M D Copenhagen, LL D Edin , F R C P E

Knud Faber was appointed regius professor of medicine in the University of Copenhagen in 1896 when he was 34 years of age During the 36 years he held office he influenced almost every side of medical life in Denmark, for he was a teacher as well as a scientist, an investigator as well as a clinician, and an administrator as well as a planner

[Schmidt New York

Besides holding the university chair he was chief of the medical department of the Royal Hospital in Copenhagen, and a fellow countryman K H K recalls that "he introduced laboratory investigations into daily clinical work and wrote the first manuals on laboratory methods He inspired an almost constant flow of contributions to contemporary clinical and theoretical medical science—articles, theses, and books And he lectured on clinical medicine for 36 years to every man or woman who qualified as a doctor in Denmark His own scientific work was mainly concerned with diseases of the alimentary tract—gastritis and peptic ulcer, colitis and anæmia, and diabetes mellitus

"His vivid and crystal-clear mind and his strong personality led him into a long and fierce battle for a system of medical administration which today is accepted by everybody in our country, but which caused a revolution 50 years ago He wanted a firm *medical* control of the administration of public health, of hospitals, nursing, pharmacy, dentistry, midwifery, and the treatment and prevention of tuberculosis He succeeded in creating each of these branches of medical administration, though it took 18 years of laborious negotiations

"Fifty years ago he organised the fight against tuberculosis , and he lived long enough to see empty sanatoria As dean of the University of Copenhagen he was an enthusiastic promoter of the development of the new university at Aarhus—Denmark's only other university—which is now flourishing In his old age he took a special pleasure in taking part in academic meetings at the Aarhus University After his retirement in 1932 his firm hand was still felt in decisions taken by his successors in his many fields of activity He wrote books on his public and private life, and even in his later years he spoke on several occasions Faber has served his country as very few have done, and his personal contribution to the promotion of the health of his countrymen has never been surpassed "

But Faber also served medicine outside Denmark In 1926 he gave a lecture tour in the United States and in 1931 he reported on the medical schools of China He had many contacts with his colleagues all over the world and was a member of the academies of medicine in Ireland Belgium Bologna, Stockholm, and Paris In this country the University of Edinburgh had conferred on him the honorary degree of LL D and he was a fellow of the Royal College of Physicians of Edinburgh and an honorary fellow of the Royal Society of Medicine He died on May 3 at the age of 93

BERNARD HART

O B E , L M S S A

Dr Bernard Hart, radiologist to Doncaster Royal Infirmary, died on June 6 at his home at Armthorpe at the age of 72 Like so many of the early workers in radiology he was disabled by the rays he studied and for many years he faced surgical and medical treatment for the burns and anæmia which he contracted

He joined the radiological department of Sheffiel Royal Hospital as a lad and later became radiograph there At first he was mainly interested in technic problems, but his work turned his attention more a more to the growing clinical possibilities of the new ray Shortly before the 1914–18 war he began to study med cine, but his qualification was delayed by active serv with the Royal Navy He finally took the L.M S S , 1923 and within a year or so was appointed to the staff Doncaster Royal Infirmary Despite ill health he carrie on his practice there for many years

EDWARD NORMAN JAMIESON

O B E , F.R C S E, L D S

For many years the name of Norman Jamieson h been a household word in the Outer Hebrides H work as surgeon to the Lewis Hospital was centred Stornoway, but his help and advice were availab to the most remote island croft from the Butt of Lew to Barra Head

He qualified, both in medicine and dentistry, fro the Edinburgh medical school in 1924, and after holdi resident appointments at the Edinburgh Royal Infirma he spent some years in Paris as resident surgical offic to the Hertford British Hospital He returned to Scotlan to take the Edinburgh fellowship in 1928 and the became registrar at Perth Royal Infirmary In 19 he was appointed to the Lewis Hospital in Stornow He found it a small cottage hospital with meagre faciliti Twenty-five years later, mainly thanks to his ener and foresight, it is an up-to-date general hospital wi 61 beds in its wards and plans for a further 30 a well advanced

Jamieson's professional life was shaped by his islan practice In the early years at least he had to offer h patients treatment in all surgical specialties with th help of a general-practitioner anæsthetist Indee at first he also acted as unofficial consulting physici to the hospital Later, modern transport and th improved facilities under the National Health Servic enabled him to bring his patients to hospital an increased his surgical scope His mastery of many specialties, and his enthusiasm for them al made him a valuable teacher, and his house office and registrars found Lewis an effective if unrecognis postgraduate school Despite many years of ill healt and his arduous and exacting work, he often visite the Edinburgh medical school for refreshment and stud and he was in Edinburgh when he was taken ill H died there on June 3 at the age of 56 He leaves a wido and a daughter

J C R-G writes "Norman Jamieson was a gener surgeon of the highest order Much of his work w obstetrics, a specialty in which he was particular interested and skilled, but he was equally at home gynæcology, orthopædics, ophthalmology, surgery the ear, nose, and throat, dentistry, and radiolog His work was done with meticulous care for detail an with insistence on the highest standards

"His visits to patients across land and water migh entail travelling by car, plane, or boat, over fords b horse and cart, or many miles on foot , journeys whic must have been a severe strain on his health Yet h courageously overcame the effects of a serious flyin accident and the tragic death of his younger daughte adjusting his life to ill health in a way that made o almost forget that he carried these additional burdens

"No matter how busy the day, he always remaine calm and unruffled , welcoming the visitor with a smi and anxious to show the stranger over the hospital— the growth and development of which he had pla such a large part and in which he was justifiably prou The kindness to the stranger and the welcome to h many friends reached their height in the hospitalit of his home where, in his quiet unassuming manne he would discuss photography fishing, and shootin He was a keen and knowledgeable sportsman and it w a pleasure to see him return to work refreshed an invigorated after a holiday in Harris the island he love so much and knew so well He will long be remembere with respect, gratitude, and reverence in every islan home ' and a good synergist to bemegride[1]—thus the cumulative effect of antagonising the barbiturate by a combination of both drugs would help to restore the patient to the safe state sooner After all, in a patient constantly liable to respiratory depression, no harm is done by using a respiratory stimulant, such as amiphenazole, which has been proved to be quite safe[1–3 5–]

Hope Hospital
Salford
M S PERINPANAYAGAM

FORT MIT DEM SPRAY!

SIR,—In your leader of June 2 prominence was most appropriately accorded to Henry of Mondeville and his progressive injunctions against surgical interference with wounds It may be of interest to record a previous appreciation of Mondeville in your columns[8] given on the occasion of the discovery and first edition of his great surgical work by Julius Pagel (1851–1912) Mondeville stands out as one of the most original figures in medicine and surgery of all times It should be added in fairness, however, that he continued the tradition of Theodoric and his predecessor Hugo of Lucca at Bologna It is the latter whom Julius Pagel called "the intellectual instigator of pus-less wound treatment" The *Surgery* of Theodoric embodying Hugo's views is now being translated into English (by E Campbell and J Colton) Books I and II have already appeared,[9] and I am reviewing them in the forthcoming issue of *Isis*

London N W 10
WALTER PAGEL

ANÆSTHESIA IN OBSTETRICS

SIR,—Perhaps your readers might be interested in the following simple method, which I have used and taught for many years, for preventing inhalation of vomit during obstetrical anæsthesia I call it the "two-pillow technique" and it is for use where the obstetrical bed cannot be tilted, when anæsthetising for forceps delivery, &c

One pillow is placed beneath the patient's scapulæ and a second pillow is placed under the patient's head The anæsthetic sequence is nitrous oxide, oxygen, trichloroethylene, and ether (or similar) from a semiclosed circuit The anæsthetist's attention is focused on the patient's breathing, and, in the light plane of anæsthesia used, impending vomiting or actual vomiting is immediately recognised with experience, by some irregularity in the breathing If this occurs, the pillow under the patient's head is immediately whipped away and the head turned to one side The patient is now in the "tonsil" position and any vomit will travel away from the larynx by gravity and can be dealt with by appropriate means

I regard this simple manœuvre as a safeguard to be used in addition to the usual precautions when anæsthetising patients who may have stomach contents, and I have not personally encountered any difficulty in managing such patients by this technique

River Hospitals
Joyce Green
Dartford Kent.
JOHN BULLOUGH

SIR,—Two questions which deserve answers have so far received little attention

Why is the danger from vomiting less when anæsthetics are given in domiciliary midwifery? Is not this fact related to the use of anæsthetic machines in hospitals by persons not familiar with them?

Vomiting under an open mask is quickly perceived and compels attention towards clearing the airway Vomiting under a mask strapped on to the face is often mistaken for coughing by the inexperienced administrator, who therefore sits tight and hopes for the best, with disastrous consequences

London S W 18
D A. BUXTON HOPKIN

PARAPLEGIA FOLLOWING SPINAL ANÆSTHESIA

SIR,—In his letter of June 2, Sir Francis Walshe refers to my citing my "single experience of the ampoule contaminated through invisible cracks by the coloured fluid in which it was immersed" Your readers should not infer that the incident is unique Came[1] reports 12 contaminated ampoules, revealed by discoloration of the contents, in his own practice as an anæsthetist while Steinberg[2] detected in this way 4 faulty ampoules in the course of "approximately 1000 spinal anæsthetics" Steinberg continues "If I had used the four ampoules mentioned, it is conceivable that I might have had 4 serious neurologic sequelæ which would have placed spinal anesthesia in a very unfavourable position"

Dr Lerman (June 9), having witnessed in the East an assembly of patients suffering from the complications of spinal analgesia, advocates that the procedure should be abandoned He makes no mention of the training, skill, and experience of the anæsthetists concerned Nor does he mention the number of silent witnesses in the local graveyards despatched by general anæsthetics incompetently administered Surely he would not, by the same argument, recommend that general anæsthetics should be discontinued

Oxford
R MACINTOSH

HORMONES AND BREAST CANCER

SIR,—In your leading article of May 12, you rightly conclude that, despite increasingly radical surgery and more intense radiation, there is "little improvement in survival-rates and often only questionable benefit to the patient" Indeed, reading about the poor results after adrenalectomy or the destruction of the pituitary gland with radon implants or similar methods, one wonders whether the authors of these methods are not in danger of losing sight completely of more basic principles and reality, in the glamour of severe surgical procedures In these I include ultra-radical mastectomy, pelvic exenteration in advanced genital cancer, and bilateral oöphorectomy followed by adrenalectomy or hypophysectomy

For about seventy years the ovaries have been removed in recurrent breast cancer, in the belief that the flow of œstrogens is undesirable and may provoke further carcinogenesis But after removal of the ovaries it is above all the thyroid gland which begins to elaborate more thyroid hormone, which in turn acts as a metabolic anti carcinogen and improves the condition of the cancer patient Why then should one continue to remove the ovaries if simple thyroid medication has the same effect, especially when thyroid hormone is coupled with androgens?

Already in ancient Egypt women with breast cancer were given seaweed in order to increase the working capacity of the thyroid gland by means of the iodine content of the seaweed, and an improvement in cases of breast cancer was observed (Ebers Papyrus)

Furthermore, as you remark, we know that after bilateral oöphorectomy the adrenals elaborate more undesirable steroid ovarian hormones, counteracting our endeavours to eliminate from the body the last traces of œstrogen After adrenalectomy, it is the thyroid gland—to a certain extent an antagonist of the suprarenal gland—that elaborates more thyroid hormone than before Why then is *it* necessary to remove an endocrine gland, especially the adrenal gland, when thyroid by mouth improves the hormonal metabolism of the cancerous body at least *to* the same extent, if not to a great deal more?

Adrenalectomy in cases of advanced cancer is a retrograde step The immediate disappearance of pain after adrenalectomy is due to the administration of cortisone, but cortisone could be given together with thyroid if one

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5 Holten C *Lancet* 1955 i 181
6 Montuschi E Wickenden P D *Ibid* p 622
7 Webb J W S *Brit med J* 1955 ii 56
8 *Lancet* 1890 ii 846
9 See *Ibid* 1955 ii 910

1 *J Amer med Ass* 1946, 132 685
2 *Anesthesiology*, 1950 11 257

BENNO SILBIGER

M.D Prague. LL.D Graz M R C S

Mr Benno Silbiger, consultant ear, nose and throat surgeon to Paddington Green Children s Hospital and associate chief assistant to the E N T outpatient department of St Bartholomew's Hospital London died on May 10

He was born in Brno Moravia, in 1895 and studied law in Vienna and Graz, where he took his doctorate in 1919 Attracted to medicine he began his medical studies at the University of Vienna and continued them in Prague graduating M D in 1923 The same year he joined the E N T department of the German University clinic in Prague and two years later, with a Czechoslovak State scholarship, he was sent to Vienna for postgraduate training at the laryngo-rhinological department under Hajek, and the department of otology under Neumann In 1926 he returned to Prague where he became deputy director and later acting director of the university E N T department

In 1939 political events forced him to leave and he came to England where he took the Conjoint diploma in 1942 from St Bartholomew s Hospital Medical College In 1942 he was appointed E N T surgeon to the Central Middlesex Hospital an appointment which he held until 1946 when he joined the staff of Paddington Green Children s Hospital He was also honorary consulting E N T surgeon to the School of Opera

W G writes "Not only was Benno Silbiger a well known E N T surgeon he was also well known as a lover of music and he seldom missed a concert or operatic event He had personality, charm and wit and he leaves many friends and colleagues to whom his death came as a sad shock In their memory he will always be cherished"

Diary of the Week

JUNE 17 TO 23

Monday, 18th

KING S COLLEGE Strand W C 2
5 15 P.M Prof. C N H Long (Yale University) The Glycogenic Function of the Adrenal Cortex

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road W 12
4 P.M. Dr Lynne Reid Pathology of Chronic Bronchitis

INSTITUTE OF NEUROLOGY National Hospital Queen Square W C 1
5 P M Prof Eric Cruickshank (West Indies) Dietary Neuropathies in Jamaica

Tuesday, 19th

KING S COLLEGE
5 15 P.M Professor Long Observations of the Secretory Mechanisms of the Anterior Pituitary

INSTITUTE OF DERMATOLOGY Lisle Street W C 2
5 30 P.M Dr D I Williams The Use of Vitamins in Dermatology

Wednesday, 20th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr D W Henderson Laboratory Studies in Respiratory Infections

INSTITUTE OF DISEASES OF THE CHEST Brompton S W 3
5 P.M Dr George Simon Some Difficulties in Interpretation of Tomograms of the Chest

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr Henry Haber The Dyskeratoses

Thursday, 21st

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
8 P.M *Urology* Dr W Gillespie Dr W Goldie Dr K F Anderson Urinary Infections

KING S COLLEGE
5 15 P.M. Dr Stephen Kuffler (Johns Hopkins University) Mechanism of Inhibition.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE 26 Portland Place W 1
7 30 P M Prof P C C Garnham Looking for Parasites in Brazil

Friday, 22nd

ROYAL SOCIETY OF MEDICINE
8 15 P.M *Obstetrics and Gynaecology* Mr Philip Rhodes Prolapse of the Umbilical Cord

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M Prof F C Ormerod Surgery of Postcricoid Pyriform Fossa Carcinomata

INSTITUTE OF NEUROLOGY
5 P M Dr W. A. Cobb Dr Michael Yealland A Case of Subacute Progressive Encephalitis (Film)

Notes and News

THE HEBERDEN SOCIETY

THE annual Heberden Round was conducted by Dr GEORGE KERSLEY at the Bath Royal United Hospital on June 1 The round is a clinical tour de force at which uncommon or controversial aspects of one or more mesenchymal diseases are discussed before an informed and critical audience After the round some scientific papers were presented

Dr D P PAGE THOMAS and Mr J T DINGLE (Bath) described their studies of the in vitro respiration of normal and rheumatoid synovial membrane The diseased membrane was found to have a relatively higher rate of anaerobic respiration They also demonstrated the effects of serum from rheumatoids and normal controls upon the growth of embryonic bone This work was still in its preliminary stages and no conclusions were drawn Dr D G SCOTT and Dr A G S HILL (Stoke Mandeville) were concerned with the possible antigenic potentialities of synovial membrane They had injected human synovial tissue into rabbits Antibodies from the rabbit serum were later tagged as globulin, with fluorescein and applied in solution to microscopic sections from a number of human organs The labelled antibody globulin was seen to react specifically with reticulin Antibodies to renal glomeruli similarly prepared did not so react

The shortcomings of cortisone in the treatment of rheumatoid arthritis has directed attention back to gold Dr M R JEFFREY (Bath) described his work on the distribution of ^{198}Au labelled calcium aurothiomalate after its injection into laboratory animals No significant localisation was found The presence of inflammation appeared to hasten the absorption and excretion of the injected gold, normally a very slow process

The apparent specificity for rheumatoid arthritis of the modified Rose-Waaler tests led Dr ROWLAND ALEXANDER (Edinburgh) to attempt to track down and isolate the agglutinin responsible He described the methods used to precipitate the active fraction from the serum proteins and to partially purify it by electrophoresis on filter-paper The highly concentrated fraction was tagged with fluorescein and then allowed to react with sensitised sheep red blood-corpuscles as in the Rose Waaler test As yet he has not been able to locate the specific fluorescent material on the agglutinated cells

Reports that the metabolism of 17-ketosteroids in gout was abnormal led Dr E R COOK (Bath) to study the pattern of excretion of 17 ketosteroids in this disease By chromatography he measured the relative concentrations of dehydroisoandrosterone etiocholanolone and androsterone, the three major components of urinary 17 ketosteroids His preliminary results showed no difference in the pattern of gouty and normal individuals

Mr J H PEACOCK (Bristol) spoke of his investigations of the peripheral circulation, by arteriography and plethysmography in Raynaud s disease acrocyanosis and rheumatoid arthritis, and in normal individuals Contrary to expectation, he did not find that the incidence of abnormalities among the rheumatoid patients he studied differed appreciably from his controls Dr J H GLYN (London) followed the course of rheumatoid arthritis, in a group of patients receiving cortisone with a battery of serological tests The tests did not prove of any practical value in distinguishing between non-specific disease suppression and true disease remission; Finally Mr NORMAN CAPENER gave a delightful account of the integrated movements of the pelvic and lumbar joints of erect man in action He emphasised the importance of this subject to the understanding and treatment of disorders of the hip joints

DESIGNING CENTRES FOR PRACTICE

IF in the National Health Service, an architect makes a building cost more than it need, he is depriving the public of some other building somewhere else In an address to the Architectural Association in London on May 30 Dr STEPHEN TAYLOR said that the new challenge to architecture was to combine efficiency with economy—and humanity The purpose of a N.H S building was not to glorify the doctors the committee or the architect, but to serve the *patients* (One way of judging whether it was good or bad was to see who was going to use the front door) The efficiency needed could be attained only by endless attention to detail does not prefer really massive doses of testosterone with thyroid.

And now all the furor against endocrine glands is directed against the hypophysis, and destruction of this gland is attempted with sword or atomic fire. But here again, after destruction or removal of the gland, it is thyroid and cortisone which must be administered to keep the body going. Technical surgical perfection, at which we all aim, cannot replace common sense in cancer therapy.

After all, cancer is essentially a disease of cell metabolism brought about by some failure in the intracellular enzyme systems, which are under the control of the thyroid gland, so surely it is to this that our activities should be directed?

As far back as 1932, it was shown by means of the Warburg apparatus that hormones influence cell respiration. The transformation of a normal cell into a cancer cell depends on the respiratory quotient of the tissue. How far hormones, and especially thyroid, can influence cell respiration and fermentation, via phosphorylation, cannot for the moment be said. But it seems to me that cancer formation starts and goes on when a carcinogenic substance hits continuously thyroid-deficient tissues. If that is so, our therapeutic marching orders are clear.

London, W.1 A. A. LOESER.

TREATMENT OF NEPHROSIS WITH PREDNISOLONE

SIR,—Dr Arneil (April 14) does considerable service to the interests of prednisolone in the treatment of nephrosis by drawing attention to the effect of this drug on the albuminuria.

Owing to the salt-retaining effect of the earlier cortisones, as a result of which a diuresis, which was believed to be the beneficial result, tended only to take place when the treatment was stopped, there has been a tendency with many to feel that steroid therapy merely acted like mersalyl, urea, and other diuretics of limited value in this condition. As was clearly evidenced, however, in cases recently under my care treated by prednisolone, the effect on the albuminuria is obviously a most valuable one, and, even though this may have no specific effect on the disease proper, the fact that the drainage of albuminuria is at least in part a cause of the œdema would suggest that its relief must have a decidedly beneficial effect on the outcome of the illness, when one remembers that one of the chief causes of its mortality (though admittedly less since antibiotics were introduced) was the liability to intercurrent infection to which the waterlogged and bedridden patient was particularly exposed.

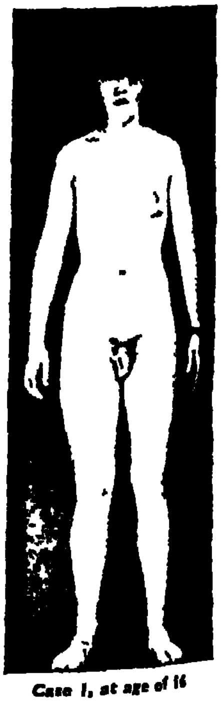
Dr Arneil treated his cases by continuous dosage for a period rather than by intermittent therapy (for example, three days a week) which the older diuretic concept made a popular regime. As with other chronic conditions amenable to steroid therapy, the continuous method would seem to be the more rational. He gave the impression, however, that all his cases were cured after the forty days' treatment. It would be interesting to know if they were followed up long enough to be certain that relapse did not take place later. This occurred in one of my cases where, when dosage was reduced to a practicable maintenance level, moderately heavy though much less severe albuminuria recurred.

Though of course no criticism of Dr Arneil's paper, an interesting and unexplained feature is why, unlike steroid therapy which in most cases seems to have to be continued for long periods, the originally used measles often cleared up the condition completely with one single "shock" as it were. This was very striking in a case under my care in 1933 when I was physician to Dr Steeven's Hospital, Dublin. This child had been waterlogged with œdema and had had profuse albuminur for months. After the child contracted measles the œdema and the albuminuria cleared up in a most remarkable manner in a matter of a few days. When seen recentl he was found to be a perfectly healthy adult. The detail of this case, which if published at the time might possibl have been the first recorded case of the effect of measl on the nephrotic syndrome, are appearing in the Ir Journal of Medical Science as a historical note.

Dublin R. E. STE

NUCLEAR SEX IN KLINEFELTER'S SYNDROME

SIR,—A syndrome characterised by gynæcomasti small testes with aspermatogenesis, normal or moderatel reduced function of the Leydig cells, and increased excretion of *follicle-stimulating hormone* was fir described by Klinefelter et al.,[1] who reported 9 ca In testicular biopsies hyalinisation of the seminiferou tubules was seen, and breast tissue showed hyperpla of the duct epithelium and much proliferation of th periductal connective tissue. Klinefelter et al. regarded the degenerative lesion of the seminiferous tubules a primary, and the gynæcomastia as due to secondar hormonal disturbances. Nelson and Heller[2] and de la Balze et al.[3] reported additional cases of Klinefelter's syndrome. They agreed that the disease should be regarded as primarily affecting the testes, and suggested that abnormal proliferation of fibroblasts in the tubular wall led to complete hyalinisation and atrophy of the germinal epithelium.



Case 1, at age of 16.

The technique of determining chromosomal sex from smears[4] has thrown new light on different forms of genital malformations. In accordance with a suggestion by Prof. M. L. Barr,[5] we have recently examined two patients with Klinefelter's syndrome.

CASE 1.—No previous illness during childhood; lived as a normally developed boy. From age 11 increasing growth of mammary glands. At age 14–15 spontaneous male pubertal development: deepening of voice, enlargement of genitalia, growth of pubic hair, &c. Admitted at age of 16 on account of gynæcomastia.

On examination, general somatic development corresponding to that of a boy aged 15, except for somewhat broad hips (see figure). No obesity. Height 168 cm., no eunuchoid skeletal proportions. Development of secondary male sexual characteristics, including muscular strength, normal for age. Penis (61 mm. long) and scrotum well developed. Testes very small (diameter 9–10 mm.), firm. Large bilateral gynæcomastia vera, corpus mammæ about 6 cm. in diameter.

Hormone excretion per 24 hours: total neutral 17-ketosteroids 9.3 mg.; androsterone 2.5 mg., etiocholanolone 2.8 mg.; gonadotrophins 25 mouse units.

Testicular biopsy.—Complete hyalinisation of seminiferous tubules; no spermiogenesis. Interstitial tissue filled with dense masses of Leydig cells.

Course.—Followed 2½ years after surgical removal of mammary glands. Despite normal 'male' excretion of

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1. Klinefelter, H. F., jun., Reifenstein, E. C., jun., Albright, F. J. clin. Endocrin. 1942, 2, 61
2. Nelson, W. O., Heller, C. G. Ibid 194[illegible], 5, 13.
3. de la Balze, F. A., Arrillaga, F. C., Irarra [illegible], Mancini, R. E. Ibid 1952, 12, 1426.
4. Lancet, 19[illegible], ii, 6[illegible]4.
5. Plunkett, E. R., Barr, M. L. Anat. Rec. 1956, 124, 348.

The general practitioner carried an enormous burden of serious illness, including most terminal illness Ideally he should have as his agents and helpers the home nurse, the health visitor, and the midwife, he should run clinics for his own mothers and babies, and he should look after his patients at work as well as at home All this was now generally accepted but far from generally achieved The years since 1950 (the turning point for general practice) had seen very important advances—the growth of rota schemes, the growth of group practices, the holding of clinics by practitioners for local authorities, and experiments with health centre buildings designed to bring practitioners and local authority services together The parts of the local authority services concerned with patients had come into being to fill gaps left by National Health Insurance general practice, and under the N H S the family doctor should in theory cover them himself In practice it was an immense help to have the assistance of local authority staff The family doctor could run maternity clinics (on local authority premises or his own) with the health visitor and/or midwife in attendance, and health visitors could act as general practitioners' social workers just as district nurses (home nurses) acted as their domiciliary assistants

All this depended largely on proper accommodation and in the National Health Service Act stress had been laid on health centres Unfortunately, the cost of the first N H S health centre planned in London was prohibitive to accommodate all practitioners on the same scale would have cost about £600 million The large centre built in Edinburgh had also been too expensive to reproduce Hope for the future, Dr Taylor thought, lay in the more modest health centres or group surgeries established publicly or privately in various parts of the country, and by numerous plans he demonstrated what could be done, in small space and with small expenditure, if means were really related to needs Many of his examples were drawn from buildings erected with the help of the Nuffield Provincial Hospitals Trust—which he described as the most powerful instrument of social research and planning that exists in the sphere of the health services These examples included particularly the health centres of Harlow New Town, which he and his associates have lately described, with illustrations, in our columns [1]

In conclusion Dr Taylor spoke of the need, first, for accurate knowledge of the work that has to be done in the building, secondly for creative social planning, so that the demands shall be the least consistent with efficiency, and thirdly, for careful architectural planning inside the strictest possible budget

LOUIS RAPKINE ASSOCIATION

ON the lines of the Horse Shoe Club, which fosters friendship between American, Canadian, and British workers in medicine, the Louis Rapkine Association has been formed for French and British doctors and medical scientists who have held scholarships and bursaries in each others countries The members, grouped into British and French sections, undertake to give what advice and help they can to visitors from the other country, and the plan is that each section shall hold an annual reunion The British section was inaugurated on May 14 at the Ciba Foundation, when Dr Etienne Berthet, director of the International Children's Centre, gave an address entitled Evolution et Tendances de la Medecine Contemporaine

Among those attending the inauguration were Madame Rapkine, widow of the French biochemist after whom the association is named A brief account of Rapkine's life, from his birth in White Russia in 1904 to his death in 1948, shows that he was indeed "a man of exceptional personal qualities who believed ardently in the need for international cooperation in science" Trained at McGill University, he went to France in 1924, and despite privation was already doing important work on cell activity before he was 21 In 1934 he started a committee for academic refugees from Fascist countries, and an international organisation was in prospect when war broke out In 1940 he was in London with a French government mission, and set about helping scientists who might be in danger in the occupied zone of France He arranged in the first instance for them to go to the United States He had to obtain their safe exit, pay their passages, persuade the Americans to give them entry, and maintain them until they could take up the research posts he had found for them Later this work was transferred to the United Kingdom, where the Mission Scientifique Française en Grand Bretagne was established Before this group returned to France in 1945 Rapkine had done much to re establish scientific contacts which had been broken by the war, and he had also persuaded the French government to maintain a permanent scientific office both in England and in the U S A to strengthen the links formed During his time in London, too, he took an active part in the foundation of that unique residential club, the Society for Visiting Scientists "The story of Louis Rapkine" as the brief biography says, "is one of the strength of the individual His integrity and complete disinterestedness gained him the support of the influential, his faith and enthusiasm won over the indifferent and sceptical, and his single minded determination cut through the barriers of officialdom and of red tape in all departments of life"

Further information about the association may be had from Dr G E W Wolstenholme, Ciba Foundation 41 Portland Place, London, W 1, or from Miss A M Vidal Hall Scientific Office, French Embassy, 22, Wilton Crescent, S W 1

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[1] *Lancet* 1955 ii, 863

University of Oxford

On June 2 the honorary degree of D SC was conferred on Prof Ragnar Granit, of Stockholm Dr G W Pickering, the new regius professor of medicine, was incorporated doctor of medicine, as a graduate of the university

The degree of D M was conferred on J C F Poole, and the degree of CH M on Harold Ellis

University of Cambridge

Dr D G Chalmers has been appointed a university assistant pathologist at Addenbrooke's Hospital

University of Manchester

Dr B J Leonard has been appointed demonstrator in pathology

University of Durham

Dr G A Smart, reader in medicine, has been appointed to the professorship of medicine in the Newcastle division of the university

Dr Smart who is 42 years of age was at school at Uppingham and graduated M B from the University of Durham in 1937 and took his M D two years later During the late war, with the rank of squadron leader in the R A F Medical Service he acted as specialist in nutrition surveys In 1948 he was awarded a Commonwealth Fund fellowship Before taking up his present appointment he was lecturer in medicine in the University of Bristol He has published papers on pituitary function and on the rôles of the adrenal cortex in diabetic acidosis

Scottish Food Hygiene Council

The 17 members of this council include Dr G Matthew Fyfe, M O H for Fife, and Dr John Smith, director of the regional laboratory, City Hospital, Aberdeen The chairman of the council is Sir William McNair Snadden

British Tuberculosis Association

The annual conference of this association is to be held in Bristol from June 27 to 30 Further particulars may be had from the administrative secretary of the association, 5 Portland Place, W 1

Royal Medical Benevolent Fund

The annual general meeting of this Fund was held on June 5 when the following honorary officials were re elected president, Lord Webb Johnson, hon treasurer, Mr F A Juler, and hon secretary, Dr R Cove Smith

British Association of Pædiatric Surgeons

This association is to hold a joint meeting with the surgical section of the American Academy of Pediatrics in London, from July 17 to 19, under the presidency of Mr Denis Browne The annual dinner of the association will be held on Thursday, July 19 at 8 P M at the Apothecaries' Hall The scientific meetings are open to non members, and further particulars may be had from the hon secretary, Mr D J Waterston, Hospital for Sick Children, Great Ormond Street, W C 1

CORRIGENDUM *British Institute of Radiology*—In our report of Professor Spiers's presidential address (June 2 p 839), we wrongly included the statement that the ^{40}K body content was now established at about 0 2% of body weight This figure in fact refers to the *total* potassium content of the body

Prof A C Frazer head of the department of medical biochemistry and pharmacology in the University of Birmingham has been elected president of the British Food Manufacturing Industries Research Association

Hospitals Directory for England and Wales 1955—A new edition of this directory has been published this week Copies may be had from H M Stationery Office, price 15s androgens and prolonged treatment with testosterone the patient retained a rather infantile appearance and no moustache developed

Case 2—In childhood lived as a normally developed boy At age of 14 spontaneous start of puberty with deepening of voice and growth of genitalia and pubic hair, but at the same time increasing obesity with feminine distribution of the fat Admitted at age of 18 on this account

On examination general appearance markedly feminine and somewhat infantile Moderate obesity with pronounced feminine fat distribution broad hips and large nates and mammæ On palpation of the fat in mammary region glandular tissue was not felt with certainty Height 172 cm no eunuchoid skeletal proportions Voice somewhat higher than normal muscular strength considerably less than in normal men of the same age Dense growth of pubic hair axillary hair scanty moustache almost absent Penis hypoplastic and very short (39 mm) scrotum well developed Testes very small (diameter about 13 mm.), firm

Hormone excretion per 24 hours total neutral 17 ketosteroids 5·7 mg androsterone 2·2 mg etiocholanolone 1·4 mg gonadotrophins >50 mouse units

Testicular biopsy—Complete hyalinisation of seminiferous tubules Between tubules large dense masses of Leydig cells

Oral and urogenital smears in case 1 showed typical chromatin-positive (“female”) nuclei The sex diagnosis was kindly confirmed by Professor Barr Unfortunately we have not been able to examine epithelial smears from case 2 but several blood smears were obtained These showed—as in case 1—typical “drumsticks” which denotes that the preparations had a female character

These surprising findings must be interpreted as an indication of a sexual “shift” early in fœtal life Grumbach et al[6] have reported various investigations concerning the fœtal sexual development of patients with “gonadal dysgenesis” They concluded that lack of testicular tissue converts the fœtal sexual development in males in a feminine direction It is difficult to explain the reported findings in patients with Klinefelter's syndrome unless one imagines the presence of a hypothetical strong male “inductor” in the early weeks of their embryonic life

We look forward to other reports on nuclear sex in cases of Klinefelter's syndrome At present we do not even know whether chromatin-positive nuclei are invariably present, or whether a minority of the cases show nuclear sex of male type.

Kobenhavns Amts Sygehus
Gentofte and Rigshospitalet
Copenhagen Denmark

Povl Riis
Svend G Johnsen
Johannes Mosbech

SUICIDE AND PHYSICAL TREATMENTS

Sir,—16 deaths by suicide have occurred during the past two years among patients discharged from the mental hospital at which I work All but 1 had received physical treatment of a more or less drastic kind

The 4 female patients had all received electroconvulsive therapy (1 of them leucotomy too) Of the remaining 12 male patients 7 had had E C T 2 had undergone a modified deep narcosis and 2 passed through a three weeks course of modified insulin—up to 80 units

The Registrar General reports an increase in the number of suicides throughout the country from 3447 in 1944 to 5033 in 1954 That is an increase of 1586 deaths by suicide

My own figures show an average of 8 deaths by suicide per annum for 1954 and 1955 If this experience were to be repeated among more than 100 mental hospitals in the country then the increased suicide rate could be substantially accounted for by the psychiatric cases leaving mental hospitals after physical treatment Especially so if as must be remembered the cases came to my notice by casual (though confirmed) report

This letter can only be regarded as a preliminary note to a more searching investigation

Chester

I Frost

NIKETHAMIDE IN RHEUMATOID ARTHRITIS

Sir—During the past eighteen months I have treated 38 successive cases of rheumatoid arthritis with nikethamide and have had 38 cures The patients were all Africans aged 25–60 and were nearly all women. They had had symptoms for between six months and twenty-three years The treatment is very simple—2 ml of nikethamide (‘Coramine’) is given thrice weekly for three or four weeks There have been no relapses so far that I am aware of and the effects are apparently lasting There are no side effects and no contra-indications and improvement often starts with the first injection

2 cases are reported here but the others are just as striking

Case 1—The patient was a woman aged about 55, who had had the disease for twenty-three years When first seen she was sitting huddled in front of her hut knees under her chin spine bent and arms folded in front of her in the position of least discomfort There was pronounced ulnar deviation of the fingers and wrists whose joints were grossly deformed and tender The other joints were not so obviously deformed but were nevertheless painful and tender, and even the spine was involved The joints of the feet had over all about 60% of normal movement and there was progressive deterioration upwards to the hands which had at most 10% The skin over the hands and forearms was atrophic and shiny and that of the face showed the crazed porcelain effect so often seen in these patients

As this was the first case I had treated with nikethamide I gave her daily injections for twenty-one days and thereafter twice weekly for a further three weeks She reached maximum improvement after two weeks At this stage she could place both hands behind her neck for the first time in many years and could close both hands tightly except for the two ring fingers which were the seat of an unyielding ankylosis at their two interphalangeal joints The pain and tenderness had disappeared but the ulnar deviation and a good deal of the deformity persisted The neck had a full range of movement and the knees were greatly improved but there was a little stiffness of the hip joints The skin of the hands and forearms had regained a normal appearance but that of the face was unaltered Formerly a helpless cripple unable even to dress herself she was now able to do most of what a normal woman of her age could do The only treatment apart from the nikethamide was manipulation of the wrists fingers neck and knees because the patient lacked the confidence to move these joints sufficiently herself I have not seen the patient for fifteen months but inquiries a few months ago revealed that she was still well

Case 2—This patient was a man aged 45 He was employed as a labourer by the South African Railways and was referred to me for certification of unfitness because he was so often ill It was found that he had rheumatoid arthritis and had had symptoms for eight years I asked that he be allowed three weeks sick leave to have a course of treatment If he was not cured after this time he would be boarded The worst trouble was in the joints of his shoulder girdle but hands elbows and knees were also involved He had nine injections of nikethamide and went back to work with only 5° less than full extension of the right arm at the shoulder All other movements were full and normal It is nine months since his treatment and he has never been absent from work since nor had any further treatment

Circumstances here in the bush do not permit of adequate investigation of each case and neither radiography nor estimation of the erythrocyte-sedimentation rate has been undertaken Moreover it is quite impossible to persuade Africans to attend for follow-up examinations They would certainly return however if they had a recurrence of symptoms All the patients must come to the dispensary for treatment and for most this involves a walk of several miles each time This may have some bearing on the treatment Nikethamide was found to have no effect on infectious or traumatic arthritis or osteo-arthritis

Without basic research which is impossible here I do not want to discuss any theory But apparently the

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[6] Grumbach M M, Wyk J J van, Wilkins L. *J clin Endocrin* 1955 15 1161

CHRONIC PYELONEPHRITIS *

JAN BROD
M D Prague
ASSISTANT PROFESSOR OF MEDICINE, CHARLES UNIVERSITY, DEPUTY DIRECTOR OF THE INSTITUTE FOR CARDIOVASCULAR RESEARCH, PRAGUE KRČ, CZECHOSLOVAKIA

"CHRONIC pyelonephritis" denotes inflammation which has spread to the kidney from an infected renal pelvis The inflammation is interstitial and scars and destroys the surrounding parenchyma in a patchy distribution, and there are great differences in the extent of inflammation and destruction not only between the two kidneys but also between different parts of one and the same kidney The structures affected most seriously by pressure, interference with nutrition, and the toxic by products of inflammation are the tubules, which are atrophic and often cystic and dilated, and often disappear in the inflamed tissue The glomeruli, on the other hand, retain their normal structure much longer, being destroyed only when the inflammation breaks through the wall of Bowman's capsule (the "invasive glomerulitis" [fig 1] of Kimmelstiel and Wilson [1936]) or when the afferent arteriole is damaged by hypertension (the "alterative glomerulitis" of the same workers)

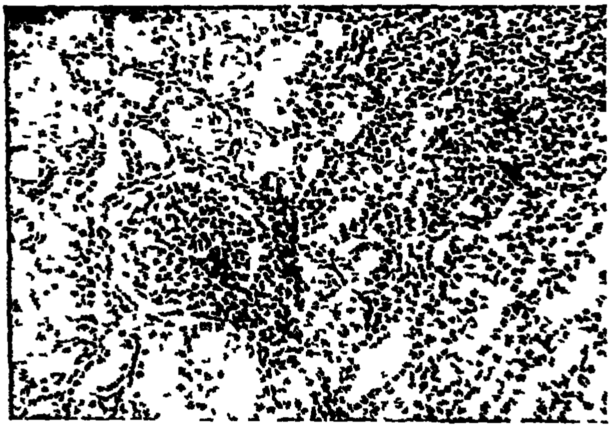

Fig 1—Invasive glomerulitis.

In two thirds of the cases the pyelonephritis is secondary, being a complication of a primary lesion elsewhere in the urinary tract, but in the remaining third the pyelonephritis is primary, there being no obvious lesions in the ureters or in the renal pelves If infection is responsible in these latter cases it must be blood borne Sampson (1903) and other workers, however, have shown that hæmatogenous infection produces pyelonephritis only if the free flow of urine has been disturbed Therefore in the absence of organic obstruction there must be functional interference with the flow of urine

Infection, however, is not indispensable in the pathogenesis of pyelonephritis Simonsen (1953), in his work on the fate of renal transplants, found morphological changes similar to those of chronic pyelonephritis without any evidence of infection, they were probably of allergic origin I do not intend to discuss here the details of the pathogenesis and the paths along which infection and inflammation spread from renal pelvis to kidney Whatever these paths, the result in the kidney is the same

Pyelonephritis has been well known to pathologists for a hundred years but little known to clinicians, and has usually been diagnosed only by urologists as a late complication of renal failure in disease of the urinary tract For decades pathologists have increasingly called attention to pyelonephritis, and some physicians have recognised its importance, especially in hypertension (Butler 1937, Longcope 1937, Weiss and Parker 1939, Pickering and Heptinstall 1953, Langley and Platt 1947, and others)

Raaschou (1948) focused the attention of clinicians and nephrologists on this important, common, and dangerous disease Using clearance techniques he showed that pyelonephritis affects the function of the kidney in rather a specific way He also established that, in Copenhagen, pyelonephritis was the commonest cause of uræmia, being found in 1 in every 14 necropsies (6 3%)

The prevalence of pyelonephritis in our population is almost exactly the same as that found by Raaschou of 1196 necropsies in the pathological department of the Thomayer Hospital, Prague, in two and a half years Horák and Kratochvilová (1955) found chronic pyelonephritis in 74 (6 18%) In 48 (65%) it was a complication of primary lesions of the urinary tract, in 26 (35%) it was a primary lesion without any obvious change elsewhere in the urinary tract Hypertension was a complication in 41 8% of the cases, being commoner in the primary cases (65 3%) than in the secondary (29 1%) A surprisingly high proportion of both primary and secondary cases had escaped clinical recognition—50 of 74 (67 5%)

The seriousness of this lack of clinical recognition of pyelonephritis is obvious from the causes of uræmia in 69 deaths from renal failure in the necropsy material of the same period although chronic pyelonephritis was less common than in Raaschou's (1948) material, it was the commonest renal cause of death accounting for 36 2% of cases of uræmia, whereas glomerulonephritis accounted for 18 8% and vascular nephrosclerosis for 14 5%, leaving 30 5% due to other and far less important causes (renal amyloidosis, polycystic kidneys, acute renal failure, &c)

These pathological data show how important it is to improve the clinical diagnosis of pyelonephritis

Material

I began to be interested in pyelonephritis in 1948, when a patient presented with what appeared to be malignant hypertension and a renal functional pattern which differed from that usually found in malignant nephrosclerosis At necropsy chronic pyelonephritis was found In a report of this case to our cardiological society I suggested that the disturbance of renal function might be specific for pyelonephritis (Brod 1948) In that same year I observed several similar cases, all of which I diagnosed as chronic pyelonephritis on the disturbances of renal function, the diagnosis being confirmed by the pathologist

Since then 132 cases have been diagnosed in this institute as chronic pyelonephritis on clinical grounds The study of this group has yielded data which may contribute to a better understanding of pyelonephritis, and to its better diagnosis by methods within the competence of almost any small general hospital

Our group comprises mainly patients treated as either inpatients or outpatients on the medical side It constitutes, however, only about half the cases of pyelonephritis The other half comes under the care of either urologists or gynæcologists, the clinical picture being primarily either urological or gynæcological

The data which we obtained on renal function in some of these latter cases did not differ materially from those in our medical patients, so perhaps the conclusions reached in our group may also be valid in the surgical cases

Correlation of Clinical Diagnosis with Pathology

Fig 2 shows that, of 22 patients who were diagnosed clinically as having chronic pyelonephritis and underwent either biopsy or necropsy (16 7% of the whole group), the diagnosis was confirmed morphologically in 20 (91% of the 22 patients) Of the 2 patients in whom the diagnosis was not confirmed morphologically, 1 had a thrombosed renal artery, and the other malignant effect of nikethamide is not similar to that of salicylate or cortisone It would be interesting to know whether Europeans and Asiatics respond to nikethamide in the same way as Africans

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* Paper read at a meeting of the Danish Society for Internal Medicine in Copenhagen, Oct 28 1955

For permission to publish this letter I wish to thank the acting director of medical services for Bechuanaland Protectorate

Government Hospital,
Maun Ngamiland,
Bechuanaland Protectorate

H F MORTON

POTASSIUM-CHLORATE POISONING

SIR,—Dr Davies (May 5) mentions among the effects of potassium chlorate "the effect of the chlorate ion, which denaturates Hb with the production of Heinz bodies, and lyses the erythrocytes"

In my own experiments (incubation mixture 0 8 ml pH 7 0 $M/15$ phosphate buffer, 0 2 ml 1 9% potassium chlorate, and 0 5 ml washed red blood-cells , temperature 37°C) I have found that the decrease of catalase activity appears prior to the denaturation extending over the whole cell I did not observe formation of Heinz bodies By the 60th minute of incubation catalase activity had decreased about 50%, and by the 120th minute 75% Probably the sensitivity of catalase is higher against the chlorate ion than that of other cell-proteins, and even in-vivo Heinz body formation is not due to the direct effect of the chlorate ion, but indirectly to the catalase inhibition

Budapest, Hungary

L MAGOS

GENESIS OF TROPICAL ANÆMIAS

SIR,—Dr Foy and Dr Kondi, in their preliminary communication of April 14 on iron losses in the genesis of tropical anæmias, appear to have modified some of their previous findings Thus, in 1952 [1] they classified the anæmias of Africans into "four well defined groups" iron deficiency anæmia, nutritional megaloblastic anæmia, sickle cell anæmia, and "splenic hæmolytic anæmia" Comprehensive data were published on the first two groups These could be clearly separated by examination of mean diameter, mean corpuscular volume, and mean corpuscular hæmoglobin concentration, and a consideration of the bone marrow in terms of megaloblasts and pathological "stab cells" Deficiencies were usually single There was, in their opinion, no overlap between the groups, which were distinct and identical with those described in other parts of the world I had always hoped that further work might reconcile apparent differences of opinion, since they were at that time unable to recognise or study anæmia due to protein malnutrition or liver damage, subjects not mentioned in their article

In an article [2] published independently by me earlier this year these divergences of opinion appear to have been reduced Within the last eight years a definite place has been accorded to the anæmia of protein malnutrition [3–6] and to that of chronic liver damage [7–10] It is not generally recognised that the latter usually produces moderate anæmia in which the red cells are macrocytic in respect of the mean diameter, and there is often an accompanying mild reticulocytosis In earlier studies of mine [11] the disturbances of protein metabolism due to diet (kwashiorkor), hookworm disease, and chronic liver damage were not clearly differentiated it was merely noted that some anæmias responded to iron and some to whole liver, but some apparently required both to complete the cure The latter anæmia I ventured to call "dimorphic anæmia" When at the end of the war, liver extracts became available it became apparent in Uganda that more cases responded to whole liver than to liver extracts This is probably because the former is rich in protein, and these cases are now treated with skim milk protein

It is now clear that Dr Foy and Dr Kondi also admit the effect of protein malnutrition, although it is not clear in any of their published observations what they consider are the morphological characteristics of the resultant anæmia when it occurs unassociated with infection or iron deficiency However, they acknowledge that microcytic hypochromic anæmia as seen in the tropics may be due to "multiple deficiencies and "the failure of some cases to respond to iron alone and the appearance of other deficiencies during iron treatment indicate the complexity of the problem" They found that some of these cases required extra protein and/or the pernicious anæmia group of hæmopoietic factors to complete cure Recent work by Tasker [12] suggests that these two types of deficiency are sometimes associated in Malaya It seems that most workers now accept the fact that anæmia in the tropics has often more than one deficiency in Uganda usually iron and protein are involved, occasionally one of the P A factors the latter is more common in Kenya and among Indians

While stressing the deficiency approach to anæmia, I must register a protest that *severe* anæmia in most tropical regions is usually due more to a tropical infection than a deficiency In young children in Uganda it is largely due to malaria, slightly older children, poor immigrant labourers, and destitute women may all suffer from "hookworm anæmia" Small blood clots can be seen in the intestine at necropsy, and it has been repeatedly demonstrated [13] and confirmed by recent work that cases cannot be cured completely by oral iron or massive injections (4 g) of intramuscular iron, large protein supplements, and large injections of vitamin B_{12} After an initial rise to 6–10 g per 100 ml , the hæmoglobin level remains stationary, in spite of a high reticulocytosis, until repeated deworming reduces the load Immediately this occurs the blood count leaps upwards while at the same time the reticulocyte count falls

It is quite true and has been known for a long time that there is no correlation in any community between hookworm loads and the hæmoglobin level, yet occasionally for reasons not understood one person becomes severely anæmic This, however, does not explain the widespread but moderate anæmia which is so prevalent in tropical communities Dr Foy and Dr Kondi suggest this may be due to iron losses in the sweat As a preliminary question one might ask whether this widespread but mild anæmia is cured by giving oral, intramuscular, or intravenous iron In my experience after an initial improvement, it is seldom possible to cure this moderate tropical anæmia, or to produce a "normal" blood count, especially high red cell counts, even after giving much iron and protein Whether this reflects, as I suggest, widespread irreversible liver damage is uncertain

One of the great difficulties in reaching agreement with other hæmatologists is terminology Thus when Dr Foy and Dr Kondi speak about a "dyshæmopoietic" anæmia or bone marrow they refer exclusively to one reflecting a deficiency of one or other of the P A group of hæmopoietic factors No other hæmatologists, as far as I am aware, restrict the term thus Surely a dyshæmopoietic anæmia occurs whenever there is a deficiency present, and there are also those due to deficiency of iron, ascorbic acid, thyroid extract, calories, protein, and other factors Many of these have distinctive morphological changes in the marrow and peripheral blood Another basic assumption of Dr Foy and Dr Kondi, substantiated by much of the literature, is that pathological giant "stab cells" even by themselves are almost proof of one or other of the deficiencies of the P A group (a "dyshæmopoietic" marrow, as they call it) While this is usually accepted due weight must be given to the opinion of others [14–17] that giant "stab-cells" may occasionally occur in the marrow smears of iron deficiency anæmia in Europe and America The truth is that few have studied the marrow in iron deficiency dyshæmopoietic anæmia or waited to see whether iron by itself in the tropics increased

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nephrosclerosis in a kidney displaced into the pelvis without obvious chronic pyelonephritis

The clinical and the pathological diagnosis agreed in 49 (91%) of 54 cases of chronic glomerulonephritis and in all 16 cases of vascular nephrosclerosis

These satisfactory results allow us to draw conclusions from our clinical group with the same certainty as from other diseases diagnosed clinically

Diagnosis

History

A very thorough history of present and past symptoms was first obtained

44 7% of the patients complained of either present or past *frequency and dysuria* (symptoms of inflammation of the urinary tract), and 64 4% of either present or past *pain* in the loins, this was of the severe colicky type in those with a history of lithiasis, but more frequently the pain was dull In 35 6% of the cases, however, there was no pain This shows that interstitial inflammation in the kidney is painless, and that any *pain present* must be due to another cause—probably spread of the inflammation to structures in the neighbourhood of the renal pelvis, or irregular contraction of the ureters

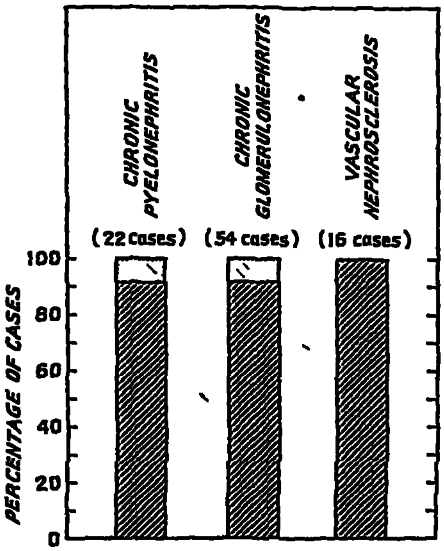

Fig 2—Incidence of agreement (hatched areas) of clinical and pathological diagnoses

Clinical Examination

Routine physical examination included that of the genitalia, palpation per rectum, and retinoscopy

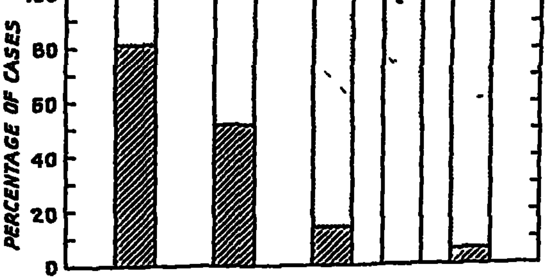

Fig 3—Incidence of pathogenic bacteria (hatched areas)

Pyelonephritis and glomerulonephritis	13 978<0 001
Pyelonephritis and healthy	38 412<0 001
Glomerulonephritis and healthy	18 038<0 001

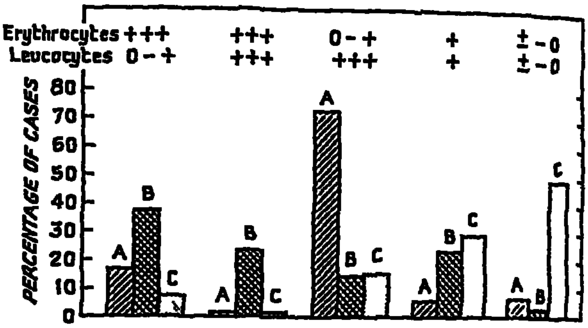

Fig 4—Cells in urinary deposit A chronic pyelonephritis, B, chronic glomerulonephritis, C, nephrosclerosis

Pyrexia, rarely exceeding 100 4°F, was found in only 25 0% of the patients

From a quarter to a third of them complained of vague *constitutional symptoms*—e g, lassitude, malaise, headache, anorexia, nausea, dyspepsia, and breathlessness on exertion In about two-thirds of the patients all these symptoms could be correlated with late renal failure hypertension, or pyrexia, but in about a third of them no such explanation was forthcoming, and the symptom had to be attributed to the focal inflammation in the kidney

17 25% of all the patients and 40 0% of those with primary pyelonephritis were referred because of a chance discovery of proteinuria, 8 33% because of high blood pressure, and 1 5% because of thirst and polyuria, but, when questioned specifically, 21 9% admitted to thirst and 11 4% to polyuria

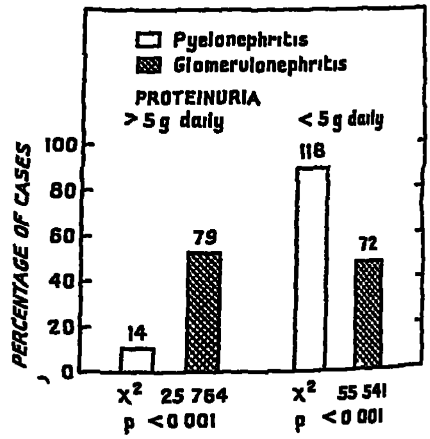

Fig 5—Proteinuria.

Routine physical examination yields practically no further information, unless pathological changes in the pelvis or in the genitalia, hypertension, or signs due to renal failure are found Although 23 patients reported having had œdema, it could be explained by extrarenal causes in 21 of them

Laboratory Investigations

Little is gained from routine laboratory examinations including chest radiography, electrocardiography, estimation of the erythrocyte sedimentation rate (E S R), blood count, and estimation of non protein nitrogen plasma proteins, and cholesterol

A rise in the E S R, a fall in the red cell count, and a decrease in the amount of *hæmoglobin* correlate best with renal failure, poorly with pyrexia, and irregularly with the inflammation in the kidneys A slight increase in the white cell count was observed in 25% of the patients with pyrexia

Thus, the history, clinical examination, and ordinary laboratory tests in pyelonephritis without renal failure afford, at most, only information about the presence or absence of inflammation in the urinary tract, without the blood-count until it became *quite* normal The disappearance of pathological stab cells after treatment by one of the P A group of substances is very suggestive

In propounding the term "dimorphic anæmia," [11] I wished to draw attention to a puzzle anæmia in the tropics was not always due either to iron deficiency or to nutritional megaloblastic anæmia There was overlap, there was confusion I must have defined the term poorly, for many who subsequently used the term gave it a different meaning I have ceased to use it, for it incorrectly and inadequately oversimplified the problem Much anæmia in the tropics is "polymorphic" It is still a puzzle, although many of the pieces are beginning to fit together

It is to be hoped that Dr Foy and Dr Kondi will continue their work on iron losses in the skin and sweat of those who live in tropical countries For my part I regret if any of my writing suggested there was some deep mystery about the tropical anæmias Much which appeared mysterious to me twenty years ago now appears explicable in terms of iron deficiency, megaloblastic deficiency, protein malnutrition, and liver disease, in which I must now have performed over 500 biopsies Much remains to be done for instance why do iron-deficiency anæmias in the tropics *rapidly* become macrocytic when iron therapy causes a reticulocytosis ? I have been unable to find any hæmatologist in temperate regions who has noticed this change, and others record data which deny that it occurs [18] I suggest this is due to intercurrent liver damage and protein malnutrition, present usually in the tropics but seldom in temperate regions

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H C TROWELL

SIR,—We have some evidence to indicate that, contrary to the opinion of Dr Foy and Dr Kondi, the rôle of hookworm in the genesis of some tropical anæmias is probably a paramount one We have "marked" the red blood cells of 22 subjects with hookworm infestation, with and without anæmia, and studied radioactivity in the fæces and in the blood

Fæces were collected in three four day periods, and radio activity was compared with that present in the blood at the beginning of each fæcal collection The same study was repeated after tetrachloroethylene treatment and recovery of the hookworm in the fæces in 15 patients We were thus able to show that each hookworm is responsible for the loss of an average of 4 19 × 10^{-2} ml per day of blood, with extremes of 0 98 to 15 53 × 10^{-2} ml per day

Generally, blood-loss per hookworm was relatively larger in patients with very low hæmoglobin, and diminished as the patients' hæmoglobin increased, either through iron therapy or after transfusions None of the group of 8 patients with light infestations (less than 200 hookworms) had a hæmoglobin below 10 g per 100 ml Of the 14 patients with severe infestations (more than 400 hookworms), 11 had hæmoglobin values below 8 g per 100 ml However, one of the latter patients, with 509 hookworms, had a hæmoglobin of 15 8 g per 100 ml, and lost only on the average 6 08 ml of blood per day (that is, 1 18 × 10^{-2} ml per hookworm per day) His diet, as contrasted to that of most of the other patients, was excellent, being both fisherman and farmer, he ate fish, milk, and vegetables daily

It is of course our impression that loss of blood is not the only factor involved, and in the last case, diet was obviously important On the other hand, it is difficult to dismiss as unimportant losses of blood which may go up to 100 or 200 ml per day Eventually the development of anæmia will depend mostly upon a balance of what comes in (including iron, protein, &c) and what goes out of the patient's body Until the various factors involved are submitted to quantitative evaluation, the final word on this problem will not be forthcoming

In preliminary studies, we have been able to show in humans that chromium tagged to red blood cells introduced into the duodenum is recovered in the fæces almost quantitatively, and that chromium derived from the destruction of circulating red cells is excreted almost entirely by way of the urine These facts strengthen the theoretical validity of our views

Somewhat similar but more limited studies have been reported by Gerritsen et al ,[1] who used radio iron, and determined, in 3 hookworm-infested patients, that the daily blood loss per hookworm was 2 6, 22, and 5 3 × 10^{-2} ml per day respectively

Instituto de Investigaciones Médicas
Fundación Luis Roche
Caracas Venezuela

MARCEL ROCHE
Director

DIAGNOSIS OF THYROTOXICOSIS

SIR,—Although the diagnosis and assessment of thyrotoxicosis can usually be made on clinical grounds alone, there is still a certain number of patients in whom the diagnosis remains in doubt In some, the clinical picture is suggestive of thyrotoxicosis without obvious thyroid enlargement, whilst others have a presumed non-toxic goitre with an associated anxiety state Further, unexplained auricular fibrillation or congestive cardiac failure may raise the possibility of "masked" thyrotoxicosis though other evidence of overactivity of the thyroid gland may be lacking

At present tests of radioactive iodine uptake can be performed only in a limited number of centres We therefore feel that more use could be made of estimations of the serum creatine level, in combination with an accurate measurement of the sleeping pulse rate, as a screening test in all doubtful cases of thyrotoxicosis

Serum creatine

Griffiths [2] has shown that a normal fasting serum creatine level of less than 0 6 mg per 100 ml in both men and women excludes all but the mildest, relatively symptomless, cases of hyperthyroidism, and differentiates the anxiety states from true thyroid disorders He concludes that patients with suggestive symptoms and raised serum creatine levels should be regarded as thyrotoxic and treated accordingly, even if the basal metabolic rate is normal

In our small series, serum creatine levels, not necessarily fasting, were estimated in 19 patients admitted with clinical evidence of thyrotoxicosis under the care of the consultant staff at the Royal Devon and Exeter Hospital Using the method described by Peters,[3] the accepted maximal normal value of 0 6 mg per 100 ml was exceeded in every case studied In the more severe cases, the serum creatine levels ranged from 1 0 to 2 3 mg per 100 ml Within a few days of starting medical treatment with propylthiouracil or carbimazole, or alternatively following subtotal thyroidectomy, the levels had frequently fallen to within normal limits In every case normal values were obtained before the end of the sixth week In fact it would appear that the maintenance dose of anti thyroid drugs can be controlled satisfactorily using this test 6 patients with non toxic nodular goitres, confirmed on histological examination, had normal serum creatine levels prior to operation

It should, however, be remembered that the serum creatine is raised in other conditions, associated with disordered muscle metabolism For example, one of us (D M) has frequently found raised levels in patients with rheumatoid arthritis

Sleeping Pulse rate

A raised sleeping pulse rate is one of the classical signs of thyrotoxicosis Accurate recordings are, however, notoriously difficult to obtain without waking the patient We have used the sensitive pulse indicator described by Simpson [4] for this purpose and thereby obtained accurate sleeping pulse rates throughout the night The instrument is simple to construct and can easily be operated by the nursing staff It utilises a small carbon throat microphone which is strapped to the pulp of the great toe with 'Sellotape' Light flex, several feet long, connects the microphone to the instrument placed on the locating it when present To do this it is necessary to study the urine and renal function This study consisted in analysis of the urine, an Addis count, a twenty four-hour curve of the glomerular filtration-rate (assessed by endogenous creatinine clearance), concentration and dilution tests, intravenous pyelography, and, when necessary, urological examination, including ascending pyelography and estimation of separate concentration indices ($\frac{U}{P}$ ratio) of endogenous creatinine

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[18] Wintrobe M M Clinical Pathology London 1951 figs 79 and 129

[1] Gerritsen T Heinz H J Stafford G H *Science*, 1954 119, 412

[2] Griffiths W J *Lancet* 1951 ii, 467 *Brit med J* 1954 i, 640

[3] Peters J H *J biol Chem* 1942 146, 179

[4] Simpson D C *Lancet*, 1955, ii, 596

Bacteriology

The causal micro organisms can often be cultured from the urine Fig 3 shows that pathogens—i e, bacteria other than *Staphylococcus albus*—were found in the urine of 81% of the patients, irrespective of sex and of whether the pyelonephritis was primary or secondary This is in striking contrast with the findings in 30 healthy people, in whom pathogens were present in the urine of only 6% Moreover in healthy females, from whom bladder urine was obtained through a catheter, pathogens were not found at all, whereas in healthy men, who provided mid stream specimens, pathogens were found in 14%, but never any *Escherichia coli* The pathogens in male urine obviously came from the urethra

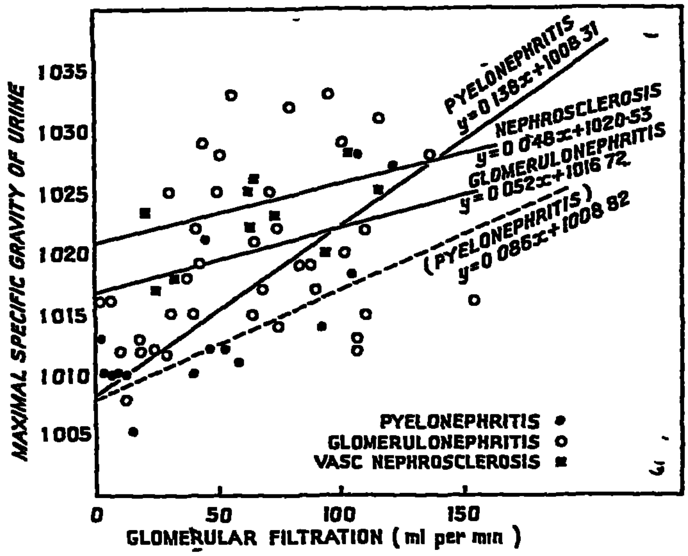

Fig 8—Correlation of glomerular filtration-rate and maximal specific gravity of urine If 2 cases of chronic pyelonephritis with unusually high powers of concentrating urine are excluded regression line is as shown by interrupted line

In chronic glomerulonephritis there was an unexplained and relatively high prevalence of pathogens in the urine (no sex difference was found in this disease), but the prevalence of infected urine in chronic pyelonephritis was significantly higher Among these organisms *Esch. coli* was the most frequent (45%) *Staph aureus* (28%) and *Streptococcus fæcalis* (27%) came next, while proteus (3 27%) and *Pseudomonas aeruginosa* (4 26%) were found in only a few of our patients—no doubt because there were no heavily infected urological cases among them

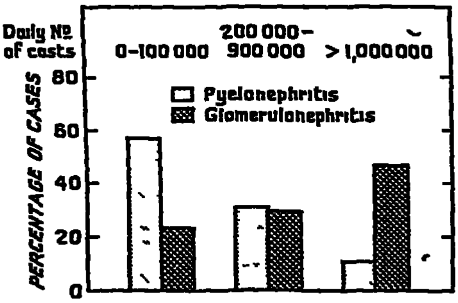

Fig 6—Casts in urinary deposit.

Addis Count

The second most important sign of inflammation of the urinary tract, simultaneously indicating its severity, is the quantity of leucocytes in the urine, estimated by the Addis count Leucocytes formed the greater part of the urinary deposit in 76% of the patients (fig 4) In glomerulonephritis and vascular nephrosclerosis this happened in only about 14% of cases

In 16% of the patients with chronic pyelonephritis there were more erythrocytes than leucocytes in the urinary deposit Most of these patients had a history of either cystopyelitis or lithiasis, and the bleeding was obviously due either to hyperæmia or to trauma of the mucosa of the urinary tract In glomerulonephritis, on the other hand, this happened in more than a third of the cases, and in vascular nephrosclerosis in only 7%

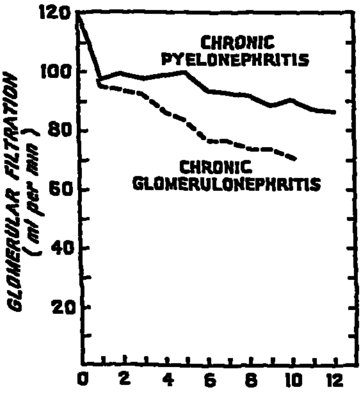

Fig 7—Changes in glomerular filtration-rate

Large and equal increases of both erythrocytes and leucocytes argue against chronic pyelonephritis and in favour of glomerulonephritis The most typical finding in vascular nephrosclerosis was a very small urinary deposit with very slight and equal increases of both erythrocytes and leucocytes

With only this indirect and direct evidence of infection and inflammation we could not, of course, localise the inflammation Only if we find signs of functional renal damage due to the spread of inflammation to renal interstitial tissue, and to damage and destruction of the surrounding structures, can we be reasonably certain about our diagnosis of pyelonephritis

Proteinuria

The late destruction of the glomeruli in pyelonephritis has been emphasised, but the presence of a severe toxic process in the immediate neighbourhood of the glomeruli will damage their finest structures (the walls of the capillaries) so much that they will leak protein, and proteinuria will ensue Contrary to what happens in glomerulonephritis, which attacks the glomeruli primarily, the quantity of protein in the urine in pyelonephritis rarely exceeds 5 g daily (fig 5)

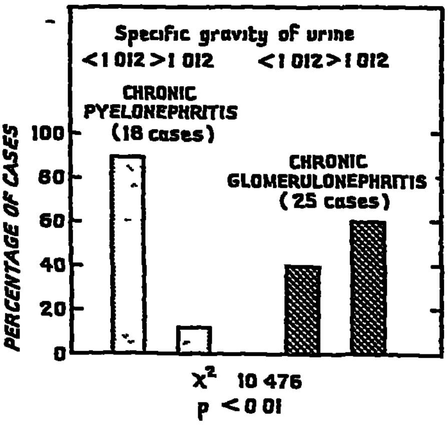

Fig 9—Incidence of inability to concentrate urine to sp gr >1·012, with glomerular filtration rate <30 ml per min

Protein in urine in the tubules and degenerated cells of the tubules yields material from which ca patient's bed table We have found that patients soon get used to this and sleep is not disturbed

We have placed further emphasis on these established methods in the hope that they may assist others in the differential diagnosis of thyrotoxicosis and anxiety states We suggest that serum creatine levels can be estimated on such patients during their first outpatient attendance Those with raised serum creatine levels can then be admitted to hospital for a few nights so that an accurate recording of the sleeping pulse-rate can be made Further confirmation of overactivity of the thyroid gland will be provided if a definite fall in serum creatine levels and sleeping pulse rate occurs after the administration of Lugol's iodine for three weeks

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London, W 1 — D MATTINGLY

SALMONELLA OSTEOMYELITIS

SIR,—The article by Dr White and Dr Meynell (April 7), in which they describe a case of paratyphoid-C osteomyelitis, prompts us to comment on a particular aspect of salmonella osteomyelitis which has so far not been adequately considered

They state that their patient is a Jamaican, which, to our mind, means that he is, to some degree, of Negro descent If this is true, it is a pity that the patient has not been examined for the presence of one of the varieties of sickle-cell disease

All observers have stressed the utmost rarity of salmonella infections of the bones This is less true in countries where sickle cell anæmia is prominent At the native hospital of Leopoldville we have observed in less than two years 5 cases of salmonella osteitis, all occurring in infants suffering from sickle cell anæmia [1] This is not a pure coincidence in the available literature we found 8 further cases of this association and recently we came across a 9th published case [2] In one of these publications, the existence of sickle cell disease was apparently not suspected by the author, but the hæmatological data of the patient could hardly fit better with this diagnosis [3]

One of us,[4] reviewing the epidemiology of salmonellosis in the Belgian Congo, referred to 14 salmonella cultures, all isolated from osteomyelitis in Negroes with sickle cell anæmia

These facts seem to suggest that the pathogenetic relationship between the two conditions is very close, and any description of salmonella osteomyelitis in a Negro is incomplete when it gives no information on the presence or absence of sickle cells

In the data given by Dr White and Dr Meynell, the patient's hæmoglobin value is too high for the diagnosis of homozygous sickle-cell anæmia, it is however perfectly compatible with sickle cell/hemoglobin C disease, a hæmoglobinopathy which is known for its ability to provoke bone changes Recently, we reported a case of this disease, with long standing suppuration of one hip [5] Unhappily, the pus was not examined bacteriologically

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Institut de Medecine Tropicale
Princesse Astrid
Leopoldville Belgian Congo — E VAN OYE

SIR,—The article by Dr White and Dr Meynell was very interesting to us here I wish, however, to draw attention to some inaccuracies

Dr White and Dr Meynell reported that " in the West Indies by far the commonest type of salmonella infection is paratyphoid C ", actually, paratyphoid C is rare and the commonest type of salmonella infection is *S typhi*

They also state that 584 cases of paratyphoid were notified in Jamaica in 1952 The W H O report to which they refer gives this figure under the heading " typhoid and paratyphoid fevers cases ", in actual fact, all 584 cases were typhoid fever, and none were paratyphoid

Only a few months ago we diagnosed our first case of paratyphoid C in Jamaica, and this has attracted so much interest that we are publishing the case shortly

Pathology Department
University College of the West Indies,
Jamaica — LOUIS S GRANT

USE OF VITAMIN K IN THE NEWBORN

SIR,—We would like to draw attention to the possible dangers of overdosage with water-soluble vitamin K analogues, when administered parenterally, especially in premature babies

Until recently, it had been thought that vitamin K was entirely non-toxic and might safely be given repeatedly in doses of 10 mg , but recent investigations[1] suggest that in premature babies these doses may lead to the development of kernicterus

There is good evidence that an intramuscular injection of 0 5–1 mg (e g , menaphthone *B.P C*) is more than adequate for the prophylaxis of hæmorrhagic disease of the newborn, due to hypoprothrombinæmia [2] In cases of established hæmorrhagic disease of the newborn due to this cause a dose of 1–2 mg should suffice to restore the plasma-prothrombin to normal levels

N B CAPON
V M CROSSE
W GAISFORD
R LIGHTWOOD
F W MILLER

PHENYLBUTAZONE IN THE TREATMENT OF PROLAPSED INTERVERTEBRAL DISC

SIR,—I should like to draw attention to the remarkable effect of phenylbutazone in cases of herniated intervertebral disc

In starting this treatment rather over a year ago, I thought that the drug might have an anti inflammatory action at the nerve root, and so diminish the pain of the condition, but so constant has its effect proved in relieving the pain and reducing the physical signs (e g , straight leg raising and areas of altered cutaneous sensitivity) that I now believe that it exerts a direct action on the disc itself, possibly by altering its fluid content differentially as between the annulus fibrosus and the nucleus pulposus In fact, I believe that it performs a " medical manipulation "

Now that I have treated well over 50 cases of disc hernia (cervical, thoracic, and lumbar) with an estimated 90% success rate, I feel the time has come to make known the method so that someone better qualified than myself can produce a properly controlled series, with some research into the mode of action of this extraordinary drug I have been able to find only one report of its successful use in this condition [3]

The dosage I employ is 200 mg three times a day for two days, and then twice a day for two days, making a total of 2 g There is no point in prolonging the administration of this potentially dangerous drug beyond that, since, if it is going to work, it produces dramatic relief in the first thirty six to forty hours, but it has very little effect on the lesser discomfort and stiffness of the healing phase If the condition is not cured in

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[1] Vandepitte J Colaert J Lambotte Legrand, J , Lambotte Legrand C , Périn, F *Ann Soc belge Med trop* 1953 33 511

[2] Ellenbogen N C Rain, J Grossmann L *Amer J Dis Child* 1955 90 275

[3] Carrington, G , Davison W *Bull Johns Hopk Hosp* 1925 36 428

[4] van Oye E *Ann Soc belge Med trop* 1955 35, 229

[5] Vandepitte J , Colaert J *Ibid* p 457

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[1] See *Lancet* 1955 i 669, 819 *Arch Dis Childh* 1956 30 501

[2] Hardwicke S H *J Pediat* 1944, 24, 259

[3] Brunelli G *Min Med Torino* 1954, 45 1819

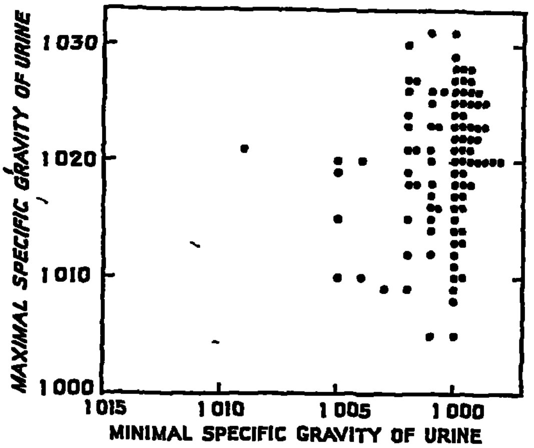

Fig 10—Correlation of maximal and minimal sp gr of urine in chronic pyelonephritis

be formed. It is therefore surprising to find that the number of urinary casts in chronic pyelonephritis is much smaller than that in glomerulonephritis, seldom being more than 1,000,000 a day (fig 6); more than 2,000,000 a day was quite exceptional. The reason for this difference between the two diseases is not clear.

Glomerular Filtration

The changes of glomerular filtration over several years in pyelonephritis and in glomerulonephritis are shown in fig 7.

Fig 7 was constructed on the assumptions that (1) before the start of their disease, all the patients had a normal average glomerular filtration rate of 120 ml. a minute; (2) glomerular filtration decreased regularly from this rate to that found on our first examination; and (3) it continued to decrease regularly from then to subsequent examinations in our laboratory. Data for the intervening years were interpolated. Although the assumptions are unwarranted, the individual deviations from the regular course are certainly in both directions and cancel each other.

A greater obstacle distorting the result is the difficulty of establishing the time of onset of pyelonephritis. The onset was assumed to coincide with the first symptoms; this was almost certainly wrong in most cases and tended to make the course of the disease appear shorter than it was and to give the graph a steeper downward trend. We have to bear this in mind when analysing the diagram.

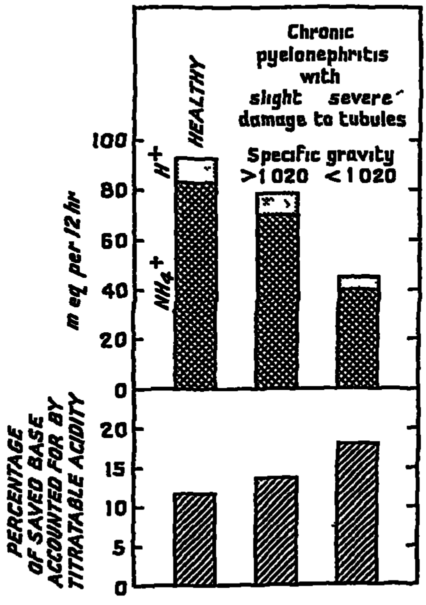

Fig 11—Changes in base-saving in chronic pyelonephritis

The diagram, however, shows clearly that in chronic pyelonephritis glomerular filtration is gradually decreased, but not so fast as in glomerulonephritis. This is in good agreement with the anatomical facts.

Function of Tubules

Grave damage is done to the tubules from the onset of pyelonephritis and disturbs their function. Many nephrons become passive channels which have more or less lost the power of fine differential reabsorption and active excretion.

Little work has been done in our laboratory on the functions of the proximal tubules in pyelonephritis, so I cannot add to the findings of Raaschou (1948). These functions can only be assessed by rather tedious techniques requiring well equipped and well staffed laboratories.

The distal tubules are also damaged from the onset. These tubules form the section of the nephron which, according to current views, reacts sensitively to changes of the blood level of the antidiuretic hormone. By excreting urine of a higher or lower osmolarity than that of the extracellular fluid the distal tubules regulate changes of osmotic pressure (and possibly of volume) of the *milieu interieur*. Also, by exchanging sodium (which accompanies acid radicals in the extracellular fluid and glomerular filtrate) for hydrogen, potassium, and ammonia ions, they help to regulate the acid base balance of the *milieu interieur*.

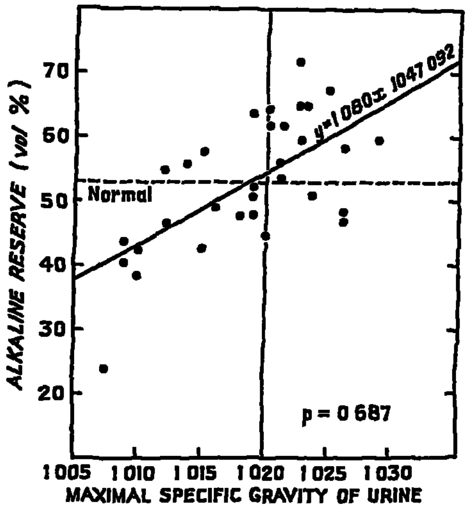

Fig 12—Correlation of maximal sp gr of urine and alkaline reserve

Functional disturbances of the distal tubules can be found in the earliest stages of chronic pyelonephritis by methods practised in most general hospitals. Thus, in almost every case of acute pyelitis, or even transient obstruction of the urinary tract, there is protracted impairment of the concentrating ability of the kidneys. It was this loss of concentrating power, quite out of proportion to the degree of impairment of the glomerular filtration-rate, that brought our attention to this particular disturbance of function.

The dissociation between the reduction of glomerular filtration and the concentrating ability was one of the

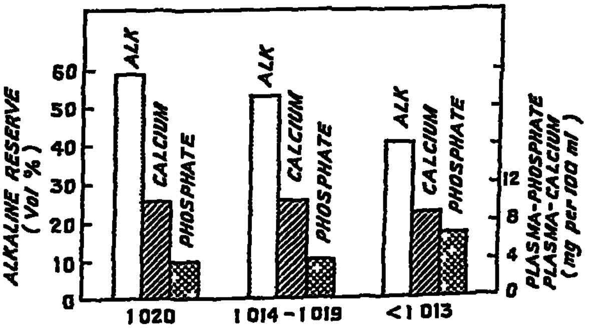

Fig 13—Correlation of maximal sp gr of urine and alkaline reserve plasma-calcium, and plasma phosphate levels

the first four days, phenylbutazone must be abandoned and recourse had to bed rest or other remedies If it is cured, prolonged administration of phenylbutazone will not prevent a relapse, but it will cure such a relapse if exhibited again after an interval It is not necessary to prescribe rest at all in this treatment if the pain is really severe the patient will have to rest whether advised to or not, but lesser degrees of pain are equally well relieved if he carries on with his normal work, and in fact I believe this course is preferable, since it partly prevents stiffness and weakness during convalescence

If anyone is sufficiently convinced by my findings to want to put this treatment to the test, I should be delighted to afford him any help in my power

Kingston upon Thames
Surrey
CHARLES STEER

THE WELFARE OF SPASTICS

SIR,—I was naturally very interested in your annotation of May 5 Because of your suggestion that the National Spastics Society may have ignored the need for "plodding and dispassionate scientific study," I would like to refer to what has for obvious reasons been a little known aspect of our work—research

The Society is setting aside £45,000 for a five year scheme of medical research and has recently allocated £25,000 towards this sum The project is being conducted by Dr Paul E Polani, in collaboration with the Society's medical research committee, and is the most far ranging investigation, prospectively and retrospectively of the ætiological and clinical aspects of infantile cerebral palsies Particular regard is being paid to the association and effects of prematurity and infantile cerebral palsies, and close collaboration is to be maintained with maternity centres It is hoped by this means to procure new evidence on the causation of cerebral palsy

This is the most substantial of the projects comprised in the Society's medical research programme, which however, embraces three other investigations of immediate importance

In Bristol the Society is sponsoring the scientific study of cerebral palsy by a team under Prof A V Neale professor *of child health*

In the sphere of psychology and education a subcommittee is investigating intellectual assessment of those suffering from cerebral palsy

The society is also sponsoring a fourth research project an investigation of intelligence levels at St Margaret's School, Croydon, forming part of the study of the background of cerebral palsy

At this stage it would be wrong to add any more, but I trust the above will suffice to show that the N S S has a well defined policy for tackling this problem

I D DAWSON SHEPHERD
Chairman
London W 1 National Spastics Society

5-HYDROXYINDOLE ACETIC ACID IN URINE

SIR,—The quantitative estimation of the urinary output of 5 hydroxyindole acetic acid has been suggested as the method of choice for a comprehensive evaluation of the general metabolism of 5-hydroxytryptamine under normal, experimental, and pathological conditions

Without precautions to preserve the acidity of the urine—particularly twenty-four-hour specimens—results will not be reliable and comparable This is especially important in cases where the daily excretion of 5 hydroxyindole acetic acid is low, as in some diseases of the blood and liver—e g, Werlhof's disease and other thrombocytopenic diseases[1]

5 hydroxyindole acetic acid is rather unstable to both light and air and in alkaline solution, owing to the presence of a phenolic and an indole group This feature could also explain the red colour of the urine in some patients with an intestinal carcinoid with metastases, where the urinary output of 5-hydroxyindole acetic acid is greatly increased Therefore, when urine is being continuously collected it is absolutely necessary to collect all samples in a dark bottle, which should contain a small quantity of concentrated hydrochloric acid, and if possible the bottle containing the urine should be stored in a refrigerator The addition of the acid to the urine maintains it at the correct acidity (pH 4·0) for the subsequent purification, extraction, and estimation

Department of Obstetrics
and Gynæcology
University of Edinburgh **F J SCANDRETT**

OXYGEN FOR EMPHYSEMATOUS PATIENTS

SIR,—The treatment of emphysematous patients with incapacitating dyspnœa is disappointing, but now, thanks to Dr Cotes and Dr Gilson, whose article appeared last week, domiciliary oxygen therapy is a possibility I eagerly await the results of extended trials and improved apparatus I hope that in their further studies they will be able to estimate the oxygen of the arterial blood by the manometric Van Slyke method, since I have found that the oximeter is quite inaccurate with oxygen saturations of less than 80% It would also be interesting to know the partial pressure of carbon dioxide in the arterial blood in these patients

In regard to their remarks about addiction to oxygen, I do not think there is any great danger since in hospital practice I have had only 1 such case in 5 years, during which I have treated many patients suffering from chronic respiratory insufficiency for long periods with oxygen

I do not want to appear pessimistic, but it is well to remember that one must always be cautious in assessing results, since it is well known that, in emphysema, any form of treatment is liable to produce temporary benefit

Chase Farm Hospital
Enfield Middx **THOMAS SIMPSON**

TUBAL OCCLUSION

SIR,—Twenty-three years ago in Germany there arose a man who postulated that if you say a thing loud enough and often enough, eventually it will be accepted as a fact About the same time a far greater man (Winston Churchill) said at the Royal College of Physicians "The longer you can look back the further you can see forward"

The reason I write thus is that the statistics of a certain hospital have been so often copied, reiterated, and repeated that there is some chance of their being generally accepted I refer to the statement that among patients attending infertility clinics who are found to have blocked tubes, spasm, irritability, anæsthesia, nerves, or even frailty in deductions and methods, are the causes of tubal occlusion in all but 6–7% of cases

There is danger in such a doctrine, for thirty years' clinical experience of hysterography and carbon dioxide insufflation, together with the published figures of three continents, show that, except in Australia, tuberculosis alone accounts for 5–6% of all occlusions Moreover, if the records of infertility clinics are carefully dissected, it will be found that not less than 8–10% of tubal blockage is due to gonorrhœal, pneumococcal, staphylococcal, or *Escherichia coli* infections—to say nothing of endometriosis and those particularly interesting types of complete cornual occlusion where, owing to streptococcal infection of secundines (often following criminal or induced abortion), it will be found that the outer two-thirds of the oviduct in over 80% of cases remains absolutely healthy in its mucous membrane and musculature, and therefore can very readily be used for tubo uterine implantation

To dismiss tubal occlusion airily is hurtful to the community as well as to those who are working, or have worked, in the great cities of the world, for although plastic operative repair can do little for the majority of the first types mentioned it has proven, in capable hands, here and in Paris, to give a 38% success rate from the point of view of subsequent full-term pregnancy, in those young women who have had the misfortune

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[1] Bigelow, F S *J clin Invest* 1953 32 [illegible]

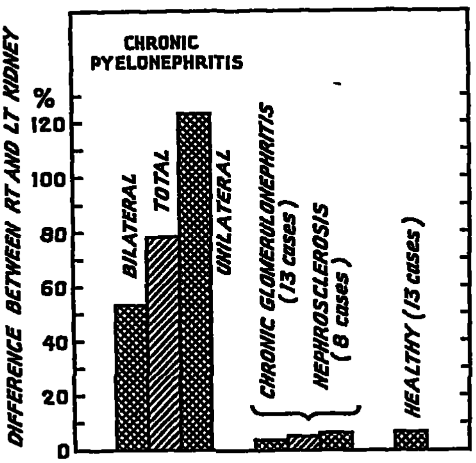

Fig 14—Comparison of concentrating powers of right and left kidneys

main criteria of the clinical diagnosis of chronic pyelonephritis It was therefore necessary to verify the validity of this criterion in 20 cases in which the clinical diagnosis was confirmed by either biopsy or necropsy The findings were compared with those in 49 cases of chronic glomerulonephritis and 16 of vascular nephrosclerosis similarly confirmed (fig 8)

In fig 8 the regression line correlating glomerular filtration with maximal concentrating ability is lower in chronic pyelonephritis than in glomerulonephritis, which gives a lower regression line than does vascular nephrosclerosis This fact supports our previous conclusion that, at all stages of reduction of the glomerular filtration-rate, the impairment of concentrating ability is more severe in chronic pyelonephritis than in chronic glomerulonephritis It also confirms that the loss of function of the distal tubules in vascular nephrosclerosis is gradual and late

Closer inspection of fig 8 reveals another theoretically interesting and clinically important feature of the isosthenuria of pyelonephritis In patients whose glomerular-filtration-rate has fallen below 30 ml a minute the specific gravity of the urine is less than 1 012 (sometimes less than 1 010) more often in pyelonephritis than in chronic glomerulonephritis This is still more obvious in fig 9 Only 10 of 25 patients (40%) with chronic glomerulonephritis, with isosthenuria, and such low average glomerular filtration rates, excreted urine of maximal specific gravity less than 1 012, whereas 16 of 18 patients (89%) with chronic pyelonephritis with a similar reduction of the glomerular filtration rate excreted urine of so low a specific gravity This difference explains why patients with advanced chronic pyelonephritis had more severe polyuria than had patients with chronic glomerulonephritis In pyelonephritis the polyuria can be severe enough to lead to the erroneous diagnosis of diabetes insipidus

In applying the ability to concentrate the urine to the assessment of the extent of the renal lesion one must not forget that, owing to the irregularity of spread of pyelonephritis, the specific gravity of the urine is that of a mixture of urine from damaged or destroyed nephrons with urine from relatively intact tubules Thus, a specific gravity of 1 020 can be the result of either moderately severe pyelonephritis of both kidneys or of a mixture of highly concentrated urine from one healthy kidney and of isosthenuric urine from the other kidney, but, when the specific gravity indicates isosthenuria, it means that there is widespread damage of both kidneys

A urinary specific gravity below that of plasma ultrafiltrate shows that, even with the most severe damage to their cells, the tubules can still absorb some electrolytes from the urine This is further shown by the result of the dilution test (fig 10) Though the ability to concentrate the urine is impaired in practically all cases of pyelonephritis (in some to a very considerable extent), the ability to dilute the urine to a specific gravity of at least 1 002 remains, with few exceptions, up to the last stages of the disease Like the concentration of the urine, the dilution of it is connected with the formation of an osmotic gradient between the blood and the urine in the tubules Fig 10 suggests that dilution and concentration cannot be viewed simply as two aspects of one and the same process, and that, of the two functions, concentration is much more vulnerable than dilution The reason for this difference is unknown

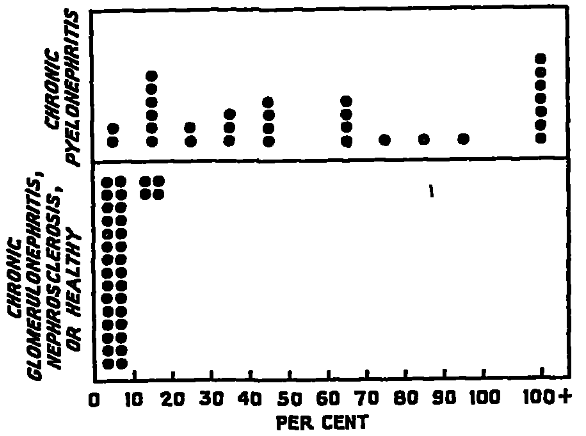

Fig 15—Individual differences in concentrating powers of right and left kidneys

The rôle of the distal tubules in regulating the acid base balance has so far been but little studied in disease and not at all in chronic pyelonephritis, where an alteration of this function may be expected V Fencl (unpublished work) therefore investigated in our laboratory the ability of our pyelonephritics to save base after the administration of ammonium chloride 5 g daily for two days In his preliminary studies he examined the twelve hour urine of the second night for ammonium and titratable acidity—i e, sodium ions exchanged in the distal tubules and used to replenish the alkaline reserve

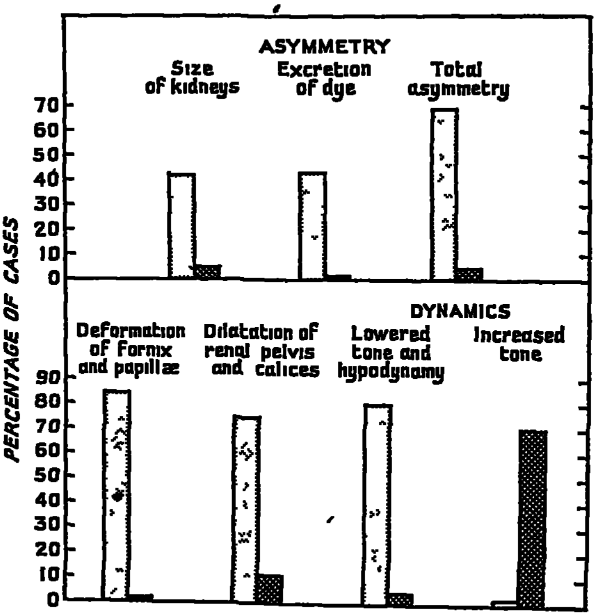

Fig 16—Radiological findings in 96 cases of chronic pyelonephritis (stippled) and 53 of chronic glomerulonephritis (cross hatched)

to suffer criminal or induced abortion, or sometimes *to have had their tubes tied inopportunely*

The incidence of extra-uterine gestation after such surgery has never been as high as 2% in London

London, W 1 V B GREEN-ARMYTAGE

TREATMENT OF TETANUS

SIR,—In our article in your issue of April 28 we produced evidence tending to show that the protracted administration of 50% nitrous oxide and 50% oxygen to patients with severe tetanus may lead to fatal aplastic anæmia Fairly conclusively it was shown that of the two components the acute bone-marrow depression was caused by the nitrous oxide and not by the oxygen

Major Sanders (June 2) calls our attention to the possibility that the pathological changes observed may have been caused by the prolonged use of oxygen at relatively high alveolar pressures This possibility has been in our minds, and we have consulted the available literature without encountering reports of acute bone marrow depression with fatal agranulocytosis following protracted breathing of oxygen at high partial pressures

Furthermore, as stated in our article, when in the two trials nitrous oxide was discontinued nothing else was changed in the treatment, including oxygen administration In other words, in these two patients hæmatological remission took place in spite of the continued use of 50% oxygen—nitrous oxide being replaced by nitrogen

Finally only this during the epidemic of poliomyelitis in Copenhagen in 1952 50% oxygen and 50% nitrogen was administered to more than two hundred patients treated with intratracheal positive pressure breathing This in many cases was kept up for several months without ever leading to the appearance of aplastic anæmia or agranulocytosis

Blegdamshospitalet
Copenhagen

H C A LASSEN
ERIK HENRIKSEN

PLASMA FIBRINOLYTIC ACTIVITY IN CIRRHOSIS OF THE LIVER

SIR,—We have read with interest Dr Fearnley's letter of April 14, referring to our paper with the above title[1]

When our observations were made we were aware of Dr Fearnley's important contributions[2–5] to the study of fibrinolytic activity Regrettably our facilities were not such as to permit the employment of the low-temperature technique which he has described Being fully aware of the lability of the fibrinolysin, we were at pains throughout to ensure that all specimens of plasma under test were clotted by the addition of thrombin at a fixed time, 15 minutes, after obtaining the blood Observations on a series of normal subjects and on patients with cirrhosis of the liver had established that there was *no significant difference in fibrinolytic activity* between specimens of the same plasma kept at room temperature for 10 and for 20 minutes before the addition of thrombin Throughout our communication the expression "healthy controls" was used, and the findings in these controls only represented the fibrinolytic activity encountered in healthy subjects under the same conditions as the experimental observations They were not intended to represent the activity which might be encountered in *normal* subjects under other conditions

We are very much aware that serum is possessed of antifibrinolytic activity This activity, however, is vastly different from the inhibition of plasmin by the serum plasma inhibitor of plasmin In mixtures of plasmin and normal plasma a relatively slight reduction in the ratio of plasmin to plasma converts a clot which lyses in less than 30 minutes to one which *will not lyse at all*[6] These results can be reproduced using plasmin, a solution of fibrinogen and serum Normal plasma does not appear to be possessed of antifibrinolytic activity[6] On the other hand, we have found that normal serum significantly reduces fibrinolytic activity, but our observations indicate that this is a function of the concentration of the serum and the duration of incubation of the fibrinolytic plasma serum mixture before the addition of thrombin In contrast to the plasma of healthy subjects, that of patients with carcinoma of the liver has substantial antifibrinolytic activity, and this effect is enhanced by incubation The serum from such patients possesses greater antifibrinolytic activity than normal serum, but this is not increased by incubation Of perhaps greater interest is the markedly variable antifibrinolytic activity of the plasma of blood obtained from normal spleens at operation Typical examples of our results, showing the lysis time in hours, are set out in the accompanying table

Plasma or serum tested for antifibrinolytic activity		Duration of incubation before addition of thrombin	Ratio of fibrinolytic plasma to plasma or serum under test					
			1/0	1/1	2/1	5/1	10/1	[illegible]
Healthy control peripheral blood	Plasma	Nil 2 hr	4 5	6½ 8	6½ 6	6 5	6 [illegible]	5½ 5
	Serum	Nil 1 hr 2 hr	4 4½ 5	7½ 15 21	6½ 10 14	5½ 5½ 6	5 5 5½	4 5 5
Carcinoma of liver peripheral blood	Plasma	Nil 1 hr 2 hr	4 4½ 5	26 2/3 lysed 26 No lysis 26	13½ 18 19½	6½ 9½ 9½	6½ 6 6	5½ 5½ 6
	Serum	Nil 2hr	4 5	26 25½	17½ 18	7½ 8½	6 7	5½ 6
Blood from 2 normal spleens	1 Plasma	Nil	3	No lysis in 24 hours				
	2 Plasma	Nil	3	12	12	8	6	6

The fibrinolytic plasma was obtained from 2 patients with cirrhosis of the liver, and the amount employed in each test was constant The final dilution of plasma or mixtures of plasmas in veronal acetate buffered saline was 1/25

Invariably in our cases of cirrhosis of the liver we have found a complete absence of fibrinolytic activity in the plasma of blood obtained from the spleen removed at operation, yet during operation, both before and after removal of the spleen, there was intense fibrinolytic activity in the peripheral blood—in some cases so intense as to lyse in 4 minutes the clot formed by the addition of thrombin to whole citrated plasma The antifibrinolytic activity of the plasma of the splenic blood appears to vary even more widely than that of normal splenic blood

Since writing the paper referred to by Dr Fearnley we have followed up for longer periods the patients who were splenectomised and have extended our observations to many others We have found that increased fibrinolytic activity does not always reappear after the initial phase of inhibition following operation When it does so, as in the three cases reported, it subsequently disappears and *in all patients* increased fibrinolytic activity is no longer present 2 months after splenectomy It has remained absent in the follow up ranging up to 14 months, but observations on patients who have been splenectomised for more than 2 years suggest that increased activity may return, though with reduced intensity

The application of the observation that corticotrophin inhibits spontaneous fibrinolytic activity in cirrhosis of the liver to the prevention or control of bleeding associated with intense fibrinolytic activity had occurred to us While we have found that corticotrophin cortisone,

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[1] Kwaan H C McFadzean A J S, Cook J *Lancet* Jan 21, 1956 p 132
[2] Fearnley, G R Revill R Tweed J M *Clin Sci* 1952 11 309
[3] Fearnley, G R Tweed J M *Ibid* 1953 12 81
[4] Fearnley, G R *Nature Lond* 1953 172 544
[5] Fearnley, G R Lackner R *Brit J Hæmat* 1955 1, 189
[6] Bidwell E *Biochem J* 1953 55 497
[7] Bidwell E Macfarlane R G *Ibid* 1951 49 xlii

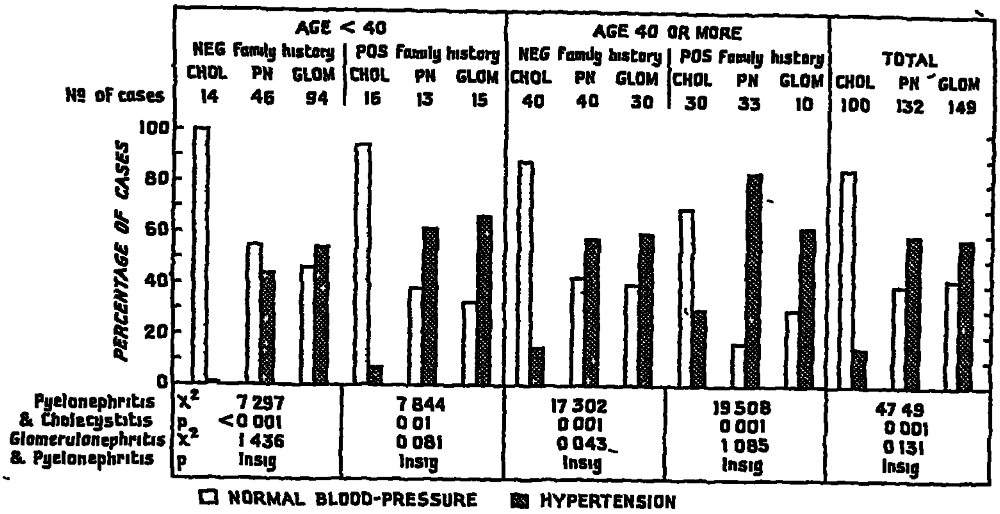

Fig 17—Incidence of hypertension in chronic pyelonephritis, chronic glomerulonephritis, and cholecystitis

A healthy man excretes in twelve hours 90 m eq of hydrogen and ammonium (fig 11) The same quantity of fixed base is saved to the body 11 5% of this saved base is accounted for by titratable acidity, and 88 5% by ammonia In chronic pyelonephritis with a mild reduction of function of the distal tubules (urinary specific gravity above 1 020) a slight restriction of this process may occasionally be found, but in patients with a urinary specific gravity less than 1 020 the efficiency of the whole exchange mechanism drops to about half, primarily owing to deficient production of ammonia This follows from the fact that the proportion of saved base accounted for by titratable acidity increases to 17 4% The hydrogen exchange is, however, limited by the concentration of hydrogen ions in the urine excreted by the tubules Hence a consequence of this reduction of the ability to excrete ammonia is the loss of fixed base which accompanies radicals of stronger acids in the urine This permanent loss of sodium from the body tends to produce dehydration, especially if a salt free diet is inadvertently prescribed for the patient

The failure of the tubules to excrete hydrogen into the urine may increase the hydrogen ion concentration within the cells of the tubules This would initiate a vicious circle by still further depressing the production of ammonia from glutamine, the optimal pH of glutaminase being 7 8 The intracellular acidosis probably causes increased loss of potassium from cells of the tubules Although potassium enters into the base saving mechanism in the urine in the tubules, being exchanged partly for sodium bound by stronger anions, its losses further complicate the disturbance of the electrolyte metabolism in advanced pyelonephritis On the other hand, this increased loss explains why we have never found potassium accumulating in the extracellular fluid, even in the most advanced stages of pyelonephritis with an extremely low glomerular filtration rate, in spite of the fact that under these conditions the accelerated breakdown of tissue proteins releases much potassium into the extracellular fluid

The restriction of sodium exchange in the distal tubules and the permanent loss of fixed base from the body decrease the alkaline reserve and produce acidosis There is a very good correlation between the decrease of concentrating power and that of the alkaline reserve to low values Fig 12 shows that only 4 patients with a urinary specific gravity above 1 020 had an alkaline reserve below our lower normal limit (53 vol %), and only 4 patients with a urinary specific gravity below 1 020 had a normal alkaline reserve The correlation with glomerular filtration-rate is slightly less satisfactory (P=0 496) However, all the patients in whom this function was severely reduced were acidotic No doubt, in these patients ther was a very severe lesio of the tubules and katabolism exceeded anabolism

Calcium and Phosphoru Metabolism

Chronic acidosis i usually connected wit disturbances of calcium and phosphorus metabolism a fall in the plasma phosphate level, whereas the plasma calcium level is normal o slightly below normal, provided the glomerula filtration rate is normal Fig 13 shows that th was not what happened in our pyelonephritics We found changes in the ratio of plasma calcium and plasma phosphorus levels in only the most advanced cases with a urinary specific gravity below 1 013 These changes, however, consisted in a rise in the plasma phosphate level and a fall in the plasma calcium level

Simple parathyroid hyperfunction as a consequence of increased urinary excretion of calcium in these acidotic patients was clearly an inadequate explanation Analysis revealed that the rise in the plasma phosphate level was the primary event This was obviously a consequence of the much reduced filtered load of phosphate, even the greatest possible increase of parathyroid secretion in these patients who were chronically losing calcium in their urine and a great reduction of the power of the tubules to reabsorb phosphate were insufficient to restore their plasma phosphate level to normal Probably the plasma calcium level dropped partly as a consequence of its increased urinary excretion in acidosis This excretion, however, was not significant enough to produce detectable osteoporosis Although the amount of alkaline phosphatase was slightly increased in the patients in this last group, no significant demineralisation of the bone, or cyst formation, was found on radiography in any of our patients with a far advanced renal lesion Biopsy specimens of bone obtained in some of our patients during lumbotomy did not reveal any changes in the structure of bone

Ureteric Catheterisation

I have been dealing so far with the effect of interstitial renal inflammation on the function of the neighbouring

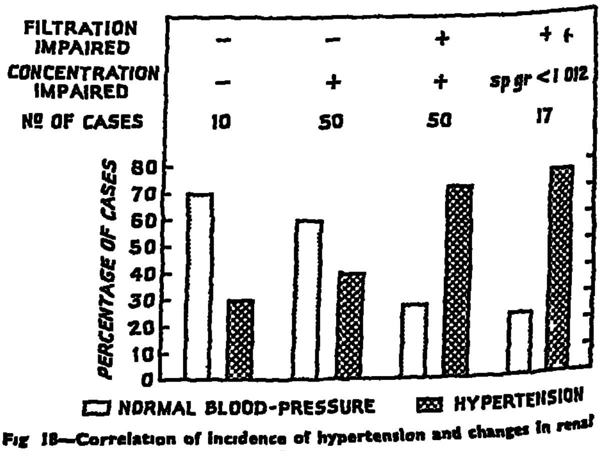

Fig 18—Correlation of incidence of hypertension and changes in renal function

control have ceased to be employed. It appeared to me that then only could the proper study of insanity begin, the removal of restraints, and of all violent and irritating methods of control, then first permitting the student to contemplate disorders of the mind in their simplicity, and no longer modified by exasperating treatment. Patients could then be presented to their observation as subjects of study and reflection." [7]

Psychiatrists were for the first time enabled to study and investigate in detail the minds of their patients. This in turn led in 1853 to the issue of the first number of *The Asylum Journal of Mental Science* published "by the Authority of the Association of Medical Officers of Asylums and Hospitals for the Insane" ‡. The further development of psychiatry in the second half of the nineteenth century bears ample evidence of the fruits of Conolly's labours.

THE RETURN OF RESTRAINT

A despondent, perhaps prophetic, state of mind to which Conolly was at times subject led him to fear lest the selfish interests of mankind might lead to reaction, and that much of his work might after all be lost to the world. "It seems to have been in some such mood that at the conclusion of his last work he was led to express an anxious hope, that nothing should be allowed to interfere with its continuation, that no future economy and no delusive theories would ever lead to the abandonment of '*non-restraint*' *in the treatment of the insane*." [10] §

In insanity the dividing line between treatment and restraint is very fine, and Conolly's forebodings were justified. "Chemical restraint of the cells of the sick brain" took the place of the old "mechanical restraint of the body." [11] Thus bromides (1857), chloral (1869), paraldehyde (1882), and barbiturates (1903) were all in turn considered harmless non-addicting specifics for mental disorders, and each allowed restraint disguised as treatment to slip back unobtrusively into the care of the insane. Some recognised the danger.

> "The successful argument against mechanical restraint was, that although it kept the patient's body quiet, it really *aggravated his malady*. *the question now which should be* considered is, whether chemical restraint does permanent good, or whether by diminishing excitement at the ultimate cost of mental power it 'makes a solitude and calls it peace.'" [11]

Since the 1930s psychiatry, jealous perhaps of the therapeutic advances in general medicine, has seen a spectacular rise and spread of "physical methods of treatment." In various forms such methods have always enjoyed a vogue ‖. Like the drugs which in part they replaced, they also were not abandoned in mental-hospital practice when they failed as therapies. Like drugs they remained as instruments of restraint in the guise of treatment. hypoglycæmic, electrical, and neurosurgical. The frequently made statement that electrical or chemical restraint is essential for keeping the peace in chronic or refractory wards of mental hospitals is shown by the experience of Cameron et al [8] to be fallacious. They demonstrated once again that better results can be achieved by skilled mental nursing. New drugs continue to be synthesised and with them claims that during their administration disturbed patients require less physical treatments. At the same time reports are published demonstrating reduction in drug bills made possible by more regular use of E C T. "since the introduction of electrical *treatment, the modern trend has* become more to rely on this in intractable cases." [13]

A KEY POSITION LOST

What does this development mean to the status of the mental nurse, deprived of the very functions to which mental nursing owes its inception—that is, to counter alienation by sustained, kindly human understanding and contact. When patients are controlled or suppressed by drugs or electricity all respect for them as mentally sick persons is lost. "when the patient is tied up, all regard for him ceases." [7]

The latest edition of the Royal Medico-Psychological Association's Handbook for Mental Nurses [13] speaks openly of restraint. It has almost nothing to say on the nurse patient relationship, which does not appear in the index of the book. To restraint there are three references.

> "*If a patient shows continued or oft repeated violence*, special measures may be necessary. The doctor may consider sedation advisable. This form of treatment is sometimes known as *chemical restraint*."
>
> "Under certain conditions the doctor may occasionally decide in favour of *mechanical restraint*."
>
> "'Sedation' can be effected in three main ways, by *drugs*, by *hydrotherapy*, and by *electrical treatment*. it brings the psychiatric patient to a more controlled level of behaviour."

In various parts of the book E C T is recommended as effective in the neuroses, psychoses, and organic states. Can a procedure which covers pretty well all aspects and degrees of mental illness be treatment, or is it restraint? Added to this, two new classes of auxiliaries curtail the nurse's direct responsibility for, contact with, and knowledge of the patient—social workers and occupational therapists. Under such a régime the mental nurse at worst spends her time polishing floors, at best she is allowed *to participate in the administration of physical* treatments. Her functions are reduced to less than those of a general nurse, and her status and conditions of work are often lower.

The shortage of nurses as well as of doctors for the staffing of mental hospitals is sometimes brought forward as the excuse for widespread physical treatments, ¶

> " until, by slow but very sure steps, restraints become the usual substitutes for attention, for patience, for forbearance, and proper superintendence. The tendency to neglect those who are deprived of reason still exists, and demands vigilant opposition. What the old system of treatment by restraint really was ought, therefore, not to be forgotten. Its evils were not imaginary, but real and dreadful. they must remain common, however disguised, wherever the system of restraint remains the subject of eulogy." [7]

Especially in a textbook designed for mental nurses.

Physical treatment replacing shortage of nurses starts a vicious circle of fewer nurses, more restraint disguised as physical treatment, less nursing, fewer nurses, more restraint, and so on. Dr Cameron and his colleagues have shown how much can be done with the minimum of well-guided staff. Who will have the courage to repeat the experiment on a large scale so successfully concluded by Dr Conolly in similar circumstances one hundred years ago? He will not find himself short of mental nurses when they are reinstated to their key position.

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‡ It is now called the *Journal of Mental Science*, and the association has become the Royal Medico Psychological Association.

§ The element of restraint is hardly disguised when results of physical treatments are given in terms of "social recovery" or "more controlled behaviour," which significantly appear often in reports of the most permanent form of brain destructive restraint—leucotomy.

‖ As Fulton [12] pointed out, even the use of electricity (in the shape of the electric eel or torpedo) is "a fine old Roman custom introduced in the first century A D by Scribonius Largus." Of course, the operation of trepanning with variable damage to the underlying brain is the oldest procedure known to medical history.

¶ "Dr Conolly was praised for the abolition of restraint but it was not this which ought to be admired so much as his pluck and determination in doing away with it at short and definite notice in a county asylum with a relatively small staff, where many patients had been made intractable by the abuse of restraint." [14]

10 Clark, Sir James. A Memoir of John Conolly, M D, D C L. London, 1869.
11 Maudsley, H. The Pathology of Mind. London 1879.
12 Fulton, J F. The Sherrington Lectures. Liverpool, 1952.
13 Royal Medico Psychological Association. Handbook for Mental Nurses. London 1954.
14 Newington, H H. J ment Sci 1901, 47, 74.

In England Now

A Running Commentary by Peripatetic Correspondents

AT 2.10 A.M. the other night I was wakened with the news that the girl in the room below had been badly burnt. She was warming herself in front of the gas-fire, when her cotton nightdress caught fire. I phoned the local hospital which I know specialises in burns, and has a large ambulance depot, and asked for an ambulance. I was told politely that I must dial 999. I rang 999, gave the address, and again asked for an ambulance. The operator, having taken down the name and age of the patient and my own name (though not age), announced that an ambulance would come immediately.

The owner of the house and I were administering hot sweet tea and packing a suitcase for the patient when there was a loud bang on the front-door. Four firemen were standing on the door-step, and, parked in the road was an immense fire-engine complete with a giant ladder. They inquired where the baby was. I explained there was no baby, and no fire, but eventually it transpired that the fire service turns out for every emergency call involving burns, whether or not there is a fire to be put out. The house shook as four pairs of heavy boots lumbered upstairs. The officer in charge made a note of the name and age of the patient, the name of the landlord, and the age of the house. He pointed out there was no fire-guard on the gas-fire. Finally he turned his attention to the girl on the bed, shivering from shock and cold. One of the men stamped downstairs, to return a minute later with a small cardboard box containing a sterile sheet. Then a police inspector suddenly appeared in the room, presumably let into the house by the fetcher of the sterile sheet. While I draped the sheet round the patient's burnt limbs, the police officer asked the now customary set of questions. He also commented on the absence of a fire-guard.

The room seemed a trifle crowded with five men and two women standing round the bed, but it became even more so a few moments later when three ambulance-men joined the party. Their senior officer once again asked the name and age of the patient, the name of the landlord, and the age of the house, and he, too, looked accusingly at the gas-fire and muttered something about no fire-guard. After these formalities, the patient was taken downstairs, accompanied by eight men, one stretcher, and a night-bag. Neatly parked outside the house were the fire-engine, the police-car, and the ambulance. It was then 3 A.M.

We were on the point of creeping back to bed when there was another hammering on the door. Three shame-faced firemen and one policeman stood in a row. The policeman wanted to know if we had the address of the patient's parents; the firemen had left something upstairs and went up to fetch it. It was the little cardboard box which had housed the sheet.

* * *

We flew from Accra to Freetown on a Sunday, stopping first at Abidjan (Côte d'Ivoire). The local French had turned out in force to meet a plane from Paris. In the restaurant the men, in very short shorts, sipped *apéritifs* and greeted all and sundry with perfunctory handclasps, while the women, wearing tropical clothes with all the *chic* of the Rue du Faubourg St.-Honoré, chatted vivaciously. We *transitaires* enjoyed an excellent hors-d'œuvre, followed by a *ragoût* and a bottle of Beaujolais. The only solecism was the *toilette* which was distinctly superior to metropolitan standards.

Our next stop was Robertsfield. Liberia is not an American colony (though cynics sometimes call it a colony of the Firestone Tyre Company), but it has a historic link with the States, and Robertsfield is run (with superb efficiency) by Pan-American. Well, if the French have gallicised their colonies, Pan-Am have certainly americanised Robertsfield. An air-conditioned passenger lounge, a large portrait of President Eisenhower with a warm-hearted message to travellers below it, and coffee or 'Coca-Cola' for those in need of refreshment. The final touch is provided by African airport police, in American uniform, each with a revolver on his hip and a sloping bandolier of cartridges.

* * *

As it was my third visit to the outpatient department, I knew the procedure and could watch with haughty disdain the new patient who sat and moved along with the old patients. I was surprised that she was not severely reprimanded, as I had been when I did the same on my first visit. But perhaps she was let off because the young clerk was not there to marshal us on this occasion. This was lucky, for I was able to collect my notes in front of those who were waiting patiently for authority to direct them. I took my place in the line of waiting patients and in an attempt to estimate the delay before seeing the specialist I asked my neighbour, a solid late middle aged woman, if she had been here long. I was appalled at her reply "Three years," but reassured when after a pause she added "off and on," and then dismayed again when, entirely disregarding Hippocrates and all that, she expounded her views of her husband's illnesses.

It transpired that it was he who was ill, but if she didn't come with him, he would sit in the hospital all day and let everyone go in front of him. He suffered from his nerves, an ulcer, and glaucoma. *The acidity from the stomach accumulates in his body and burns his nerves which make the eye contract so that it almost blows up at times.* The hospital had given her some wonder drops which you could only get from the hospital. They were called Tid and had to be given three times a day; she had tried to get some from the chemist for a friend, but the chemist had never heard of them. Amazing how these ignorant people were allowed to practise in the health service at all. Where would we be without the hospital doctors?

Take her own case, she developed a giddiness of her eyes *(if I got her) about 18 months ago, or was it 19?* Anyway she went to her own doctor and he said it was her nerves; then she insisted on seeing an eye specialist at the hospital and he said there was nothing the matter with her eyes. Just fancy, if she hadn't seen the specialist she might still be having treatment for her nerves. Not that she really believes in all this nerve business. Take her own husband, she always tells him it's only will power. If he really put his mind to it he needn't have any of this ulcer or glaucoma business.

At this moment Sister appeared and said, "Doctor Blank, would you come in now please." As I left my loquacious companion I heard her turn to her next neighbour and remark:

"Fancy him being a doctor. I wouldn't have told him all my ills if I'd known. Doctors aren't allowed to discuss illness you know, the Minister of Health might strike them off if he caught them. That's why some have secretaries, so they can tell the patients what's the matter with them."

* * *

Newspapers treat the hospitals more and more as though they had ceased to be institutions; but why, oh why, when someone goes to hospital, are there still only *two* alternatives open to him? He is either "detained" or "allowed to go home." Even the Liberal dailies suffer from this aberration.

* * *

In our sanatorium we sent a lot of patients home on leave for Christmas; in fact, in one ward, only six Pakistanis and an East African were left. But the carol-singing nurses who visited the ward at midnight on Christmas Eve firmly started their programme with "Christians Awake!"

* * *

At today's domiciliary visit the consultant wanted an electrocardiogram. To everybody's surprise the electrocardiograph produced sweet melodies from the nearby television station instead of T waves and Q waves.

G.P. (jokingly): "You'd better ring them and tell them to stop their show."

Cardiologist (seriously): "I certainly will." And he did.

The reply was: "In one and a half minutes we will stop for two minutes." And they did. The E.C.G. was taken without any interference.

Cardiologist: "You'd better ring them again and tell them that we are grateful for their coöperation."

G.P. on the phone: "Thank you very much for stopping; we managed fine in those two minutes."

B.B.C. Engineer: "Good show."

nephrons I have already emphasised that chronic pyelonephritis spreads irregularly, and that there are usually great differences in its extent in the two kidneys I therefore tried to assess the function of the two kidneys separately After much futile effort, we decided to make do with a study of separate concentrating indices of endogenous creatinine ($\frac{U}{P}$ ratios) in the urine obtained from the two kidneys by ureteric catheterisation The results of this study, made by my collaborator Prat (1955), are shown in fig 14, where the differences in the $\frac{U}{P}$ ratios of the two kidneys are expressed as percentages of whichever ratio was the lower This difference was insignificant in 13 healthy people (6 0%), in 13 patients with chronic glomerulonephritis (3 6%), and in 7 with vascular nephrosclerosis (5 9%), whereas in 31 patients with chronic pyelonephritis the average difference was 78 3% for the whole group, being 123 6% in those in whom there were other reasons to suspect unilateral disease, and 53 5% in those in whom no difference between the two kidneys was indicated on other grounds The diagnostic importance of this finding is clear, especially since the data for the individual cases (fig 15) show very little overlapping

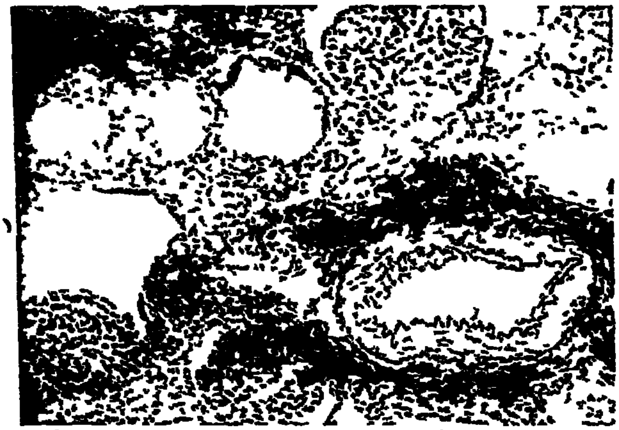
Fig 19—Section of biopsy specimen of contracted kidney in unilateral chronic pyelonephritis with malignant hypertension cured by nephrectomy

Radiography

There has been much controversy about the usefulness of radiography in establishing the diagnosis of chronic pyelonephritis Radiography is, of course, necessary to show anatomical abnormalities of the urinary tract, but it has been doubted whether it can afford further information about the state of the kidneys

Improved methods of diagnosing pyelonephritis enabled my colleague Dejdar (1955) to reinvestigate this question The result was rather surprising of 96 patients in whom chronic pyelonephritis was diagnosed on clinical grounds it was possible to demonstrate in 70% an asymmetry between the two kidneys This was shown by the size and density of the renal shadow and by the speed at which the dye appeared in the renal pelves (fig 16) In the control group of 21 glomerulonephritics such an asymmetry was found in only 4% Further, when serial radiographs were taken in the first few minutes after the injection of dye to gain some idea of the function of calices, pelvis, and ureter, and attention was paid to residues of the dye in the pelvis and calices fifteen to thirty minutes later, a failure of proper contraction and evacuation of the dye—either hypotony or atony—was discovered in 80% A hypotonic urinary tract was found not only in patients with a primary lesion in the urinary tract but also in patients with primary pyelonephritis This discovery supports the view expressed above that a functional disturbance of the urinary tract without any anatomical obstruction may facilitate infection and its further spread to the kidneys This was in sharp contrast to the findings in glomerulonephritics, such changes being found in only 3 7% of such patients, and being neither severe nor widespread On the other hand, spastic calices were found in 69 9% of the glomerulonephritics but in only 1% of the pyelonephritics in whom they were unilateral, whereas in glomerulonephritics they were bilateral

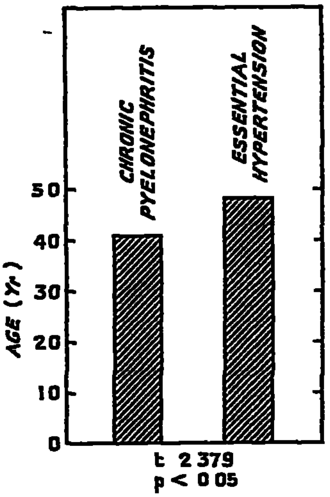

Fig 20—Average ages of patients with malignant hypertension

Hypertension

Our progress in the clinical diagnosis of chronic pyelonephritis shed more light on hypertension in chronic pyelonephritis Investigators in this field are divided into several groups most of them seem to accept that hypertension is present, at least in the late stages, but opponents of this view—e g, Bell (1950)—do not acknowledge any link between pyelonephritis and hypertension Goldring and Chasis (1944), who deny such a connection, at least in unilateral pyelonephritis maintain that hypertension is then coincidental Schroeder and Steele (1941) hold the extreme view that chronic pyelonephritis underlies most cases of essential hypertension, their conclusion being based on minor abnormalities in the pyelograms

We therefore compared the prevalence of hypertension (blood-pressure over 145/95 mm Hg, special attention being paid to the diastolic pressure) in our 132 pyelonephritics and in 100 patients with chronic cholecystitis selected at random (fig 17) The controls were selected from patients because of our previous finding that any organic disease might disturb the vasomotor mechanisms (Brod et al 1954) We also studied hypertension in glomerulonephritis

The average age of our patients with cholecystitis was somewhat higher than that of those with pyelonephritis,

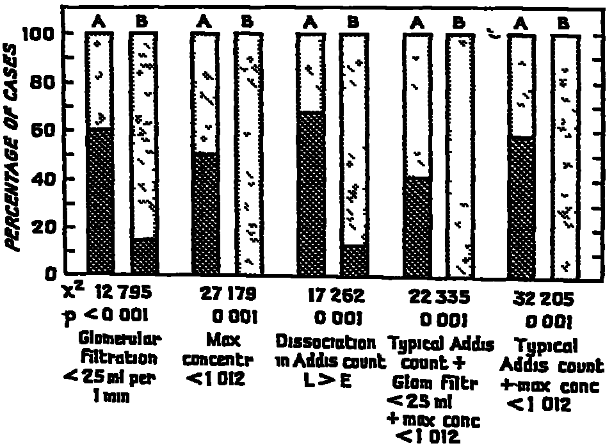

Fig 21—Renal function in malignant hypertension due to chronic pyelonephritis (A) and in essential hypertension (B)

(2) Postoperative bleeding necessitating reopening of the wound, evacuation of clot, and suture of a bleeding point on the right side—the right nerve was damaged.

(3) A large retrosternal gland on the left side, but the right nerve was damaged.

(4) A second operation with a retrosternal prolongation on the right side, and the right nerve was injured.

No Recovery of Movement of Cord

Of the 22 cases (7·3%), including 2 bilateral cases, in which no movement of the cord was recovered, 14 showed excellent compensation by the opposite cord. This occurred soon after operation and compensation was complete in 10 cases. So good was the compensation in these 10 cases that when they were examined recently for this review, it was not suspected until the larynx was examined that the cord had not recovered. These patients could sing and shout and described their voices as perfect. 4 of them had not noticed any abnormality in their voices even shortly after operation. The other 4 had compensated fairly well but still had some huskiness or found that their voices were easily fatigued, being normal for only the first few minutes of speech. Nevertheless all had shown considerable improvement and did not consider that they were handicapped by this weakness.

This left 8 cases (2·7%) with no improvement and included the 2 cases with bilateral paralysis where compensation was obviously impossible. All these patients had voices which were husky and easily tired, and in the bilateral cases the voices had a “ brassy quality ” with some inspiratory stridor.

In 15 of these cases difficulties were noted during the operation, whereas in the other cases the operation appears to have been uneventful. The difficulties were as follows:

(1) A second operation for removal of a diseased right lobe with a retrosternal prolongation. The inferior thyroid artery could not be seen on the right side and was not tied. There was considerable bleeding during the operation, and two days later the wound was reopened for evacuation of clot and control of bleeding. The right nerve was damaged.

(2) A large retrosternal prolongation on the left side. The left nerve was damaged.

(3) A very vascular gland which bled postoperatively and necessitated reopening of the wound on two occasions for evacuation of clot and control of bleeding.

(4) A second operation with a difficult dissection, and the nerve was seen to be divided at operation.

(5) A large friable gland with a retrosternal prolongation on the left. The left nerve was damaged.

(6) A large gland with retrosternal prolongations on both sides, and the left inferior thyroid artery was not tied. The left nerve was damaged.

(7) A large retrosternal prolongation on the right side. The right nerve was damaged.

(8) A second operation with a retrosternal prolongation on the left side. The left nerve was damaged.

(9) A retrosternal prolongation on the right side. The right nerve was damaged.

(10) A second operation with a difficult dissection on the right side. The right nerve was damaged.

(11) A second operation, and the left inferior thyroid artery was not tied. There was considerable bleeding, and the left nerve was damaged.

(12) A retrosternal prolongation on the right side and the inferior thyroid artery on the right side was not tied. The right nerve was damaged.

(13) A very large nodular right lobe. The right nerve was damaged.

(14) A very large hæmorrhagic gland. Both nerves were damaged.

(15) A second operation with a retro œsophageal prolongation on the left side. The left nerve was damaged, and the right nerve had been damaged at the first operation in 1925.

There was no record in any case of any abnormality in the anatomy of the neck except in so far as it was produced by the diseased gland.

The following is a summary of the difficulties met with in 19 cases:

11 cases with retrosternal prolongation of a lateral lobe.

7 cases where a second operation was being done.

5 cases in which hæmorrhage was severe, and in 3 cases the wound had to be reopened.

1 case where there was a retro œsophageal extension of a lateral lobe.

There were 21 cases in which no difficulty was noted at operation. In these cases the proportion of right nerves injured to left nerves injured is 2 : 1 (14 : 7 cases). This is higher than the proportion for the whole series (23 : 18) and seems to be significant.

Discussion

The first important fact emerging from this review is the frequency of 13·3%, which was far higher than expected. This shows a close correlation with Wade’s (1955) conclusion that 15% of recurrent nerves are in absolute or partial danger during thyroidectomy. This fact is revealed because each case was examined irrespective of whether the patient complained of a voice change or not. If we had examined only those who complained of voice changes at a follow-up attendance, the frequency would have been 4–5%.

It was to be expected that a damaged recurrent nerve could recover. It is presumed that, in cases showing early recovery, the nerve lesion was due to stretching, causing neurapraxia, whereas in the few cases that took over six months to recover the axons had been damaged (axonotmesis) without disruption of the sheaths, possibly by being crushed in a hæmostat. This is suggested by the 4 cases that showed full movements of the cords but still had some slight impairment of voice function. In the 1 case where the nerve lesion initially appeared to be partial and later was certainly complete we suggest that fibrosis following hæmorrhage round the nerve had produced this effect; but it is only an isolated case and perhaps the occasional difficulty in examining the larynx soon after operation may, in this case, have led us to classify as partial a lesion which was, in fact, complete.

Although it is well known that where the nerve does not recover, compensation can be good, we were surprised to find it so good in so many cases. In the 10 cases that showed complete functional recovery great care was taken to ascertain that this was really so. Only 6 unilateral cases (2%) showed no significant recovery.

As regards the causes of damage to the nerves, in 19 cases where difficulties were noted by far the most common difficulty was that presented by a large retrosternal prolongation of the gland (11 cases). This suggests that the nerves are more vulnerable the lower the dissection proceeds. At this level a greater proportion of nerves are in an exposed position lateral to the tracheo œsophageal groove, and when the lobe is delivered the nerve is drawn forwards with it. Certainly it seems that special care is required in delivery of a retrosternal prolongation of the gland; though a blind dissection may be necessary it cannot be assumed that the nerve is out of danger.

Many workers have drawn attention to the vulnerability of the nerves when they lie in a variable relationship to the inferior thyroid artery, but the nerves are also in danger at a lower level. When a retrosternal prolongation or a lower-lobe adenoma is dislocated upwards and forwards, the nerve is also drawn forwards. Though it is debatable whether the nerve should be dissected through-but it is clear that hypertension was four times as common among our pyelonephritics as in the controls 59 7% compared with 15 0%

In patients aged more than 40 and with a family background of hypertension the prevalence was 84 85% in pyelonephritis and only 30% in cholecystitis Here we cannot deny a possible coincidence with essential hypertension, 85% being almost the sum of the prevalence of hypertension in older pyelonephritics with a negative family history and the 30% prevalence in patients with cholecystitis with a positive family background However, even in young patients with a negative family history hypertension was present in 43 5%, whereas it was not found in any control patient of the corresponding subgroup The difference between pyelonephritis and cholecystitis is statistically highly significant

On the other hand, there is no difference between the prevalence of hypertension in pyelonephritis and glomerulonephritis in any of the subgroups, and the over-all prevalences of hypertension in pyelonephritis and in glomerulonephritis are almost equal, that in glomerulonephritis being 58 1%, indicating that the blood-pressure is raised by the same mechanism in both diseases

Hypertension develops with increasing frequency as pyelonephritis progresses, but hypertension was found in 14 (43 8%) of 32 patients with a normal glomerular filtration-rate and in more than 20% of patients in whom all renal functions were only a little damaged (fig 18) Thus there can be no reasonable doubt about the causal relationship between chronic pyelonephritis and hypertension, which can be brought about even by slight disease

As regards the mechanism by which hypertension develops one can but speculate, but our biopsy studies (Brod and Benešová 1955) refute the theory of Weiss and Parker (1939) that arteritis induced in renal vessels by the surrounding inflammation may be the starting-point in 5 of our patients with grave hypertension such lesions were either absent (fig 19) or minimal, and in 3 patients with hypertension vascular changes were of the type found in experimental hypertension

A very important complication of pyelonephritic hypertension is malignant hypertension, diagnosed on changes in the retinæ Of 76 pyelonephritics with hypertension this complication developed in 15 (19 7%) This was significantly more than the 10% prevalence of malignant hypertension in our 490 patients with essential hypertension There was, however, no significant difference in the prevalence of severe diastolic hypertension (above 130 mm Hg) between chronic pyelonephritis and essential hypertension Malignant hypertension came on at an earlier average age (41 67 yr) in chronic pyelonephritis than in essential hypertension (48 59 yr) (fig 20), the difference being statistically significant

From the renal aspect an important difference was found between these two diseases as regards malignant hypertension whereas essential hypertension can become malignant at any level of glomerular filtration or concentrating ability, in chronic pyelonephritis hypertension tends to become malignant only with far advanced renal disease The difference is statistically significant ($P<0 05$) Whereas a reduction of the glomerular filtration rate below 25 ml a minute was found in 60% of patients with malignant hypertension in pyelonephritis, it was found in only 10% of patients with essential hypertension (fig 21) Inability to concentrate the urine to sp gr 1 012 was not found in malignant hypertension per se, but it was found in 50% of our pyelonephritics with malignant hypertension

The Addis count further differentiates patients with malignant hypertension due to pyelonephritis from those with malignant hypertension following essential hypertension the typical prevalence of leucocytes in the urinary deposit was found in almost 65% of the pyelonephritics but in only 10% of the patients with essential hypertension Therefore a combination of a glomerular filtration-rate below 25 ml a minute, inability to concentrate the urine to sp gr 1 012, and a majority of leucocytes in the Addis count are pathognomonic of malignant hypertension due to chronic pyelonephritis

A combination of a low urinary specific gravity and Addis count gives an equally sharp differentiation between the two diseases The diagnosis thus established was confirmed by either biopsy or necropsy in most of the later cases

Clinical Entity of Chronic Pyelonephritis

In most of the patients included in this study the clinical diagnosis of chronic pyelonephritis was based (apart from the history) on the dissociation between the disturbances of glomerular and tubular functions and the dissociation between leucocytes and erythrocytes in the Addis count New criteria were added only slowly as our experience of chronic pyelonephritis increased, and our present knowledge comes only from the analysis of the whole group Is it, therefore, possible that we have collected an artificial group which, although presenting this double dissociation, is really of heterogeneous pathology? I think that this question can be answered in the negative Not only was our diagnosis confirmed by the pathologist wherever possible, but also the alterations in almost all the functions which have been discussed separate our group of chronic pyelonephritis sharply from the other renal diseases and reveal a uniform behaviour within the group

Treatment

Little advance has been made in the treatment of chronic pyelonephritis Chemotherapy and antibiotics are insufficient The chief difficulty lies in the fact that a kidney which has once been damaged is a locus of predilection for any blood borne organisms, and that an abnormally functioning urinary tract predisposes to infection of the renal pelves We can do little towards functional restitution of the pelves once their elastic and muscular elements have been superseded by fibrous tissue

Our not very satisfactory therapeutic regimen can be summarised as follows

(1) Prevention of disturbance of the urinary tract and intensive treatment of such disturbance

(2) Prevention of infection and careful elimination of all focal infection in a patient in whom the function of the urinary tract is disturbed, and intensive treatment of every infection in the urinary tract

(3) Antibiotic therapy strengthened, if possible, by regulating the reaction of the urine

(4) Care of the bowels, with proper hygiene of the abdominal wall

(5) Sexual hygiene

(6) Saving of osmotic work of the diseased tubules by the dietetic principles of Addis

(7) Salt restriction never to be prescribed unless there is some special reason for it—e g, heart failure

(8) Possibly treatment in a sanatorium, to improve the patient's general condition and his resistance to infection

(9) Renal denervation or an attempt to remove sclerosed fat from the renal hilus in progressive cases

(10) Where unilateral disease leads to hypertension (especially the malignant sort), nephrectomy to be considered

With such purposeful treatment we have occasionally seen striking results In several cases malignant hypertension was made to recede, and in 1 case nephrectomy completely cured malignant hypertension, but such striking successes have hitherto been the exception rather than the rule Too many patients are still referred to us with irreversible changes of the urinary tract, terminal changes in the kidneys, or a seriously damaged cardiovascular system It is possible today to recognise chronic pyelonephritis even in its earliest stage by methods which out its course in the neck, it is certain that care should be taken that only the inferior thyroid veins are divided at the lower pole, and the web of tissue should be carefully teased out and scrutinised before hæmostats are applied or ligatures tied Dislocating a diseased lobe may cause an injury from which the nerve will recover, but it can easily be converted into a permanent injury

In 7 cases the gland was being explored for a second time, and it is obvious that there is then greater difficulty in exposing the gland and avoiding damage to the nerve It may be suggested that in these cases it would be wise to expose the nerves if possible, but we feel that the dissection necessary for exposure would itself cause damage In 3 cases severe postoperative bleeding necessitated reopening of the wound to control bleeding, and it is obvious that great care should be taken to avoid the nerve, but bleeding from an area near the nerve must be controlled, and the risk of nerve damage accepted

In 21 cases (7%) no operative difficulty was noted and yet one of the nerves was damaged In 14 of these cases the nerve recovered, presumably the nerve was either stretched or caught in a hæmostat in these cases It has already been pointed out that the right nerve was damaged twice as often as the left in these cases Bowden (1955) has recently concluded that, from anatomical considerations alone, there is an inherent risk of damage to the nerves during thyroidectomy She points out that the nerve takes an irregular course on the right side more commonly than on the left She also found that, at the level of the gland, only 73 of 134 nerves on the right, and 85 of 133 nerves on the left, were lying in the tracheo œsophageal sulcus, the rest were in an exposed position Again the right nerve seems to be slightly more vulnerable

Conclusions

We agree with Bowden (1955) that there is an inherent risk of damage to the recurrent laryngeal nerves during thyroidectomy, and we add that the risk is greatly increased in the presence of certain pathological conditions of the gland, of which the most important is the retrosternal *prolongation* of the lateral lobes

We emphasise the danger to the nerves at quite a low level in the neck in the presence of lower-lobe adenomata and retrosternal *prolongations*, in *addition* to their vulnerability where they are crossed by, or mingle with, the branches of the inferior thyroid artery It is in these cases that permanent damage to the nerves can be avoided

The prognosis of the damaged nerve is good Many recover In those that do not recover, compensation by the other cord is usually good and functional recovery rapid and often complete

Summary

In a series of 300 consecutive thyroidectomies 39 patients sustained damage to one recurrent laryngeal nerve and in 1 case both nerves were damaged

In 18 cases the damaged nerve recovered completely, while in 22 cases recovery did not occur The causes of damage to these nerves is discussed and their recovery of function assessed

An accurate estimate of the frequency or extent of damage to the recurrent laryngeal nerves can only be obtained if the vocal cords are examined both preoperatively and postoperatively, preferably by an ear, nose, and throat surgeon

Our thanks are due to Mr Robert Strang for permission to include his cases in this review

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AN INTRAVENOUS STEROID ANÆSTHETIC

EXPERIENCES WITH VIADRIL

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THE word "steroid" is a "generic name for a group of compounds comprising the sterols, bile acids, heart poisons, saponins and sex hormones" (Grant 1949) Fifteen years ago Selye began an investigation into the anæsthetic properties of a large number of steroids (Selye 1941a and b, 1942a and b, 1943), all of which, except pregnanedione, exhibited hormonal activity Recently these results were reviewed by Laubach et al (1955), and the results of pharmacological experiments suggested that a derivative of pregnanedione (21 hydroxy pregnane 3, 20 dione, sodium hemisuccinate) ('Viadril') might be suitable for human anæsthesia The drug was sufficiently soluble in water to be given intravenously, it had a far higher therapeutic index than thiopentone, it was not carcinogenic, and it showed no signs of hormonal activity, such as salt retention This drug was released for simultaneous clinical trials in the U S A (Gordon et al 1955, Murphy et al 1955, Howland et al 1956), Italy (Dauri 1955, Taddei 1955), Sweden (Vinnars 1956), and in this country, where we have used it An identical compound has been studied in Scotland by Taylor and Shearer (1956) The structure of viadril and some other steroids is shown in fig 1

Our First 100 Cases

The 100 operations performed with viadril as the basic anæsthetic were

Laryngopharyngectomy (first stage)	2	Appendicectomy	3
Laryngopharyngectomy (second stage)	2	Prostatectomy	1
Partial gastrectomy	6	Partial nephrectomy	1
Partial thyroidectomy	6	Cholecystectomy	1
Œsophagectomy	2	Vulvectomy and bilateral inguinal adenectomy	1
Excision of rectum	3	Disarticulation of the hip	1
Excision of colon	3	Hypophysectomy	1
Hysterectomy	4	Subdiaphragmatic abscess	1
Colporrhaphy	5	Appendicular abscess	1
Radical mastectomy	4	Herniorrhaphy	2
Cystectomy of breast	2	Mastoidectomy	1
Bilateral adrenalectomy	2	Fissure in ano	1
Unilateral adrenalectomy	1	Sigmoidectomy	1
Oophorectomy and adrenalectomy	3	Diagnostic laryngoscopy	1
		Major dental operations	38

The accompanying table illustrates our use of viadril in a few of these 100 cases The first two operations in the table illustrate how the technique has been modified in the light of experience so that less viadril is now given and most of it is administered before and during the first few minutes of the operation

Method of Administration

Viadril was originally injected as a 2 5% solution into a fast running intravenous drip (Murphy 1955), but painful venous thrombosis followed in most cases Murphy et al (1955) reported only a 3% incidence of venous thrombosis, but we did not realise that their "fast running" drip was one which was pouring through the drip chamber like a running tap By trial and error, it was found that solutions weaker than 0 5% in physiological saline produced no vein troubles A suitable solution can most readily be prepared by dissolving five 500 mg vials of viadril in the usual 540 ml bottle of intravenous saline, however rapidly it is run in, this solution is trouble free, and causes no sclerosis of veins

With a drip rate of 150 per min the average patient becomes drowsy within 5 to 7 min and falls asleep in 10 min, although he can be roused by questioning or are at the disposal of even small hospitals Our future tasks are to look for methods of treating functional disturbances of the urinary tract and to prevent this dangerous and common disease This will be possible only after we have thoroughly recognised its cause, and this, especially in the primary form, still awaits a solution

I thank Dr D Benešova for the photomicrographs used in figs 1 and 19

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IDIOPATHIC HYPERCALCÆMIA OF INFANCY

CLINICAL AND METABOLIC STUDIES WITH SPECIAL REFERENCE TO THE ÆTIOLOGICAL RÔLE OF VITAMIN D

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'Idiopathic hypercalcæmia Is this the price we pay for the abolition of rickets ? —*Lancet* 1954, ii 128

In spite of the knowledge of the preventive action of vitamin D, and also of ultraviolet light rickets remains in the Baltimore community an extremely common disease '—E A Park (1953)

Two types of infantile hypercalcæmia have been recognised one with mental defect, often other congenital abnormalities, a long course, and a poor prognosis, and the other with no associated congenital defects, a shorter course, and usually a better prognosis (Schlesinger et al 1956) Most of the published cases have been of the latter type, and it is with this type that we deal here

Ætiology

Creery (1953) suggested that alkali therapy might be a contributory cause Lowe et al (1954) concluded, from a renal biopsy, that primary renal disease was probably not responsible They and others also dismissed primary parathyroid overactivity as a cause Idiopathic hypercalcæmia has not been reported in a wholly breast-fed infant, and this has been related to the fact that the calcium content of breast-milk is about a quarter of that of cow's milk (Creery and Neill 1954) The high phosphorus content of cow's milk is, however, held responsible for neonatal hypocalcæmia by other workers (Gardner et al 1950)

An abnormal sensitivity to normal doses of vitamin D has been suggested by Lightwood (1953) as the cause Such sensitivity and an excessive intake of vitamin D were considered as likely ætiological factors by Lowe et al (1954) and Creery and Neill (1954) Bonham Carter et al (1955) gave calciferol 10,000 units daily for eleven days to a child with idiopathic hypercalcæmia and, from the coincident clinical deterioration, concluded that there was an abnormal sensitivity to vitamin D The implication of these suggestions has led the British Pædiatric Association, at the instigation of the Ministry of Health, to conduct a national inquiry into the possible relationship between the intake of vitamin D and the development of idiopathic hypercalcæmia of infancy.

Certain objections can be raised against the concept of vitamin-D overdosage or hypersensitivity Very large doses of vitamin D have been tolerated in infancy without toxic effects, and Wolf (1943) concludes that there is a very wide margin of safety between optimal and toxic dosage

Creery and Neill (1954) state that 2 of their patients with idiopathic hypercalcæmia had had no supplement of vitamin D and a total intake of only 700 units of it daily They gave, in one of their active cases, 2000 units of calciferol daily for three and a half weeks and obtained a steady clinical improvement despite a transient rise in the serum-calcium level

Idiopathic hypercalcæmia has apparently not been reported from the United States of America (*Quarterly Review of Pediatrics* 1955)

An association has been reported between hypercalcæmia and interstitial plasma-cell pneumonia (Hallman et al 1954) This latter disease has only recently been recognised in this country (Baar 1955) During its acute phase the serum calcium level often rises, and in a few cases a raised serum-calcium level persists for weeks after the child has recovered.

Case-reports

The present study is based on 5 cases of idiopathic hypercalcæmia and a possible 6th case observed during 1951–56 The main clinical and biochemical findings and progress are given in tables I and II and figs 1–5

TABLE I—SUMMARIES OF CASE HISTORIES

Case no	Age at onset (mos)	Age when diagnosed (mos)	Duration of illness (mos)	Follow-up
1	3	7	7	Æt 3½ yr wt 39 lb ht 41 in, normal intelligence and activity serum Ca 12 0 mg per 100 ml plasma-cholesterol 185 mg per 100 ml
2	10	13	9	Æt 3 yr wt 27 lb ht 33½ in normal intelligence and activity serum Ca 10 4 mg per 100 ml plasma-cholesterol 167 mg per 100 ml
3	6½	8	10	Æt 2 yr wt 26 lb ht 33 in normal intelligence and activity serum-Ca 10 4 mg per 100 ml plasma-cholesterol 197 mg per 100 ml
4	4	8	8	Æt 2 yr wt 22 lb ht 33 in, normal intelligence and activity, serum Ca 10 2 mg per 100 ml plasma-cholesterol 229 mg per 100 ml
5	10	10½	1½	Æt 2 yr wt 26 lb ht 33 in, normal intelligence and activity serum Ca 10 0 mg per 100 ml plasma-cholesterol 194 mg per 100 ml
6	5	7	3 –	

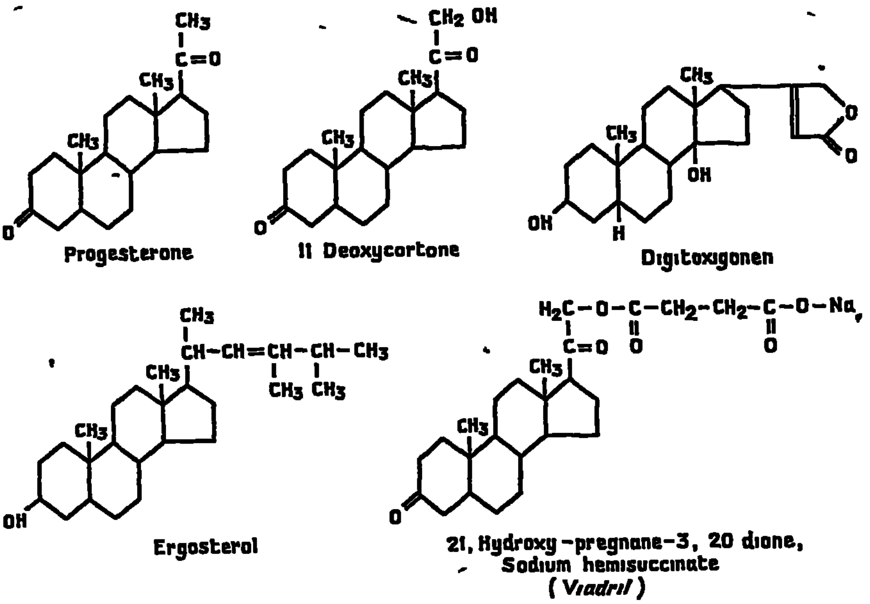

Fig 1—Structure of viadril and other steroids

touching the arm. After 15 min. he seems deeply asleep and cannot be roused by shouting or shaking, although he reacts to painful stimuli, in which respect viadril resembles intravenous bromethol ('Avertin'). At this stage a carefully inserted pharyngeal airway does not evoke the pharyngeal reflexes or cause laryngospasm. This is in striking contrast to thiobarbiturate anæsthesia, but resembles the chlorpromazine promethazine pethidine sequence ("lytic cocktail"). Laryngoscopy can also be performed, although there is slight resistance from the masseter muscles, and there may be slight but semi-purposeful limb movements. On the other hand, the vocal cords can be viewed with ease, they are wide apart and, when stimulated by touch, close and open again. This also is very different from barbiturate or thiobarbiturate anæsthesia when similar stimulation would not only send the vocal cords into spasm but produce a sphincteric closure of the proximal aperture of the glottis itself. Endotracheal intubation was sometimes possible under viadril anæsthesia alone, after which nitrous oxide and oxygen (5/2 mixture) was adequate to maintain anæsthesia for relatively simple procedures such as major dental surgery. More often, however, analgesics such as pethidine were added, and muscle relaxants as well, particularly for thoracic or abdominal surgery.

Hastening Induction

The usual induction period of 20–25 min. can be halved in the following way. Directly the patient falls asleep a mask can be held within an inch or so of the face and pure nitrous oxide administered. The mask is gradually lowered until it touches the face, when 20% oxygen is added to the mixture. After another 2 min., 30–50 mg. of pethidine is injected intravenously,* followed by a suitable dose of a muscle relaxant, in each case the doses are regulated according to circumstances in the usual way. After another minute the mask can be removed, laryngoscopy performed, and an endotracheal tube passed, nitrous oxide and oxygen are then given to maintain anæsthesia.

Electro encephalographic Changes

Steroid, barbiturate, and thiobarbiturate narcosis are indistinguishable so far as the electro-encephalograph (E.E.G.) is concerned. In each case, four arbitrary levels of anæsthesia can be distinguished by the E.E.G. (Bellville et al. 1956, Howland et al. 1956). After a few minutes of intravenous viadril the E.E.G. changes, and when the deepest level (level 4) is reached—i.e., when cortical activity has been fully suppressed—patients still move slightly when towel clips are applied. It is obvious, therefore, that cortical activity is suppressed before full surgical anæsthesia is is attained, and the E.E.G. seems to be useless for assessing the varying depths of surgical anæsthesia itself.

Respiration

Doses of viadril up to 2 g. do not appear greatly to affect either the depth or rate of respiration however rapidly they are given (fig. 2), although Howland et al. (1956) had occasional patients in whom tidal-volume was considerably diminished, and there was one who

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* Pethidine, *d* tubocurarine chloride, and suxamethonium should not be injected into the viadril drip, since the first causes milkiness and the other two produce a flocculant precipitate when added to 0·5% viadril solution. Thiopentone, thialbutone, gallamine, atropine, neostigmine, nikethamide, nalorphine, and methylamphetamine are compatible with viadril.

EXAMPLES OF OPERATIONS PERFORMED WITH VIADRIL AS BASIC ANÆSTHETIC

Operation	Time *		Viadril (0·5%)			Adjuvants					Patient		
			Dose (mg.)	Time of infusion		Pethidine (mg.)	Muscle relaxant (mg.)	Tr	N₂O	O₂	Sex	Age	Condition
	hr	min		hr	min								
Laryngopharyngectomy	4	23	1560	4	29	50	Nil	Tr	N₂O	O₂	F	59	Fairly fit
Laryngopharyngectomy	5	5	1130		37	60	S M 50	Tr	N₂O	O₂	F	50	Fit
Œsophagectomy	2	46	1170		30	50	T C C 20		N₂O	O₂	F	60	Fairly fit
Œsophagectomy	3	21	1255		31	70	T C C 15		N₂O	O₂	F	72	Frail
Partial gastrectomy	1	27	1100		15	80	T C C 33		N₂O	O₂	M	49	Fit
Partial gastrectomy	1	39	975		40	90	T C C 35		N₂O	O₂	M	48	Fit
Perineal resection of rectum	1	9	1150	1	5	30	T C C 10		N₂O	O₂	M	79	Frail
Anterior resection—anastomosis of rectum	1	50	1250		25	70	T C C 33		N₂O	O₂	F	65	Fairly fit
Disarticulation of hip	2	28	1170		32	100	G 120		N₂O	O₂	F	50	Fit
Partial thyroidectomy	1	23	1000		22	30	T C C 10		N₂O	O₂	F	63	Thyrotoxic otherwise fit
Partial thyroidectomy	1	4	960		49	60	T C C 15		N₂O	O₂	F	47	Thyrotoxic and frail
Total colectomy	2	27	1470		32	90	T C C 20		N₂O	O₂	F	49	Ulcerative colitis, otherwise fit
Bilateral adrenalectomy	1	6	1170		33	70	T C C 15		N₂O	O	F	59	Diabetic otherwise fit

* Including induction of anæsthesia.
T C C = *d* tubocurarine chloride. G = gallamine ('Flaxedil'), S M = suxamethonium ('Scoline' 'Brevedil'). Tr = trichlorethylene in minimal concentration to settle coughing if head was moved or after tracheostomy and passing of sterile endotracheal tube.

TABLE II—BIOCHEMICAL FINDINGS

Case no	Serum-calcium (mg per 100 ml)	Serum alkaline-phosphatase (K A units)	Serum phosphorus (mg per 100 ml)	Plasma cholesterol (mg per 100 ml)	Blood urea nitrogen (mg per 100 ml)	CO_2 combining power (vol %)	Urine	Serum proteins (mg per 100 ml)
1	11 3–15 4	8	2 4–5 0		20–30	54–61	Acid	6 90–7 00
2	10 7–16 4	10–11	5 0	212–283	7–44	26–44	Acid no amino aciduria	7 25 *
3	9 6–15 6	8–13	4 2–6 7	156–306	13–18	54	Acid no amino aciduria	6 15–6 25 *
4	10 2–16 2	10–16	2 6–6 0	145–262	30–44	45	Acid, no amino aciduria	7 05–7 34 *
5	10 7–11 2		6 5	263	14	46	Acid	
6	9 8–13 6	14	5 2	158–249	24	55	Acid	7 10–7 60 †

* Normal electrophoretic pattern † Increase in α' and β globulin

Case 1 —Male birth weight 9 lb 1 oz Breast fed for eight weeks, then given National dried milk (N D M) without additional vitamin supplement Normal progress for three months but thereafter vomited, lost weight, and became pale, anorexic, listless, and constipated

Admitted to hospital æt 5 mos Continued to vomit and required subcutaneous saline solution frequently Very ill when serum calcium level first estimated (12 7 mg per 100 ml) Improved two weeks later, when serum calcium level had risen to 15 2 mg per 100 ml Radiography showed increased peripheral density of metacarpal, tarsal, and metatarsal bones

Diet in hospital predominantly cow's milk except for period of low calcium diet (meat purée and sweetened fruit juice) No clinical improvement during latter diet although serum calcium level fell (fig 1)

Ultimately recovered satisfactorily, and three years later height and weight were well above normal for his age and at the 90th percentile of the values given by Mitchell Nelson (1950) for healthy children

Case 2 —Girl birth weight 7 lb 13 oz Breast fed for two weeks, then given N D M until weaned at one year Half a teaspoonful of cod liver oil daily until 3 mos old, thereafter no vitamin supplement until after onset of symptoms When 10 mos old vomiting, anorexia, constipation, loss of weight, pallor, and listlessness developed

Admitted to hospital æt 14 mos, underweight Characteristic radiological bone changes present Temporary spontaneous initial improvement followed by a relapse

Low calcium diet (as for case 1) given for three weeks Serum calcium level fell and clinical improvement took place and continued after reintroduction of a milk diet, although the serum calcium level rose to 16 1 mg per 100 ml (fig 2)

Discharged home after five months in hospital At the age of 3 years was considerably below the expected weight and height, at the 10th percentile and below the 3rd percentile respectively of the values given by Mitchell Nelson (1950)

Case 3 —Male identical twin of case 5 Birth weight 7 lb Breast fed for a month, then cow's milk Given cod liver oil a few drops a day in the early weeks, increasing progressively to a teaspoonful at 6 mos, when all vitamin supplements were stopped

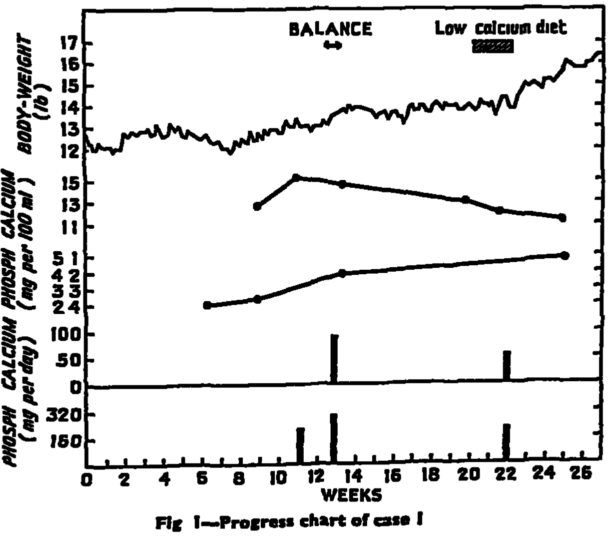


Fig 1—Progress chart of case 1

At 3 mos developed a respiratory infection treated with penicillin At $6^1/_2$ mos began to vomit and shortly thereafter developed an acute episode of vomiting and diarrhœa, which lasted five days Vomiting continued, and he gradually became constipated, pale, and apathetic

Admitted to hospital æt 8 mos, underweight and with continuing symptoms Some increased density of femoral metaphyses and periphery of tarsal bones

Began to recover after six weeks in hospital (fig 3) discharged after four months A year later below expected weight and height, at the 25th and the 10th percentile respectively (Mitchell Nelson 1950)

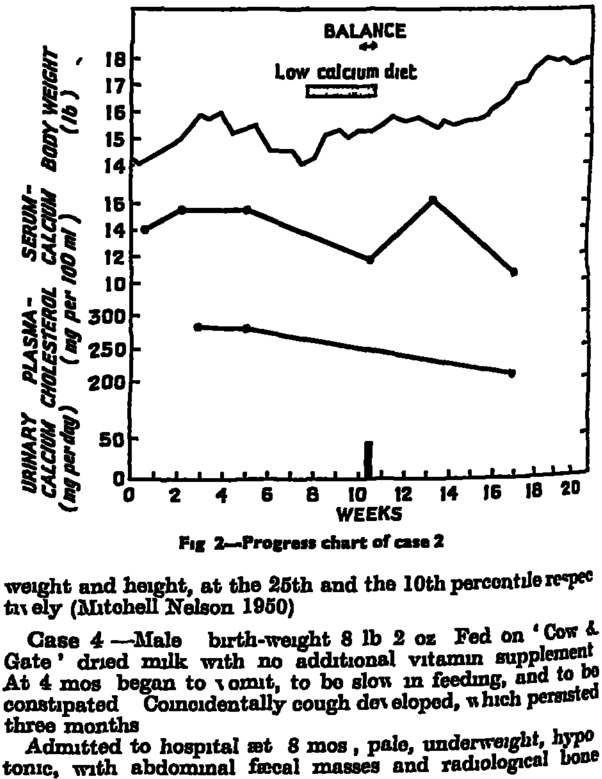


Fig 2—Progress chart of case 2

Case 4 —Male birth-weight 8 lb 2 oz Fed on 'Cow & Gate' dried milk with no additional vitamin supplement At 4 mos began to vomit, to be slow in feeding, and to be constipated Coincidentally cough developed, which persisted three months

Admitted to hospital æt 8 mos, pale, underweight, hypotonic, with abdominal fæcal masses and radiological bone changes of idiopathic hypercalcæmia

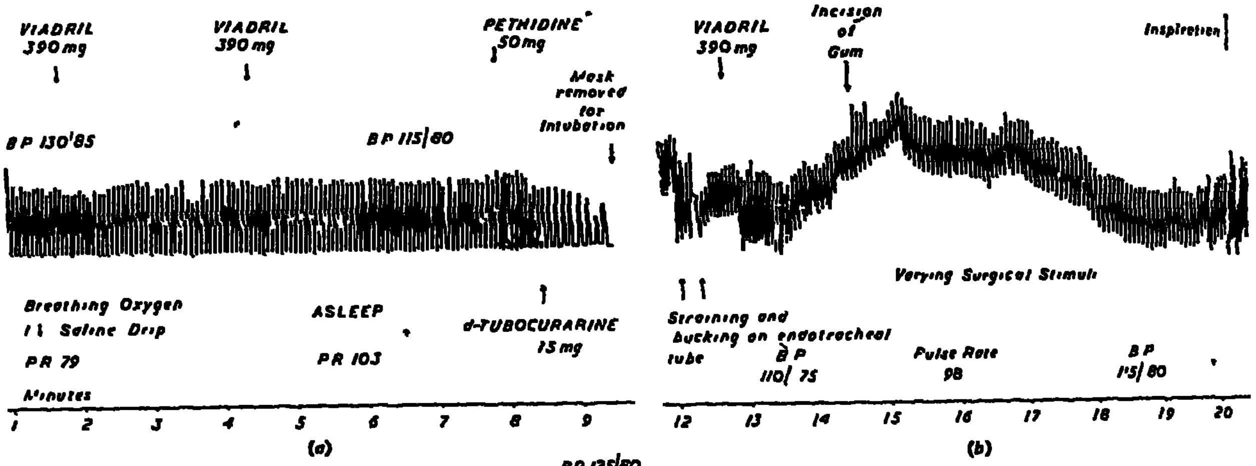
In hospital for five and a half months (fig 4)

At the age of 2 years very much underweight and underheight, at the 3rd percentiles (Mitchell Nelson 1950)

Case 5 —Identical twin of case 3 Birth weight 5 lb Breast fed for five weeks, then cow's milk Given cod liver oil a few drops a day in the early weeks, increasing to a teaspoonful at 6 mos and remaining at that amount At 6 mos respiratory infection developed At 9 mos given a ten day course of ultraviolet light At 10 mos vomiting anorexia, and loss of weight developed, with initially a four day episode of diarrhœa, then constipation

Admitted to hospital a fortnight after onset of symptoms Began to recover after three weeks

This child's illness was very similar in onset and symptoms to that of his twin His mother and the family doctor considered the illnesses to be the same The



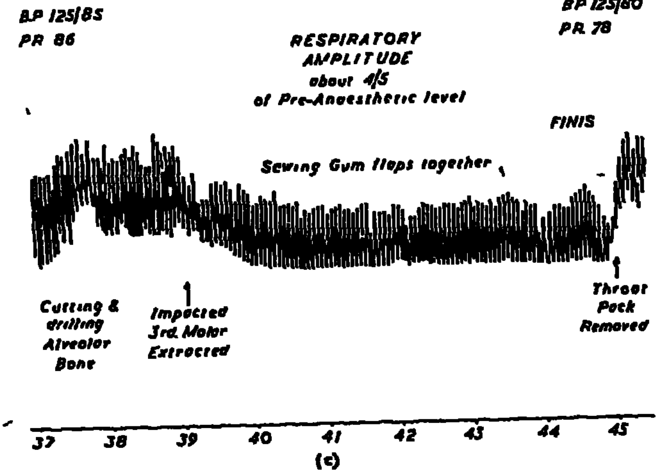


Fig 2—Respiratory tracing during removal of impacted 3rd molar in woman of 29

(a) Viadril (2·5% solution) and other drugs injected into intravenous saline drip On each occasion 390 mg of viadril was injected in two minutes

(b) Transnasal endotracheal intubation 3 min before this part of tracing N_2O and O_2 via tube

(c) Endotracheal N_2O and O_2 continuing (CO_2 absorption)

required artificial respiration for 30 min It may be significant that these patients were all "general surgical patients admitted to a hospital for neoplastic diseases," and many were, presumably, toxic and elderly subjects When controlled respiration is attempted, we agree with Murphy et al (1955) that respiration is more easily "taken over" than it is with thiobarbiturate anæsthesia For instance, during an abdominothoracic œsophagectomy, using 1225 mg of viadril and lasting 3 hours 21 min, controlled respiration was easily maintained under nitrous oxide and oxygen, with the addition of 50 mg of intravenous pethidine and a dose of *d* tubocurarine chloride as small as 15 mg (the entire dose of tubocurarine was given before endotracheal intubation)

Reflexes

As we mentioned, the pharyngeal reflex is soon suppressed—i e, when 500–600 mg of viadril have been given At this stage, also, there is no laryngospasm when the vocal cords are stimulated, although their momentary closure suggests that they have preserved their sensitivity After intubation, the endotracheal tube is more easily tolerated than it is under thiobarbiturate anæsthesia Even when anæsthesia is extremely light, movement of the tube rarely produces more than a few seconds breath holding there is a remarkable absence of the "bucking" so common under all other forms of anæsthesia Again, bronchospasm is rare Controlled respiration is easy, perhaps because of facilitation of the mechanism whereby the respiratory centre is depressed by continued rhythmic inflation of the lungs When surgical anæsthesia is attained, the pupils are small and no longer react to light

Circulation

We agree with Taylor and Shearer (1956) that the pulse rate is very much higher than is usual under other forms of intravenous anæsthesia, although we cannot entirely agree that this is due to the fact that viadril i more of a hypnotic than an anæsthetic Were this view entirely correct, one would expect the pulse rate to be rapid only during surgical stimulation whereas rates of 85–105 per min have been noted during induction, even when the infusion rate was slow On the other hand, intravenous pethidine, a known analgesic, has significantly reduced the pulse-rate during the actual operation Another unusual feature, which makes it hard to be dogmatic about the absence of analgesic properties, i the fact that painful stimuli, which would appreciabl increase the rate and amplitude of respiration during thiobarbiturate anæsthesia, have little or no effect during steroid anæsthesia, despite a relatively high pulse rate Moreover, even during exceedingly painful procedure the respiratory-rate has remained steady at rates of from 14 to 26 per min

Sharp falls of blood-pressure have occasionally been noted but we did not find that they were confined to elderly subject (Taylor and Sheare 1956) In ou experience th blood pressure al falls in youn people, though les often than in th old (fig 3) Suc falls are much les likely if the dru is administere slowly—i e, 60-10 drops per min— but unfortunatel this slows a already tard induction

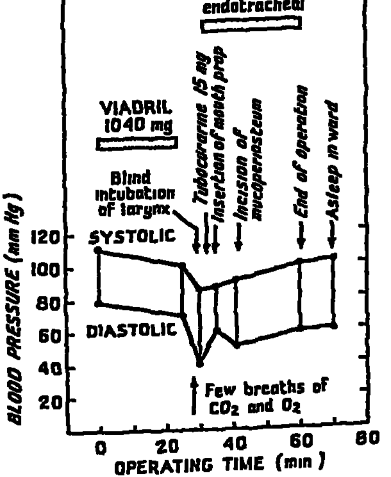


Fig 3—Fall of blood pressure during extraction of impacted upper and lower 3rd molars in woman of 30 Spontaneous recovery

Muscles

Owing no doub to the fact that w supplemente viadril directly th patient fell aslee we have not see plasma cholesterol level as with his brother was raised It appears quite likely that he had the same disease as his brother but presenting in a milder form

The criteria of identical twinning were as follows they looked alike, the blood-groups, including A B O, Rh phenotype, and probable genotype, M N S and P, Lutheran, Kell, Lewis a and b, and Duffy, were identical, blood from both parents and the four other siblings examined in the same way showed that the probability of uniovularity was at least 98 7%, calculated by the method of Race and Sanger (1954) The finger prints, according to the criteria of Cummins and Midlo (1943) were compatible

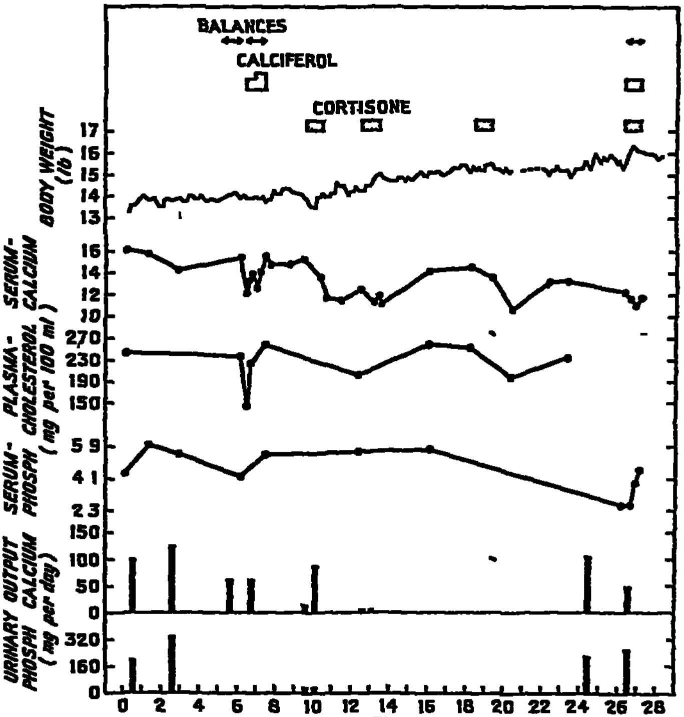


Fig 4—Progress chart of case 4

Case 6.—Girl birth weight 8 lb 12 oz Breast fed for two months then Cow & Gate milk Half a teaspoonful of cod liver oil at 2 mos, increasing to 1 teaspoonful at 3½ mos and remaining at that level 'Farex' at 4½ mos Given 'Glucose D' (1 or 2 teaspoonfuls daily) from 3 mos onwards At 5½ mos cough (which lasted a month), vomiting and constipation loss of weight, and anorexia developed

Admitted to hospital at 7 mos (fig 5) Palpable fæcal masses hypotonia and suggestive radiological changes in bones

Method

The balance periods lasted five to eight days except for the three-day balance on a low calcium diet With milk feeding an aliquot from each day's feed was kept and analysed Where a mixed diet was being given each feed was duplicated and the pooled duplicates for the day analysed Apart from case 1 when re examined at the age of 3½ years and case 2 when on a low calcium diet, the balance diet consisted of cow's milk with additional cornflour and arrow-root occasionally All the infants had been on the balance diet for at least four days before the balance studies were begun, and, except in case 6, no vitamin supplements had been given for several weeks or months previously Urine and fæces were collected daily by the methods described by Forfar and Prain (1950) Specimens for the estimation of daily urinary excretion of calcium and phosphorus were usually collected over several consecutive days

Standard biochemical methods were used Fæces and diet were emulsified with water to a convenient volume in an 'Ato mixer,' and an aliquot was examined

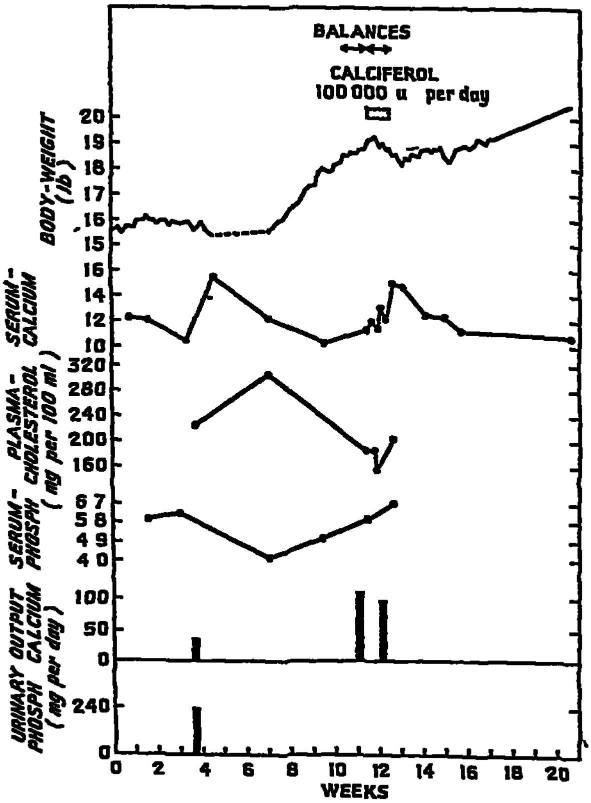


Fig 3—Progress chart of case 3

Intake of Vitamin D and Effect of Calciferol

The approximate intake of vitamin D in these cases and the form in which it was predominantly administered are shown in table III The figures are calculated on the assumption that a teaspoonful of cod-liver oil contains 700 units of vitamin D, a level scoopful of National dried milk powder 40 units, of proprietary milk powder 45 units, and cereals the amounts stated by the manufacturers

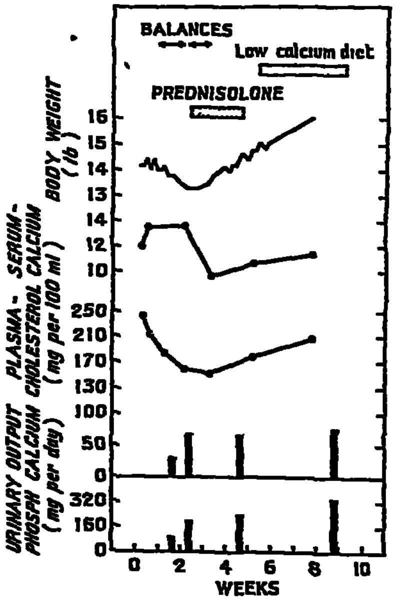


Fig 5—Progress chart of case 6

Since cases 3, 5, and (to a lesser extent) 1 had had low intakes of vitamin D, it was felt that this vitamin might twitching or rigidity of the limbs during induction (Taylor and Shearer 1956). Often, however, there was a clonic convulsive rigidity—sometimes accompanied by generalised trembling—at the end of the operation, after stopping nitrous oxide and oxygen. This usually resolved spontaneously within 1–2 min. The muscles of the limbs, neck, and trunk were involved, and the respiratory movements were not being greatly impeded.

Although controlled respiration can be instituted after small doses of muscle relaxants, the conventional doses are necessary if full muscular relaxation is required for abdominal surgery.

After-effects

We have been greatly impressed by the absence of after-effects. Only 1 of our patients has vomited during the recovery period and no others have had any nausea. The recovery times after viadril seem to be slightly shorter than we would have expected had thiopentone been the main anæsthetic.

Postoperative fatigue is greatly reduced, even compared with other forms of intravenous anæsthesia. So interesting were these findings that a comparison was made between two series of major dental operations (60 cases in all): half had thiopentone as the basic anæsthetic and the other half viadril. Those who had thiopentone all felt slightly lethargic the next day, they lacked appetite, and a few felt slightly sick. Those who had viadril were all alert, and anxious to get home, and they ate as ravenously as their dental disabilities allowed.

One young woman had two similar and symmetrical operations within a fortnight, one with thiopentone and the other with viadril. In each case pethidine was avoided during anæsthesia and the doses of suxamethonium before intubation were identical. The length of the operations was much the same (just over an hour) and a nitrous oxide/oxygen mixture (5:2) was used for maintenance. Quite spontaneously, this patient said she felt "very much better" after viadril than she did after thiopentone.

Even more remarkable was the lack of postoperative fatigue and the sense of well-being of patients undergoing major surgery.

22 hours after an abdomino perineal resection of his rectum a patient carried on an interesting conversation and said that he felt better after viadril than after three other operations (appendicectomy, herniorrhaphy, and sigmoidoscopy) all under thiopentone, *d*-tubocurarine, and/or pethidine. 26 hours after an œsophagectomy a middle-aged woman was knitting an intricately designed bed-jacket. Both these patients seemed to have the same attitude towards their pain as if they had just had chlorpromazine.

Discussion

It is interesting to compare viadril with thiopentone. By and large, viadril seems capable of replacing thiopentone (or similar thiobarbiturates) in any anæsthetic sequence. It suffers, however, from the fact that it has to be given in a very dilute solution to avoid venous sclerosis, and it is, therefore, unlikely to replace thiopentone for short operations when the induction period might greatly exceed the operating-time and appreciably prolong the operating session. Owing to the rapid suppression of the pharyngeal and laryngeal reflexes, this disability can be overlooked if smooth anæsthesia is desired for laryngoscopy, or for the opening of a submandibular cellulitis. We have been particularly impressed with viadril for thyroid surgery. Not only is there less likelihood of "bucking" on the endotracheal tube as the larynx is unavoidably moved during the operation, but the docility of the throat reflexes means that direct laryngoscopy can be performed with the greatest ease at the end of the operation for evidence (or otherwise) of recurrent laryngeal palsy. In major surgery, where intravenous infusions are almost inevitable, viadril probably comes into its own, particularly since it secures so smooth and pleasant a recovery.

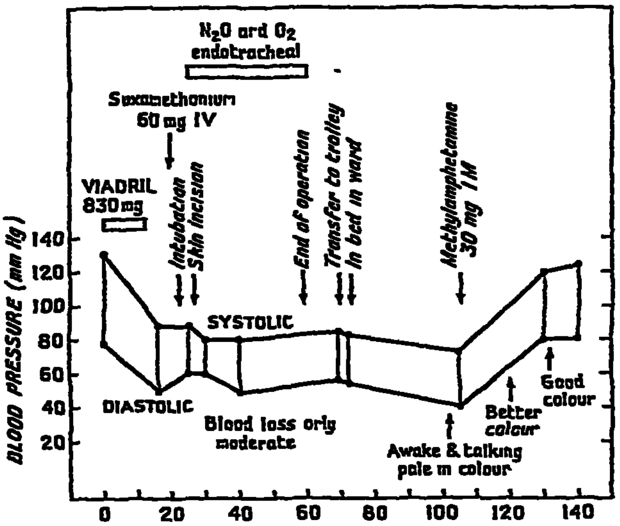


Fig. 4—Effect of intramuscular methylamphetamine on postoperative fall of blood pressure after excision of cyst of breast in a woman of 46.

The occasional falls in blood-pressure are not so alarming as they sound. In every case the patient's appearance and pulse volume was so good that the actual blood-pressure level surprised those recording it. Unlike "hypotensive anæsthesia" (with pentamethonium or hexamethonium or 'Arfonad') there seemed to be no venous engorgement of the limbs, and postural ischæmia was difficult to obtain. Methylamphetamine or similar drugs, given intravenously or intramuscularly, never failed to rectify any fall in blood-pressure (fig. 4).

As for the lack or diminution of postoperative fatigue, viadril resembles the chlorpromazine-promethazine-pethidine sequence ('lytic cocktail'). Viadril, however, has the advantage that after they return to the ward patients rarely have any fall of blood-pressure and, if they do, it can readily be restored by intramuscular methylamphetamine.

Why patients feel so fit after viadril is unknown. It may well be that the drug inhibits the excretion of adrenocorticotrophic steroids during the actual operation, and that they are thus preserved to cope with the stress of the recovery period. Alternatively, this sense of well-being may be similar to that of cortisone or corticotrophin (A.C.T.H.) therapy—the cause of which is also unknown. In this respect it is interesting to note that Hoeffer and Glaser (1950) demonstrated E.E.G. changes suggestive of cortical suppression in patients who had had corticotrophin for three to five days. We intend to take E.E.G.s during their recovery from viadril to ascertain whether they demonstrate similar findings.

Not the least interesting facet of steroid anæsthesia is the light it may throw on the rhythmic causation of sleep. It is now generally agreed that the normal state of the cerebral cortex is one of inactivity or sleep and that wakefulness is maintained only by a continual bombardment of impulses from the reticulo-activating centre of grey matter situated in the brainstem. In turn this centre is activated by centripetal impulses from the entire sensory system. Barbiturate, thiobarbiturate, and steroid anæsthesia may be regarded as depressing this reticulo-activating centre so that it no longer stimulates the cortex into wakefulness and unconsciousness supervenes. This hypothesis does not, however, explain the rhythm of sleep or the increased and overwhelming desire for sleep after long periods of wakefulness. 19th-century

TABLE III—APPROXIMATE INTAKE OF VITAMIN D BEFORE ONSET OF SYMPTOMS, AND TYPE OF VITAMIN D ADMINISTERED

Case no	Range (units)	Average daily intake (units)	Average daily intake for a month before onset of symptoms (units)	Form in which vitamin D was predominantly given
1	45–1300	550	1250	D
2	30–2000	1350	1950	D_2 and D_3
3	30–750	400	400	D_2
4	750–1500	1200	1450	D_2
5	20–760	570	750	D_2
6	33–2500	1240	2300	D_2 and D_3

have been too readily incriminated as a possible cause of idiopathic hypercalcæmia Vitamin D is stated to increase the urinary excretion of calcium by decreasing tubular reabsorption (Dent 1954) It is generally agreed that it favours the deposition of calcium in the bones Therefore, in infantile hypercalcæmia, in which the metabolism of calcium is already disturbed, the administration of additional vitamin D might be beneficial in that, under its influence, the urinary excretion of calcium and the deposition of calcium in the bones might be increased at a relatively greater rate than the alimentary absorption of calcium The work of Bonham Carter et al (1955) had not been reported at this time Pure calciferol (vitamin D_2) 50,000–100,000 units a day was therefore given by mouth to cases 3 and 4 Case 3 had a slight temporary loss of weight (fig 3), but such fluctuations in weight are common in infantile hypercalcæmia (figs 1 and 2) and this fall may have been fortuitous The serum-calcium level rose by 3 5 mg per 100 ml but quickly fell again—a similar effect to that reported by Creery and Neill (1954) The level reached, however, was lower than that which had previously been reached spontaneously Otherwise no beneficial or adverse effects were noted either during therapy or during the following eight months In case 4 there was no clinical change during or after calciferol therapy The serum calcium level fell by 3 1 mg per 100 ml and returned to its previous height the day after calciferol was discontinued Comparable normal controls given the same dosage of calciferol showed rises of 1 2 and 0 7 mg per 100 ml in 2 cases and a fall of 1 0 mg per 100 ml in 1 other

Calciferol was also given to case 1, who had been free from symptoms, had had no vitamin-D supplement for more than two years, and had a normal serum calcium level Again neither immediate nor long-term effect were noted There was no change in the serum calcium level The biological activity of the batch of calciferol used was proved by curing a case of active rickets with it

Calcium-balance Studies

The nature of the balances, the stage of the disease at which they were studied, and the results are shown in table IV

Unrestricted Diet No Vitamin-D Supplement or Vitamin D-fortified Milk

The retention of calcium was 31%, 48%, and 69% in the active cases, 16% in the recovering case, and 16% in the cured case

A very wide range of retention of calcium has been found in healthy infants on a milk diet From the work of Hoobler (1911), Telfer (1922), Daniels and Stearns (1925), Flood (1926), Stearns (1933), Jeans et al (1936), and Harrison (1936) we have obtained the results of 24 calcium balances studied in healthy infants aged 7–12 months and fed on a cow's milk diet or an evaporated milk diet with, so far as can be ascertained, a normal intake of vitamin D On an average intake of 1 17 g of calcium daily the mean retention of calcium was 32% or 0 38 g (range 0–79%) which agrees very closely with the daily

TABLE IV—CALCIUM AND PHOSPHORUS BALANCES

Balance	Case no	Age (yr)	Clinical state	Duration of balance (days)	Average daily intake (g)	Average daily output (g)		Retention	
						Fæces	Urine	Amount (g)	% of intake
Calcium Normal diet	1	8/12	Active	5	1 500	0 940	0 090	0 470	31
	4	9/12	Active	7	0 896	0 404	0 063	0 429	48
	6	7/12	Active	8	0 658	0 183	0 030	0 445	69
	3	10/12	Early recovery	7	1 096	0 811	0 109	0 176	16
	1	3½	Inactive	7	0 772	0 567	0 079	0 126	16
Normal diet plus prednisolone 5 mg daily	6	7/12	Active	6	0 793	0 426		0 367	46
Normal diet plus calciferol 100 000 units daily	4 *	9/12	Active	7	0 892	0 180	0 063	0 649	73
	3	11/12	Early recovery	7	0 907	0 500	0 096	0 401	40
	1	3½	Inactive	7	0 692	0 220	0 183	0 289	42
Normal diet plus calciferol 100 000 units and cortisone 25 mg daily	4	13/12	Active	6	1 135	0 807	0 048	0 280	25
Low calcium diet, no vitamin supplement	2	1½	Active	3	0 035	0 135	0 054	Net loss 0 154	
Phosphorus Normal diet	1	8/12	Active	5	1 500	0 600	0 300	0 600	40
	6	7/12	Active	6	0 319	0 056	0 083	0 180	56
Normal diet plus prednisolone 5 mg daily	6	7/12	Active	6	0 412	0 248		0 164	40

* Calciferol 50 000 units daily for first 3½ days of balance

physiologists used to postulate a "hypnotoxin"—i e, a noxious chemical agent accumulating in the brain "which when present in sufficiently high concentrations arrests cerebral activity which does not recover again till the alleged toxin is destroyed" (Wright 1952) Alternatively, it might be (Kalmus 1956) that an as yet unidentified steroid is secreted during the stress and fatigue associated with wakeful activity, which builds up to a sufficiently high concentration to suppress the reticulo-activating centre which, in turn, can no longer activate the cortex, so that sleep ensues ?

Summary

Viadril is the first steroid to be used in human anæsthesia and is the first departure from the derivatives of barbituric and thiobarbituric acids since intravenous anæsthesia became established in 1932 Judging from animal experiments, its therapeutic index (i e, the ratio between the dose producing apnœa and the dose causing death during artificial respiration) is much greater than any barbiturate or thiobarbiturate in clinical use as an anæsthetic

In contrast to all the ultra short-acting barbiturates and thiobarbiturates, viadril rapidly suppresses the pharyngeal and laryngeal reflexes, even under the lightest narcosis it is difficult to provoke vomiting or laryngospasm

Falls of blood pressure and a rise in pulse rate are more frequent with viadril than with thiobarbiturate anæsthesia With viadril, however, the lowering of blood-pressure often rectifies itself and, if it does not, it can readily be remedied by intramuscular or intravenous methylamphetamine or similar drugs

Vomiting is rare after viadril anæsthesia, post-operative fatigue is slight or absent and patients experience a sense of well-being during their recovery from operation similar to that produced by cortisone

In concentrations greater than 0 5%, viadril solutions unfortunately give rise to painful venous thrombosis, it must therefore be given as an intravenous drip and, consequently, the induction period is long This will probably limit the drug's use in the shorter operations For long operations, where an intravenous drip is almost inevitable, viadril causes less inconvenience from the point of view of time and may well prove the anæsthetic of choice

Whether used alone or in place of thiopentone in the usual hypnotic analgesic muscle relaxant sequence, viadril not only offers ideal operating conditions but ensures a more comfortable recovery period than any other anæsthetic or anæsthetic combination in common use

'Viadril' was kindly supplied by Pfizer Ltd

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LIVER PREGNANCY

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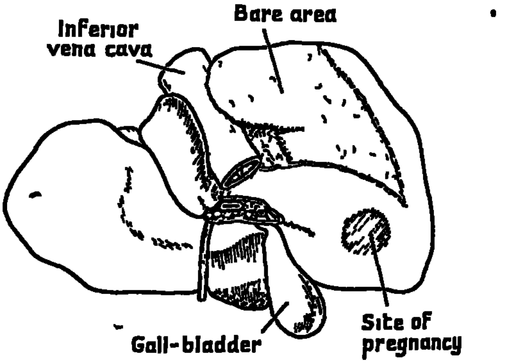
IN most extra-uterine pregnancies the abnormal placental site is in the pelvis Cornell and Lash (1933) found records of 236 pregnancies involving placental attachment to 641 sites, the great majority being in the pelvis In 8 cases one site of attachment was the liver but note was not made whether this was ever the sole area Echols (1934) and Barrett (1952) mentioned patients in whom the placental site involved several organs, one of which was the liver Billington and Goodchild (1948), Serebriakova and Kanshin (1952), and Van de Loo (1953) described placental sites solely in the liver The following is another example of this rare condition

Case-report

A woman, aged 39, was admitted to the Royal Portsmouth Hospital at 6 A M on May 19, 1955 At 10 P M on the previous evening very severe pain began suddenly in the right hypochondrium The pain became generalised in the abdomen and was referred to the left shoulder and the back The patient was nauseated but did not vomit and passed no urine, fæces, or flatus Before this illness her health had been good except for a miscarriage in 1945 She had three children aged 9, 3, and 2 years She said that her appetite had been abnormally good in the previous two weeks but that she had some epigastric discomfort immediately after food Micturition and bowel habit had been normal, and she had no abnormal respiratory or cardiovascular symptoms Menstruation had been regular, lasting 4 or 5 days in each cycle of 27 or 28 days The loss had tended to increase in recent years, and there was a slight offensive intermenstrual vaginal discharge The last period of menstruation was from April 25 to April 29, 1955

On admission the patient was shocked and in pain Her tongue was dry and furred Her chest was normal on clinical examination Her abdomen was completely rigid and tender all over and on rectal palpation of the pouch of Douglas, but especially in the right hypochondrium Bowel sounds were absent Perforated peptic ulcer was diagnosed and laparotomy was done at 9 A M on the day of admission



Posterior and inferior surfaces of liver, showing site of pregnancy

Operation—A small upper paramedian incision revealed dark blood in the peritoneal cavity Four pints of blood and peritoneal exudate was removed during the operation No cause was found in the upper abdominal organs palpable through the original incision, and the uterus was felt to be enlarged, with tumours on each side of it, the pelvis contained much blood A lower abdominal paramedian incision showed that each ovary contained several small cysts and that the uterus was enlarged by fibroids The cysts were removed, and the search for the origin of the bleeding was continued by enlarging the upper incision Fresh bleeding was detected coming from the posterior surface of the liver normally in relation to the right kidney (see figure), it came retention of calcium in a similar age group reported by Sherman and Hawley (1922) from their study of German published reports, and with the calculated requirement of the body at this age (Leitch 1937).

In our 3 active cases the mean intake of calcium was 1.02 g. a day and the mean retention 49% (0.45 g.) a day.

In view of the wide range of retention in healthy infants and even in the same infant, of the anorexia, vomiting, and constipation which make balance studies in idiopathic hypercalcæmia difficult, and of the variety of other factors which can influence the retention of calcium, individual calcium balances or small series of balances must obviously be interpreted with caution. We feel, however, that the retention of calcium in these cases, especially when considered along with the increased urinary excretion of calcium, the raised serum-calcium level, and the probably increased deposition of calcium in the bones, indicates increased absorption of calcium from the alimentary tract.

Unrestricted Diet with Additional Prednisolone

In case 6 this balance was studied in the early acute phase of the disease. Under the influence of prednisolone, 5 mg. a day, a positive calcium balance of 69%, with an average daily retention of 0.45 g., was converted to a balance of 46%, with an average retention of 0.37 g.

Unrestricted Diet with Additional Calciferol

The retention of calcium was increased in all the cases by calciferol—to 73% in the active case, 40% in the early recovery case, and 42% in the inactive case.

Honet (1946) gave a single dose of calciferol 600,000 units to a healthy infant, aged 6 months, whose retention of calcium just before the calciferol was given was 45%. Over consecutive ensuing three-day periods retentions of 67%, 47%, 70%, and 45% were observed. Previous deprivation of vitamin D also increases sensitivity (Honet 1946)—a relevant factor in our cases.

Thus calciferol caused no significant clinical change and did not appear to increase the retention of calcium to a greater degree than might have occurred in a healthy infant.

Unrestricted Diet with Additional Calciferol and Cortisone

In case 4 the balance was studied four months after the previous (calciferol) balance. The retention of calcium was 25%, which is considerably less than the retention on the same dosage of calciferol alone, and considerably less than the retention in the first study, when no calciferol supplement was given.

Low-calcium Diet

The infant had been on a low calcium diet for eighteen days before the balance was studied. A negative calcium balance resulted and, as was found by Ferguson and McGowan (1954), Russell and Young (1954), and Bonham Carter et al. (1955), there was a fall in the serum-calcium level.

Urinary Excretion of Calcium

On a normal diet without added vitamin D the daily urinary excretion of calcium (eight estimations) was 30–127 mg. (mean 83 mg.). In healthy infants of the same age on about the same intake of calcium the range of eighteen estimations published by the workers already cited above was 8–55 mg. (mean 27 mg.) of urinary calcium a day. Knapp (1947) reported 3–86 mg. a day.

In idiopathic hypercalcæmia ranges of 23–122 (mean 69) mg. a day (Lowe et al. 1954), 40–67 (mean 53) mg. a day (Creery and Neill 1954), and 34–128 (mean 82) mg. a day (Bonham Carter et al. 1955) have been reported. Thus although there is a wide individual and case-to case variation, there appears to be little doubt that hypercalcuria occurs in idiopathic hypercalcæmia of infancy.

A feature of the present study is that (with the special exception of case 1 after recovery) calciferol in the dosage given did not increase the urinary output of calcium. Dent (1954) suggests that vitamin D reduces the tubular reabsorption of calcium, thus increasing its urinary excretion. Honet (1946) has shown that in healthy infants, a dosage of calciferol comparable to that given to our patients slightly increases the urinary excretion of calcium. Accentuation of this effect might be expected in the presence of vitamin-D hypersensitivity. The failure of calciferol to increase further the hypercalcuria which was already present in the affected cases cannot be attributed to incapacity of the kidney to excrete more calcium, no matter how high the intake of calciferol might be, because in case 4, a month previously, spontaneous urinary outputs of calcium considerably in excess of that obtained with calciferol were observed (fig. 4).

Thus, although there is moderate hypercalcuria in idiopathic hypercalcæmia, there is no renal response to calciferol.

At the age of 3½ years case 1 showed more than a twofold increase in the urinary output of calcium in response to calciferol. Clinically he had long since recovered from idiopathic hypercalcæmia, and his response to calciferol was probably normal and a function of his age rather than his disease. Knapp (1947) has shown that healthy infants excrete in their urine a smaller proportion of their intake of calcium than do older children and adults, and that it is about the age of 2 years that the adult pattern of excretion is attained.

Phosphorus Metabolism

Phosphorus balances were studied in cases 1 and 6 on normal milk diet during the active phase of hypercalcæmia (table IV). The retention of phosphorus was 40% and 56% respectively.

In 24 published phosphorus balances studied in healthy infants aged 7–12 months having, so far as can be ascertained, a normal intake of vitamin D (Blauberg 1911, Hoobler 1911, Telfer 1922, Daniels and Stearns 1925, Stearns 1933, Jeans et al. 1936, Harrison 1936) the mean intake of phosphorus was 0.89 g. a day, and the mean retention 23% (0.20 g.) a day.

In our 2 active cases the mean intake of phosphorus was 0.91 g. a day and the mean retention 43% (0.39 g.) a day. There thus appears to be an increased retention of phosphorus in idiopathic hypercalcæmia. Honet (1946) has shown that the effect of calciferol on infants is to reduce the retention of phosphorus somewhat.

Random estimations of daily urinary excretion of phosphorus on a milk diet without added vitamins were made on seven occasions. The range was 85–324 mg. (mean 229 mg.) a day. In the above mentioned published balances the mean daily output of phosphorus in the urine was 437 mg. on a roughly comparable intake of phosphorus. In the cases of idiopathic hypercalcæmia there was thus a hypophosphaturia. In infancy calciferol normally causes hyperphosphaturia (Honet 1946, Fanconi and de Chastonay 1950), which might be expected in idiopathic hypercalcæmia if increased susceptibility to vitamin D were present.

Seventeen estimations of serum-phosphorus levels were made in these cases on a standard cow's-milk diet without added vitamin D. As observed by other workers, the levels fluctuated widely. The range was 2.4–6.3 mg. per 100 ml. (mean 4.9 mg. per 100 ml.) in contrast to the normal range of 4.5–5.7 mg. per 100 ml. (mean 5.4 mg. per 100 ml.) for children of this age (Bullock 1930). In hypervitaminosis D in infancy the serum-phosphorus level has been reported to be lowered (Fanconi and de Chastonay 1950) and to be raised (Jelke 1946, Ross 1952).

The serum-calcium and serum-phosphorus levels were estimated together on twenty occasions. The correlation coefficient was -0.08, thus no correlation between these could be demonstrated.

from a soft globular tumour 3 cm in diameter The tumour was enucleated with ease and the bleeding from the resulting cavity in the liver was controlled by packing the cavity with Oxycel' gauze The wounds were closed without drainage Four bottles of blood were given during the operation and the postoperative recovery was uneventful Histological examination of the tumour showed a collection of chorionic villi and highly active trophoblastic tissue

Follow up—When seen six months later the patient was in good health

I wish to thank Mr Bernard Williams for permission to publish and Dr H. Miller for the histological report

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On May 16, 1955, a woman, aged 27 aborted and a few hours later was transfused with two bottles of ABO incompatible blood The error was discovered four hours after the transfusion had been completed, and the only early sign of a hæmolytic reaction was the secretion of black urine, discovered when the patient was catheterised before operation She was immediately placed on the Bull regime she developed oliguria, nitrogen retention (blood-urea level 75 mg per 100 ml.) jaundice (bilirubin 9 2 mg per 100 ml), and inadequate circulation (pulse-rate 150, blood-pressure 85/60 mm Hg) After 54 hours she vomited and diarrhœa developed , so the strict Bull regime had to be abandoned and feeding by mouth begun , but next day, 72 hours after the transfusion diuresis set in and she thereafter made an uninterrupted recovery and was discharged on May 31

The disappearance of the transfused cells was followed by Ashby's differential-agglutination method free circulating anti-A was detected by agglutination of A cells by the recipient s serum, and anti-A adsorbed on recipient's cells by the direct anti-globulin method The results are shown in the accompanying table

Date in May	Direct anti-globulin test	Presence of B cells (Ashby)	Presence of anti A	Volume of urine (ml)
17	++	Not tested	Not tested	50
18	++	Not tested	Not tested	500
19	++	+	+	230
20	++	0	+	360
21	++	0	+	460
23	0	Not tested	0	1020

It is clear that foreign incompatible agglutinins derived from donor plasma remained in the recipient s bloodstream even longer than did the foreign red cells

Technique

The patient had been admitted on May 11 and next day was grouped by the hospital blood bank as group B rhesus positive the cells being tested against known serum and the patient's serum tested with known cells When the duty pathologist was asked for blood he did not check the patient s group but took two bottles of group-B rhesus-positive blood from the store for cross-matching by the tube-centrifuge method Agglutination took place in both tubes The pathologist took two more bottles of group-B rhesus-positive blood and repeated the test this time setting up a control with the patient's cells in her own serum , all the tubes showed agglutination, which he ascribed to an auto-agglutinin active at 37°C, although such auto-agglutinins are very rare whereas errors in ABO grouping and non-specific clumping by centrifuging at too high a speed are fairly common

The pathologist then set up a routine cross-match in saline solution and albumin, both at 37°C, and set up cells and serum for the anti-globulin test using the patient s cells in her own serum as an indicator for auto-agglutinins However when he visited the ward he concluded that the patient's clinical state warranted immediate transfusion , so after an hour s incubation he read the saline solution cross-match, which showed no agglutination and completed the anti-globulin test, which was also read as negative He then issued the blood

The blood was administered between 4 45 A M and 10 A M on May 17 and caused neither dyspnœa backache, nor rigor the incompatibility was discovered at 2 15 P M , when the blood-bank staff checked all the night emergency work It became clear that the patient s group was A and not B, and that the blood-bank staff had made an error on May 12 The original serum which had been kept was found to contain anti-B , so it must have come from a patient of group A No explanation for this error could be found

The cross-match had failed to demonstrate the error without ambiguity When it was repeated with sera collected on May 12 and 17 against a 2% suspension of donor cells at room-temperature, there was strong agglutination, with a trace of hæmolysis only, but at 37°C there was well-marked hæmolysis in both tubes, and the residual cells were uniformly distributed except for a few clumps Further tests with added guineapig complement showed that an anti-B hæmolysin active at 37°C was present in both samples of serum, causing almost complete hæmolysis at a titre of 1 and a trace at 4 whereas at room-temperature there was only a trace at 1 There was nothing to suggest an immune origin for this hæmolysin A sample collected ten days after transfusion showed a hæmolysin titre of 16 and an agglutinin titre of 256 compared with a pre-transfusion value of 32.

Comments

This incompatible transfusion occurred because

(1) The technical staff of the bank made an error in ABO grouping

(2) The duty pathologist believed the bank s result and did not check it even when he got unexpected results

(3) He set up the saline solution cross match at 37 C instead of at room temperature and did not recognise the hæmolysis

It follows that

(1) Since auto agglutinins active at 37°C are very rare if their aid must be invoked to explain the results of cross-matching tests a gross error has probably been made

(2) The most probable error in such a case is an error in ABO grouping usually of the recipient This can be checked on the tile in a few minutes If the recipient s ABO group is correct. that of the donor should be checked. with special attention to the possibility of A_2.

(3) Hæmolysis in a cross match usually indicates an ABO incompatibility this can be confirmed by a slide test or more slowly by a saline solution test at room-temperature

(4) The saline-solution cross match should be kept at room-temperature where it will easily identify anti-A anti-B anti M, anti H, and anti-P it should not be incubated at 37 C, where hæmolysins may be active

We wish to thank Dr W J Clancy and his staff for their full coöperation and Dr George Discombe for his invaluable help throughout

The serum alkaline phosphatase level tended to be low, as in vitamin-D intoxication (Fanconi and de Chastonay 1950)

Prednisolone, 5 mg a day, converted a positive phosphorus balance of 59%, with an average daily retention of 0 18 g, to a balance of 40%, with a retention of 0 16 g

Citrate Metabolism

Serum citrate levels and urinary outputs of citrate were estimated in case 6 in the active phase and in cases 4 and 6 during recovery In the active phase the serum citrate level was 0 7 mg per 100 ml, and during recovery 1 8, 2 4, 2 5, and 1 8 mg per 100 ml on four occasions Harrison and Harrison (1952) have given the mean serum citrate level in infants aged from 2 months to 2 years as 2 5 mg per 100 ml, with a range of 2 0–3 4 mg per 100 ml Thus the serum-citrate level was low in the active phase and gave no indication of increased vitamin-D effect in which raised levels up to 6 mg per 100 ml may be obtained (Harrison 1954)

The twenty four-hour urinary output of citrate in the active phase was 9 5 mg and 10 6 mg on two occasions and in the recovery phase 96 mg The output in the active phase was low and that in the recovery phase low normal in contrast to the high urinary output of citrate in hypervitaminosis D

Cholesterol Metabolism

Hypercholesterolæmia was a feature of cases 2, 3, 4, and 6 Cholesterol was not estimated in case 1 Lowe et al (1954), Creery and Neill (1954), Dawson et al (1954), and Macdonald and Stapleton (1955) have all reported hypercholesterolæmia in idiopathic hypercalcæmia Vitamin-D intoxication in infancy has been reported with either a low or a normal plasma cholesterol level (Jelke 1946, Fanconi and de Chastonay 1950) Coincidental plasma-cholesterol and serum calcium levels were estimated most frequently in case 4, and there was a striking parallelism between them (fig 4) Altogether twenty-two coincidental serum calcium and plasma-cholesterol levels were estimated in cases 2, 3, 4, and 6 The coefficient of correlation between these was +0 58, with a standard error of 0 22 There was thus a statistically significant positive correlation between serum calcium and plasma cholesterol levels

In view of this we examined the same relationship in previously published cases in which coincidentally estimated levels are available Lowe et al (1954) reported fifteen such pairs of levels in 7 cases, Dawson et al (1954) five such pairs of levels in 1 patient, and Macdonald and Stapleton (1955) nine such pairs in 2 cases By combining these twenty-nine pairs with our twenty two pairs the scatter diagram shown in fig 6 was obtained The coefficient of correlation of these results is +0 72, with a standard error of 0 14, again indicating a significant positive correlation between serum calcium and plasma cholesterol levels

Certain cholesterol derivatives will in the standard laboratory test for total cholesterol be estimated as the latter substance At the same time it is recognised that some cholesterol derivatives have a vitamin D like effect —e g, vitamin D_3 is derived from 7 dehydrocholesterol Also the healthy infant synthesises cholesterol (Gamble and Blackfan 1920) In view of the hypercholesterolæmia and hypercalcæmia and the demonstrated correlation between them it seems that the disordered metabolism of calcium in idiopathic hypercalcæmia could be related to a disorder of cholesterol metabolism It is tempting to speculate that the latter takes the form of excess production of cholesterol derivatives with a vitamin D-like effect but with other and toxic effects also It is recognised that sterols exist which are antirachitic (and can presumably therefore produce hypercalcæmia) but also predominantly toxic—e g, toxisterol The presence

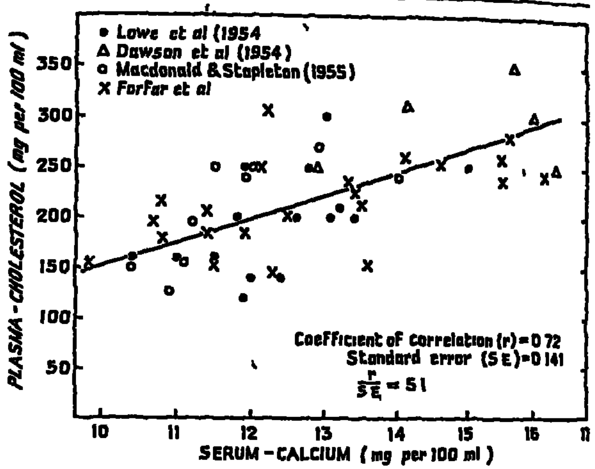

Fig 6—Correlation between plasma cholesterol and serum calcium in present and in previously published cases

of a substance of this kind would be in keeping with the symptomatology and biochemistry of idiopathic hypercalcæmia

The free cholesterol/cholesterol ester ratio was estimated seven times in the acute and early recovery phases of hypercalcæmia (cases 3, 4, and 6) and found to be 0 71–2 17 (mean 1 25) This compared with 0 35–1 03 (mean 0 56) in 10 controls of the same age The rise in the ratio was accounted for predominantly by a rise in the free cholesterol fraction

On serum electrophoresis (case 6) 11% of cholesterol was found to be attached to α lipoprotein and 89% to β-lipoprotein, compared with the usual ratio of a third to α lipoprotein and two thirds to β lipoprotein

No abnormal sterols could be demonstrated by reverse phase chromatography

Effect of Cortisone

Anderson et al (1954) have shown that cortisone reduces the serum calcium level in the hypercalcæmia which may accompany sarcoidosis, and have suggested that cortisone antagonises vitamin D

Cortisone (25 mg daily) was given to case 4 for three periods of five to seven days, and prednisolone (5 mg daily) to case 6 for three weeks On each occasion the serum calcium level fell The balances studied in case 6 showed that prednisolone reduced the retention of calcium and phosphorus (table IV) Cortisone also antagonised the effect of calciferol (table IV)

We conclude from these findings that cortisone reduced the absorption of calcium and phosphorus from the alimentary tract, and that it did so in virtue of an anti vitamin D-like effect

During prednisolone therapy a serum citrate level which had been 0 7 mg per 100 ml rose to 1 2 mg per 100 ml

Cortisone in case 4 did not produce any detectable clinical improvement In fact on three occasions its administration was accompanied by a considerable increase in vomiting It did not cause any consistent increase in weight and did not appear to improve appetite or to reduce lassitude Prednisolone in case 6 appeared to produce clinical improvement Appetite improved, vomiting diminished, and there was a steady gain in weight, which continued after prednisolone was withdrawn Further experience will be necessary before the therapeutic role of these drugs can be adequately assessed

Discussion

Fatal vitamin-D poisoning has been reported in infancy

Malmberg's (1929) patient, who had been given up to 2 teaspoonfuls of cod liver oil daily from the age of 3 weeks,

Preliminary Communication

DETERMINATION OF FŒTAL BLOOD-GROUP

By examining the desquamated cells in the amniotic fluid for the specific sex chromatin discovered by Barr and his associates,[1] it has become possible to diagnose the sex of a fœtus. This method has been described by two of us,[2] and independent development of the method simultaneously in various parts of the world has amply confirmed its reliability.[3–6] We have since tried to develop a method for determining the fœtal blood-group, and we report here the preliminary results of antenatal ABO grouping in the last months of pregnancy from desquamated cells in the amniotic fluid.

If the fœtal blood group can be determined as early as the sex—i.e., from the fourth month of pregnancy—and amniotic fluid can be withdrawn at this stage without disturbing the pregnancy (which we believe but have not yet proved), then it will be possible to diagnose both sex-linked and blood group-linked hereditary diseases at a stage when pregnancy can be safely interrupted.[7]

No simple and reliable method for determining the blood-group from tissue cells was available until Coombs and his co-workers recently described a method by which A and B antigens could be demonstrated on human epidermal cells by mixed agglutination.[8] Coombs et al. believed that this method could be applied to most tissue cells and thus afford a useful tool in studies of the antigenic structure of tissue cells. In our hands, this method has made it possible to detect A and B antigens in the cells of amniotic fluid, all of which are of fœtal origin.

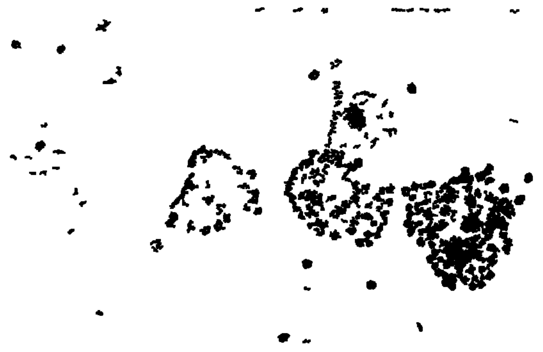

Fig 1—Mixed agglutination of erythrocytes and amniotic fluid cells. Cells do not all participate in agglutination.

Amniotic fluid was obtained by inserting a catheter into the amniotic cavity from below in cases where labour was to be induced, and by transabdominal puncture in a case of hydramnios. 2–5 ml. of each sample was centrifuged for three minutes at 1500 r.p.m. in silicone-coated conical glass tubes. The vernix and the supernatant were removed and the cellular sediment was resuspended in Ringer's solution and centrifuged again. This procedure was repeated once or twice. 10 drops of a suitable cell suspension was then incubated for one hour at 20°C with a similar quantity of anti-A immune serum, and another aliquot with anti-B serum. After this the samples were centrifuged again for three minutes, and the sediments were washed twice with Ringer's solution. Erythrocytes of groups A, B, and O were washed twice, and 1% suspensions with Ringer's solution were made. 4 drops of the cell suspensions was then mixed with similar amounts of the erythrocyte suspensions in silicone-treated test tubes in the following way:

(1) Amniotic cells incubated with anti-A + A erythrocytes.
(2) Amniotic cells incubated with anti-B + B erythrocytes.
(3) Amniotic cells incubated with anti-A + O erythrocytes.
(4) Amniotic cells incubated with anti-B + O erythrocytes.

The tubes were centrifuged and the sediments were then carefully resuspended in the supernatant by gently shaking the tubes. A drop of each cell-erythrocyte mixture was inspected on a slide under cover with an ordinary light microscope or a phase-contrast microscope.

Where agglutination occurred, appearances very similar to those described by Coombs et al.[8] were seen (figs. 1 and 2). The erythrocytes adhered in large numbers to the surface of the much larger amniotic fluid cells, but no agglutination of erythrocytes or of cells alone was seen. When agglutination occurred in mixture no. 1, a fœtal blood-group of A was diagnosed; agglutination in mixture no. 2 was diagnosed as group B; agglutination in both as group AB; and no agglutination as group O. No agglutination occurred in mixtures nos. 3 and 4 in any instance, thus providing a control.

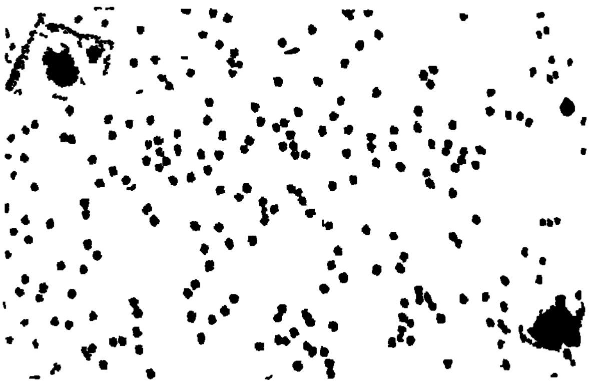

Fig 2—Cell-erythrocyte mixture showing no agglutination.

So far we have studied twelve samples of amniotic fluid, six of which were examined by two of us independently of each other. One sample was found at the first centrifugation to contain blood; contamination with maternal blood was assumed, and this was confirmed by the subsequent examination. In one case very weak agglutination was obtained in mixture no. 1 by both investigators. Postnatal blood grouping of umbilical-cord blood indicated group A. In all the remaining cases except one the results agreed with the blood-groups determined postnatally on cord blood. Only in one case did one of the examiners fail to obtain agglutination in mixture no. 2, where the blood group later turned out to be B. In two instances one of us saw slight erythrocyte agglutination in cases of group O, but no mixed cell-erythrocyte agglutination, which alone is taken as a positive test.

Although the number of samples is small there is no doubt that the fœtal ABO blood group can be diagnosed by this method. How early in pregnancy it can be done is not known, nor has any attempt been made to determine the Rh group as yet. A knowledge of the fœtal Rh-group would be of practical value in cases of Rh immunisation. At present we induce labour in such cases about two weeks before term if the fœtus is estimated at 2800 g. or more; but even in cases where the mother has a high titre of antibodies the fœtus may be Rh negative, and antenatal diagnosis of the Rh group would make it possible to avoid induction of labour in such cases.

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died at the age of 4 months with generalised œdema, rickets, and cardiac degeneration

Putschar (1929) described an infant who had been ill from birth and died at the age of 5 months after having had a moderate excess of vitamin D for ninety days

The dosage of vitamin D is given in only one of Thatcher's (1931, 1936) cases About 1500 units daily was given after the first signs of disease had appeared

At necropsy both of Thatcher's cases and Putschar's case had renal calcification in and around the tubules—a lesion now recognised to occur in idiopathic renal acidosis with nephrocalcinosis None of these patients was subjected to biochemical studies They appeared to have been ill before any increase of vitamin D was given, and it is difficult to accept them as proved cases of vitamin-D poisoning or of idiosyncrasy

A more convincing case has been reported by Ross and Williams (1939) in an infant who had been premature at birth and had received vitamin D 20,000–40,000 units daily for several months He died of pneumonia and at necropsy had widespread visceral calcification

Non fatal cases of vitamin D poisoning have been reported by Ross and Williams (1939), Jelke (1946), and Fanconi and de Chastonay (1950) The dosage was 20,000–100,000 units a day for weeks or months

Thus indisputable vitamin-D poisoning in infancy has been associated with very high intake of vitamin D, and even with dosages of this order recovery, if it occurred, took place within a month to six weeks of withdrawal of vitamin D, a considerably shorter period than is required for recovery in many cases of idiopathic hypercalcæmia

It is clear that many of the features of idiopathic hypercalcæmia are in keeping with an excessive vitamin-D effect, but there are also features significantly out of keeping with the known effects of calciferol These two groups are contrasted in table v The hypothesis of hypersensitivity to vitamin D will not accommodate some of the features of hypercalcæmia, unless it is also postulated that the hypersensitivity is accompanied by a profound disturbance of response to vitamin D

TABLE V—FEATURES OF IDIOPATHIC HYPERCALCÆMIA

Evidence of vitamin D like effect	Unlike calciferol effect
Symptoms Radiological changes in bones Increased absorption of calcium from alimentary tract Increased retention of calcium Hypercalcæmia Hypercalcuria Azotæmia Serum alkaline phosphatase level lowered	Vitamin D intake may be low Absence of significant clinical change on administration of calciferol Absence of renal response to calciferol Possible duration of illness after withdrawal of vitamin D Increased retention of phosphorus Hypophosphaturia Hypocitræmia and hypocituria

The postulation that idiopathic hypercalcæmia of infancy results from a disturbance of cholesterol metabolism with the production of a hypercalcæmic but toxic substance could explain most of the features The low intake of vitamin D and prolonged course in certain cases would be understandable The administration of vitamin D might add insult to injury already present but would be unlikely to produce any severe hypersensitivity reaction The lowering of the serum calcium level by a low-calcium diet or by cortisone would, in so far as hypercalcæmia is itself harmful, be beneficial It would not necessarily obviate other toxic effects As a corollary we observed some dissociation between the serum-calcium level and the patient's clinical state symptoms were not worst when the serum-calcium level was highest, nor were they least when the serum-calcium level was lowest If case 5 is accepted as one of idiopathic hypercalcæmia sine hypercalcæmia, his illness cannot have been related only to his serum calcium level, but the conception of a substance predominantly toxic and only moderately hypercalcæmic would explain such a case It would need to be accepted that the mode of action of such a substance differs a little from that of vitamin D—e g, in certain aspects of phosphorus and citrate metabolism

The arithmetical product of the serum calcium and plasma cholesterol levels may have some diagnostic significance In ten estimations on infants aged 6–15 months who were convalescent from, or in the active stage of, other diseases the range of this product was 1007–2726 (mean 1717) In case 5 (serum calcium 11 2 mg per 100 ml) this product was 2946 When he had recovered, the product had returned to within normal limits (1940) So, too, on recovery did the products in cases 2, 3, and 4 become normal (1786, 2047, and 2333 respectively) The term idiopathic hypercholesterocalcæmia would perhaps more accurately describe this disease and would embrace those cases which appear to be of the same disease but by definition are excluded by the term idiopathic hypercalcæmia

There are certain analogous features between idiopathic infantile hypercalcæmia and the hypercalcæmia which may accompany interstitial plasma cell pneumonia, and Hallman et al (1954) suggest that there may be some relationship between the two None of our patients exhibited the clinical features of interstitial plasma cell pneumonia, but 3 of them had had fairly prolonged preceding respiratory infections, which in 1 case lasted three months The clinical course and usually self-limiting nature of idiopathic hypercalcæmia of infancy would be in keeping with an infective ætiology

Summary

5 cases of idiopathic hypercalcæmia are described, together with a possible 6th

In 3 cases the intake of vitamin D was somewhat below that normally accepted in this country, and in only 1 was it above 2000 units a day

Balance studies showed that there was increased retention of calcium and phosphorus

Calciferol produced no significant clinical change and did not increase the retention of calcium more than might be expected in a healthy infant

Moderate hypercalcuria was present, but calciferol did not further increase the urinary output of calcium

The urinary excretion of phosphorus was low

The plasma cholesterol level was usually raised in the active phase of hypercalcæmia This was due to a rise in the free cholesterol fraction There was a significant positive correlation between the plasma cholesterol level and the serum calcium level

The serum citrate level and the urinary output of citrate were those of hypovitaminosis D rather than of hypervitaminosis D

These results are interpreted as showing that, although there is evidence of a vitamin-D like effect in idiopathic hypercalcæmia, neither excessive ingestion of vitamin D nor specific hypersensitivity to vitamin D explains all the features

We suggest that in idiopathic hypercalcæmia a disturbance of cholesterol metabolism produces a cholesterol derivative with hypercalcæmic and toxic effects

The possibility that this disturbance of cholesterol metabolism is due to infection is considered

A low calcium diet induced a negative calcium balance and a lowered serum calcium level without producing any consistent clinical improvement

Prednisolone reduced the absorption of calcium and phosphorus from the alimentary tract

Cortisone lowered the serum-calcium level and antagonised the effect of ingested calciferol

We wish to thank Prof R W B Ellis for his support

References overleaf

Reviews of Books

Peopling the British Commonwealth

G F McCLEARY, M A, M D Camb London Faber & Faber 1953 Pp 174 18s

INTEREST in demography tends to be limited to specialists But the facts it reveals are the concern of us all, as Dr McCleary proves in his balanced survey of the population problems of Britain and the Commonwealth Vital statistics are often dull reading, but he tells his story with skill and a wealth of interesting historical detail By collecting in readable form facts and opinions which are difficult of access to the general reader he has made a useful contribution to the understanding of problems which are being increasingly forced on public attention

Dr McCleary has deliberately confined his book to countries with immigration potential After sketching the historical and political background, he follows the tangled threads of the birth and death rates, and of immigration and emigration since the end of the last century, first in Britain, then in each of the four Dominions In 1883 Seeley predicted that within fifty years the white population of these countries would exceed 100 million In fact seventy years later, it is still only 79 million, and, relative to resources, the distribution is unbalanced Tracing causes and consequences, Dr McCleary shows how voluntary birth prevention has limited the development which was so confidently forecast Can the Commonwealth survive as a viable unit unless the birth-rate rises above replacement-level ? What can be done to redistribute the overcrowded population of Britain to the underpopulated and underdeveloped Dominions ? To these questions Dr McCleary propounds no dogmatic answers He surveys the alternatives and leaves conclusions to the reader, indicating only his preference for planned mass emigration and his realisation that our collective future may depend on switching the contemporary preference for material pleasures to the less immediate but more lasting happiness of a fuller family life

An Outline of the Cytology and Pathology of the Reticular Tissue

A H E MARSHALL, Freedom research fellow, Bernhard Baron Institute of Pathology, London Hospital With a chapter on the Lipidoses by J B CAVANAGH. Edinburgh Oliver & Boyd 1956 Pp 274 116 illustrations 42s

Dr Marshall combines a factual account of our knowledge of the reticular system with a critical appraisal of the many hypotheses which veil the important gaps waiting to be filled in He is not afraid to express his own views, which are based on the records of the London Hospital and the Oxford Lymph Node Registry and supported by his own experimental work At the same time he is commendably cautious in his comparison of human reticuloses and experimental reticuloses in animals

He pays much attention to the often overlooked work of Hortega and de Asua (1921 and 1924) on the presence of microglia like cells in organs other than the brain This is the essential starting point of his work, for he has demonstrated, mainly by the Weil-Davenport technique, the presence of "metalophil" cells throughout the reticular system and in such unexpected places as the advancing edge of the histological tubercle

In reviewing the various clinical and histological types of reticuloses and reticulosarcoma, he largely follows Robb Smith he seems to favour classification by further analysis rather than synthesis His account of 30 cases of lymphohistiocytic medullar reticulosis (Robb Smith 1947), of the Kurloff cell, of Boeck s sarcoidosis, and of mycosis fungoides are particularly helpful of this last disease he insists that the diagnosis should be reserved for cases with a typical clinical course and a predominant skin localisation and should not be applied to examples of generalised reticular tissue neoplasm in which some dermal infiltration has taken place

Dr Cavanagh, of Guy s Hospital, contributes a chapter on the lipid storage diseases which helps to clarify a subject which is becoming increasingly confused

The illustrations of this stimulating book are of a high order

Office Procedures

PAUL WILLIAMSON M D Philadelphia and London W B Saunders 1955 Pp 412 87s 6d

THE title suggests to the British reader that this book is written for the business man in fact, it is full of useful medical information The American doctor's "office" is equipped on a more ambitious scale than is usual in this country, and the procedures which are carried out there include many customarily delegated here to the minor-operation theatre or hospital ward sideroom

Each section contains clear accounts of all the manipulations, manœuvres diagnostic tests, and procedures likely to crop up in general practice The section on pædiatrics, for example, deals, among other things, with treatment of birth fractures and injuries venepuncture, lumbar puncture, examination techniques, numerous sideroom tests, management of herniæ, hydroceles, immunisation and vaccination techniques and circumcision The other sections are built up in the same way, and those on minor surgery, proctology, gynæcology, and the musculoskeletal system are particularly comprehensive

Clear line drawings help the text, and those in the section on minor surgery are especially good They show that, though his equipment would be considered generous in this country the author can improvise shrewdly, finding many uses for an item of equipment found in any office"—the straightened paper clip

Dr Williamson has enjoyed writing his book He writes easily and well, wisely and wittily His book will find eager readers in every casualty department, and among those in group practice It will appeal also to single-handed general practitioners who have a theatre and some occasional help to turn to

The British Pædiatric Association, 1928–1952

H C CAMERON, F.R C P London British Pædiatric Association. 1955 Pp 107

THIS is the story of the first twenty-five years of the British Pædiatric Association The association is as fortunate in its choice of a historian as it has been in so many of its activities Dr Cameron, the biographer of Lord Lister and Sir Joseph Banks and the historian of Guy's Hospital, has written this account of the pædiatricians with delightful grace The birth of the association is portrayed in the frontispiece drawing by Mrs Donald Paterson, in which her dynamic husband, with James Spence in the wings, is persuading a doubtful Dr Still to give the project his authoritative blessing

The newborn association began as a friendly clinical club and has continued, in the atmosphere of Windermere, to maintain this spirit while developing its medicopolitical responsibilities Dr Cameron's story makes it plain that this remarkable fusion of objectives was achieved by the devotion of the men who directed the association s development, such as Frederic Still, Leonard Parsons, and James Spence, their work now completed and Robert Hutchison, Charles McNeil, Cameron himself, and Donald Paterson, still exerting a friendly influence

The book concludes with obituaries in which the author (unlike that famous Guy's man, Samuel Wilkes, whose *vale* to departed colleagues was said to "add a new terror to death"), by his appreciation of the good in the men he describes, makes it appear an "easy and pleasant thing to die." This history happily records the work of a generation who created, we may hope, an enduring tradition for pædiatrics

International Review of Cytology

Vol IV Editors G H BOURNE and J F DANIELLI London Academic Books Pp 396 $9

THE editors have again ranged widely in their choice of topics—from micromanipulative technique to electrochemistry

M J Kopak describes the triumphs of instrumentation by which he is able to investigate the enzymatic activity contained in one millionth of a c.mm of cytoplasm, so much has been achieved in this direction that when the writer states that "it is theoretically possible to identify a single

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THYROIDECTOMY AND THE RECURRENT LARYNGEAL NERVES

A D Roy
M B Glasg , F R C S , F R C S E
LATE SENIOR SURGICAL REGISTRAR

R H Gardiner
M Ch Oxfd F R C S , F R C S E
CONSULTANT SURGEON

W M Niblock
M A Camb , F R C S
CONSULTANT E N T SURGEON

THE AYLESBURY HOSPITALS, BUCKS

"Damage to one recurrent nerve produces a permanent huskiness of the voice " These words from a well-known textbook on surgical anatomy represent a widely held opinion on the results of damage to the recurrent laryngeal nerves during thyroidectomy

It has always been our practice for an ear, nose, and throat surgeon to examine both preoperatively and postoperatively the larynx of patients undergoing thyroidectomy and, where there is evidence of damage to a nerve, to follow these patients and to assess the degree of disability In doing this, it has become clear that the problem could not be stated so simply as in the quotation given above, nor is the picture so gloomy We therefore decided to investigate the frequency of damage, any predisposing factors that increase the risk of damage, and the subsequent condition of such patients

We examined the records of 300 patients operated on between January, 1949, and December, 1954, for non malignant conditions of the thyroid gland All the cases showing nerve damage were followed up for at least a year , the last case in the series occurred in October, 1954

Operative Technique

The technique of thyroidectomy has remained unchanged for years, being based on that of Joll (1932)

The gland is exposed by a collar incision with separation of the infrahyoid muscles in the midline These muscles are rarely divided, and in no case in this series was it considered necessary to do so In no case was the sternum split to deliver an intrathoracic goitre The inferior thyroid artery is ligated in continuity in the areolar tissue lateral to the capsule of the gland and as close to the carotid sheath as possible, but in a few cases it was not found in this position, and a prolonged search was not pursued The recurrent nerves are not looked for and identified, reliance being placed on leaving a slice of the posteromedial surface of either lobe to protect the nerve To trace the course of the nerves in the neck is only possible after dislocation of the lateral lobes, especially when they are enlarged, and there is little doubt that many injuries to the nerves occur during the dislocation The cut surface of the gland is stitched to the fascia covering the trachea to control bleeding, and only the superficial layer of the wound is drained We always aim at accurate hæmostasis in the area deep to the "strap" muscles, however tedious and time consuming it may be The extent of the resection, of course varies with the condition of the gland, but when the gland is toxic about seven eighths of each lobe is removed

The larynx is examined four days before operation and five days after operation , and, if there is any doubt about whether the nerve is injured or not, the larynx is examined again a month later

Frequency of Damage

In 40 cases there was evidence of damage to one or both of the recurrent laryngeal nerves—a frequency of 13 3% In 22 cases the right nerve was damaged, in 17 cases the left nerve, and in 1 case both nerves were damaged Of these patients 18 recovered completely and 22 did not The bilateral case did not recover In 1 case one nerve had been permanently damaged at a previous operation and the other nerve was damaged in this series There was again no recovery, and a bilateral paralysis resulted

Recovery of Full Movement of Cord

Of the 18 cases (6%) in which full movement of the cord was recovered, 6 had initially a partial lesion of the cord, manifesting itself as sluggishness of the cord and weakness in adduction of the cord, and all these cases recovered rapidly and completely, 5 before leaving hospital and the other 1 within a month Only 2 of these patients noticed any change in their voices

In 11 cases there was initially complete paralysis of a cord in the paramedian position midway between adduction and abduction, and in 1 case the paralysis was partial within six days of operation and complete a month later All these patients recovered full movements within a year The most rapid recovery was in two months, and the slowest in almost a year With recovery in movements went recovery of a full range of voice except in 4 cases 1 patient was still slightly husky, and the other 3 stated that under an emotional strain (usually anger) their voices tended to "fade away," which seemed to indicate early fatigue in the affected muscles

In 4 of these cases difficulties were met with at operation and noted, but in the other 14 cases the operation was uneventful The difficulties were as follows

(1) A large gland displacing the trachea to the left and retrosternal on the right side—the right nerve was damaged

enzyme molecule " the reader is inclined to accept the practicability of doing so as well The second essentially technical paper is by M Wolman and is a useful critical discussion of the mode of action of fixatives and their effects on tissues as subsequently visualised Two interesting communications deal with bacterial morphology, in the first A Marshak discusses the bacterial analogues of the cellular inclusions of higher organisms, and in the other R Vendrely discusses from a histochemical point of view the staining characteristics of bacteria, and includes a consideration of the basis of Gram staining

The papers by D P Hackett on plant mitochondria, and by K Muhlethaler on the structure of chloroplasts are most timely in relation to recent biochemical work on the pathways of photosynthesis N B Kurnick's review of the histochemistry of nucleic acids is notable for a good discussion of the pitfalls of photometric measurements on histological preparations, while R Couteaux's chapter on the localisation of cholinesterases contains some splendidly reproduced photographs and drawings—although the element of subjectivity in drawings is, as always, difficult to evaluate

The contribution by L E Wagge on amœbocytes concentrates on those of molluscs and is in the descriptive tradition, similarly that of H Moe on goblet cells is also broadly descriptive histology, but it includes some quantitative data on the distribution of such cells in the intestine of the cat, though the significance of these data is not altogether clear The remaining papers comprise an informative but inconclusive account of the structure and chemistry of nucleoli by W S Vincent and a short note by E J Conway which summarises recent studies on the redox pump theory of ion transport

This work is not, of course, addressed primarily to a medical public, but the histochemical sections of the book are likely to be very valuable to pathologists who are not specialists in this branch of histology, while many of the other sections will appeal to bacteriologists and biochemists

Tropical Medicine for Nurses

A R D ADAMS and B G MAEGRAITH, School of Tropical Medicine, Liverpool Oxford Blackwell Scientific Publications 1955 Pp 314 30*s*

THE nursing profession now has a more substantial volume on tropical medicine than hitherto For many years the staff of the Liverpool School have taught this subject to general-trained and registered hospital nurses before they went overseas, and it is for them that this book has been written It is definitely not a book on nursing, but it gives an idea of what they may have to contend with in isolated stations in the tropics The subjects are arranged in alphabetical order and each disease is dealt with simply but adequately The 32 figures are very clear and well produced, and the book is admirably suited to its purpose

Bibliotheca Walleriana

A Catalogue of the Erik Waller Collection Vols I and II Compiled by HANS SALLANDER Stockholm Almqvist & Wiksell 1955 Pp 1000 Sw Kr 200

THE Royal University Library of Uppsala was greatly enriched in 1950 when the Swedish surgeon, Erik Waller, presented his library It contains almost all the major medical works published before 1800, as well as a highly representative selection of later literature The famous collections of Osler and Cushing each comprised some 8000 items, but Waller's includes nearly 21,000, and is also superior in quality

The main part of the library consists of old medical literature, including numerous rare and unique books These, together with the 150 incunabula form the first volume of the catalogue The second volume deals mainly with literature of the natural sciences, the history of medicine and science biography, bibliography, and various other subjects, including the collected works of famous scholars and scientists The items are listed under full titles Unfortunately there are no annotations but they would have been an immense job and would have greatly increased the cost

These volumes will be useful to medical and scientific libraries as a check list for exact titles and editions In these days of photo-copying, a catalogue of this kind often reveals the location of a rare book The production of the two volumes is excellent

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La Lèpre (2nd ed Paris Expansion Scientifique Française 1955 Pp 310 Fr 3800)—In this book Dr Roland Chaussinand, of the Pasteur Institute, has drawn from his own considerable experience in Indo China and has added much of value from the work of others He has substantially enlarged the 1950 edition, and he gives a sound and h description of the disease, its history, epidemiology, bacteriology, immunology, prophylaxis, and treatment There are 130 excellent photographs, of which 18 are coloured and a comprehensive bibliography He condemns compulsory segregation, calling it " illogical, ineffective and dangerous and he emphasises the importance in prophylaxis of case finding and early treatment He also develops his view that tuberculosis and leprosy, by virtue of the relative cross immunity they produce, are mutually antagonistic diseases and he brings the reader up to date on B C G in the prevention of leprosy In his chapter on treatment he clearly states his preference for D D S (diaminodiphenyl sulphone), and deals comprehensively with other aspects such as physiotherapy and surgery It is a pity that so little space is devoted to the histology of leprosy and to describing reactive states there is only a fleeting reference to erythema nodosum leprosum and Lucio's phenomenon is not mentioned Further, many leprologists will disagree with the view that borderline cases always evolve from major tuberculoid and can therefore be considered benign, particularly since 100% have positive skin smears, 86% are negative to lepromin, and the majority become lepromatous These criticisms apart, this is a concise and informative work

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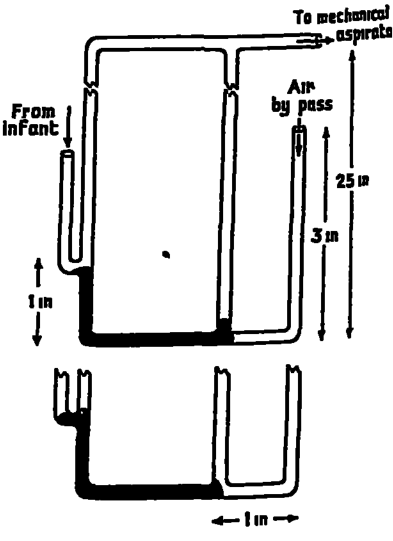
New Inventions

A MUCUS-ASPIRATOR FOR INFANTS

THERE is little doubt that a thorough clearance of the upper respiratory passages is the most important measure in the resuscitation of the newborn This is most commonly achieved by swabbing the mouth and aspirating mucus While this is being done the attendant often sucks and blows through the extractor, which consequently becomes contaminated by micro-organisms Most of the mechanical aspirators designed for suction of the adult respiratory passages are capable of a suction force of 650 mm Hg, which is sufficiently strong to cause serious damage to the pharyngeal mucosa of the newborn



A mucus-aspirator has been designed (see figure) with a "mercury break" introduced between the mechanical force of suction and the infant When the suction force rises above 25 mm Hg, air enters through the by-pass and the pressure returns to atmospheric The oscillation of the column of mercury produces gentle intermittent suction

This mechanical aspirator facilitates early aspiration of the fœtal respiratory passages, especially during cæsarean section and breech delivery, under sterile conditions

J M HOLMES
M D Lond, M R C O G

Guy's Hospital, London

Letters to the Editor

CORONARY-ARTERY DISEASE

SIR,—Dr. L Schmidt's comments (Dec 24) are best answered by relating some results of short-term fat-feeding experiments which have been conducted under controlled conditions on volunteers with low serum-cholesterol levels The details of these experiments will be published soon

The basic diet has consisted of maize meal and white bread (estimated fat content 3% of calories) supplemented by sugar and casein in order to maintain by suitable adjustment an isocaloric and isonitrogenous state To this diet various fats and oils have been added in amounts to increase the percentage of calories derived from fat from the basic 3% to approximately 45% and on occasion 70%

Under these conditions, animal fats in the form of beef dripping, butter, eggs, and beef were associated with a prompt and significant elevation of the serum cholesterol level No elevation followed the feeding of equivalent amounts of vegetable oils such as olive oil, sunflower-seed oil, and ground nut oil When ground-nut oil was fed in the hardened or hydrogenated form a prompt rise in the serum cholesterol level occurred One result of the hydrogenation process is the destruction of certain of the highly unsaturated fatty acids, which form only a small percentage of the fatty acid composition of the animal fats used above

By fractional crystallisation we separated out a highly unsaturated and a saturated fatty acid fraction from sunflower seed oil We fed the ethyl esters to a patient whose serum cholesterol level had been raised by a cholesterol (3 0 g) supplement to the basic diet Despite the continued dietary cholesterol supplement, the serum-cholesterol level promptly fell following the feeding of the unsaturated fraction, and an elevation occurred when the saturated fraction was fed later

In Dr Schmidt's criticism of your leading article of Nov 26 on the animal fat theory of coronary heart-disease reference was made to the feeding habits of the Eskimo The animal fat intake of the Eskimo is largely derived from marine animals [1] Marine oils in the form of fish oil, seal oil, and whale oil approach vegetable oils in their fatty acid composition, having a high proportion of the unsaturated fatty acids We have fed seal oil to two volunteers No elevation of the serum cholesterol level followed

In these experiments, then, changes in the serum-cholesterol have been determined by the fatty acid composition of the fats fed, and the consistency of the results has not been affected by alterations in the caloric or protein intake or by switching from maize meal to "baker's cones," a highly refined maize meal from which most of the germ has been removed Nevertheless the views held by Dr Schmidt on maize and bread are somewhat similar to ours, except that we are more interested in the high content of the unsaturated fatty acids in the germ of wheat and maize and not the vitamin E content Burr [2] and Deuel et al [3 4] have shown that the highly unsaturated fatty acids have biological activity in the rat and that the requirement increases as the fat intake increases There is, in addition, a sex difference in the requirements of young rats

Compulsory reversion to the use of naturally occurring vegetable and marine oils, due to the scarcity of animal fat and to bomb damage to hydrogenation plants, could, in our view, explain the striking fall in mortality from circulatory diseases in Norway soon after the German occupation This concept depends on the acceptance of the relationship between the serum-cholesterol level and the incidence of coronary heart disease, but we fully appreciate that more than one mechanism may be operative

Department of Medicine,
University of Cape Town,
South Africa

B BRONTE-STEWART
L EALES
A ANTONIS
J F BROCK

RECRUITMENT FOR THE OVERSEA MEDICAL SERVICE

SIR,—May I endorse Mr Seddon's important letter last week ? We all must agree that it is the duty of this country to help those parts of the Commonwealth where the medical services are inadequate

As far as specialist services are concerned, the seconding of registrars can only meet the need to a very limited extent—for two reasons

Firstly a registrar, however skilled, will not have the same prestige as a consultant, not only will this make it harder for him to carry out his work, but the implication that a registrar is good enough is almost certain to provoke resentment in the recipient country In some cases in its early days the World Health Organisation made the mistake of sending personnel of inadequate status, as a medical ambassador only the best is good enough

Secondly, a registrar will inevitably have at least one eye on vacancies at home and will probably think more of the coveted consultant appointment than of his present work

The only satisfactory way to provide adequate specialist service for underdoctored areas is to second consultants —preferably of some years' standing Nor should a period of work abroad be looked on as a loss or sacrifice, I both benefited professionally and made many friends

Finally, important as it is to provide medical aid where it is needed, this aid is as likely to create ill-will as gratitude, especially as the "undeveloped" countries of the Commonwealth become more "developed", at the earliest possible moment a programme of exchanges should be substituted for aid

Robert Jones & Agnes Hunt
Orthopædic Hospital, Oswestry

ROBERT ROAF

BLOOD-TRANSFUSION

SIR,—With much of your leading article of Dec 31 we would agree, but the last paragraph has been too much for us and we must protest against it You quote Dr French as saying that junior residents should not do emergency cross matches, but that the pathologist himself should be called out if necessary You continue, with slight horror in your voice lest Dr French should hear, to reveal the fact that in *some* hospitals technicians are called in for emergency cross matches We declare now for all to hear, including Dr French, that this has been the practice in this and very many other hospitals for some time, and that it is as safe and as satisfactory as any other arrangement, provided the technician is always able to call in a pathologist in any case of difficulty

It has long been known that the greatest dangers in grouping and cross matching are ignorance, haste, and the little slips and errors that human flesh is heir to These dangers are best overcome by good training in the technique and constant day-in and day out experience Technicians have this training, and for the benefit of those who still regard them as "lab boys," able to do the washing up but good for little else, we would point out that the *final* I M L T hæmatology examination is a searching one based on a comprehensive syllabus in which all aspects of transfusion laboratory work are covered in some detail, and in which mistakes are not tolerated Technicians also have the experience, for they do the vast majority of the routine work both in hospitals and in the National Blood Transfusion Service—and you have yourself commented favourably on the accuracy of the

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[1] Sinclair H M *Proc Nutr Soc* 1953 12 69
[2] Burr G O *Fed Proc* 1942 1 221
[3] Deuel, H J Greenberg S M Anisfeld L Melnick D *J Nutr* 1951 45 535
[4] Cheng A L S Kryder, G D Bergquist L Deuel H J *Ibid* 1952, 48 161

S M S Medical College LIBRARY 1377

blood-grouping work done by the latter No medical qualification can compensate for lack of the necessary technical training or for lack of constant experience in the routine For this reason junior residents are entirely unsuitable for emergency work of this nature, and even pathologists are likely to be less safe than technicians, for there are few, however knowledgeable they may be in transfusion work, who put up routine cross matches Resident clinical pathologists are in this respect better than the clinical residents, but it must be remembered that they are frequently in their first laboratory post and have neither the training nor the experience in serology of a qualified hæmatological technician What are their advantages over qualified technicians who daily undertake this work and who can call on a pathologist in case of need? Is it not nonsense, therefore, to say, as you do, that hospitals without resident clinical pathologists are thereby unfitted to undertake work in which transfusion is often needed?

If, as you suggest, a pathologist is necessary for emergency grouping and cross matching, it follows that he is also necessary during the day-time when it is no less important and no less dangerous As we employ two technicians full time and one part time on grouping and cross matching, it would be necessary for the total medical staff of this laboratory to spend its whole time doing transfusion work And even you, Sir, in spite of your leader, would agree that this would be absurd

We seriously question the wisdom of dividing patients into "dangerous" and "safer" recipients Dangerous recipients there certainly are, but would it not be better to avoid the use of the word "safer" lest it mislead anyone into believing that the cross match is a mere formality? You suggest that when "safer" recipients are to be transfused the emergency can be coped with by "the normal resident staff" with Dr Discombe's book to guide them We presume this means the clinical residents, and we feel that we cannot do better than quote Dr Discombe's good counsel on this subject, on p 14 he states

> "If a clinician is faced with an exsanguinated patient and himself has to decide to administer blood transfusion, to group the patient, and crossmatch a bottle of blood, he must be exceptionally experienced or exceptionally phlegmatic to endure the long wait between starting the test and reading the result Even British phlegm is rarely equal to this task, so that a young clinician hurries over his tests He may easily make an error in the Rhesus group and miss a low titre antibody, or sensitise some young girl to the Rhesus factor and make it unlikely that she will ever have healthy children Every hospital, therefore, must see that the junior clinician on duty need not, whatever the emergency select blood for his own patients"

In conclusion, we would like to say that if a transfusion were to be done on one of us (which God forbid) we would be happiest for the cross match to be done by a technician trained and experienced in hæmatology, knowing that his day-to day familiarity with the technique would guard to a large extent against slips, and knowing that if he was unable to get a perfectly clear cross-match he would call in the other of us, who would decide what was to be done We should be considerably less happy for the cross-match to be done by anyone, pathologist or not, not constantly engaged in this work, however great his theoretical knowledge of blood group serology Technician and pathologist each have their part to play The former carries out prescribed tests and in the vast majority of cases is able to issue blood with an assurance that there is no important incompatibility present In the minority of cases where a clear cross-match cannot be obtained, it is for the pathologist to decide what is to be done next, as here the risks of transfusing and the risk of not transfusing the patient have to be carefully weighed The use of a pathologist for routine cross matches is rather like the use of a steam hammer to crack a nut—not only wasteful of power but also not in the nut's best interests

Pathology Laboratory,
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JOHN B PENFOLD
J W NICHOLAS

SIR,—May I support your commendation of D George Discombe's booklet[1] In it he expresses t hope that it will be read by housemen It should also b studied by pathologists and technicians, but above a surgeons should read and re-read it, for the commone cause of laboratory error in blood grouping and matchi as Discombe has pointed out,[2] is the worrying clinic who wants blood at short notice

In desperate emergencies group O Rh(D) negati blood (which should be available in every blood bank should be used without direct matching, when th urgency is somewhat less, rapid methods of groupi and direct (cross) matching, taking about half an hou are used It cannot, however, be overemphasised that th quicker the method the greater is the risk to the patient not only of a transfusion reaction but of death Zeitlin[3] states that 1 death results from 2000 transfusions

In your leader you imply that properly matched bloo can be provided within two hours from the arrival of the specimen in the laboratory This is correct only if the patient's group and Rh(D) type is already known and if separated serum is available

If these are not available, using modern approved techniq two hours' incubation is necessary to determine the group an the type of the patient's blood[4] After this has been do two more hours' incubation is necessary for the direct matc (the so called cross match)[5] So, assuming the patient's grou and type are unknown, a minimum of four and a quart hours of laboratory working time is needed (the quarter o an hour being allowed for washing the donor's cells, setti up the tubes, and reading the results) To expect blood to b ready in four and a quarter hours presupposes that a pathologist or technician will be ready to drop whatever he is doi and deal with the request

Many clinicians, remembering the days when bloo was grouped on a tile and matched on a slide in a matte of minutes, but forgetting the not infrequent transfusion disasters, feel that pathologists today are being unreason ably difficult Not infrequently requests for blood fo non urgent cases that are to be operated on arrive so late that there is often less than four hours' working time In such circumstances the pathologist should urge the postponement of the operation unless he is prepared to risk a transfusion reaction or fatal catastrophe To my mind it is unfair that he or the technician should have to take the responsibility for the surgeon's thoughtlessne

Many pathologists would not agree with your paragraph in which you question the reliability of technicians to do grouping and direct matching I am convinced that properly trained and experienced technicians who have had recent practice in the work are entirely reliable A technician or a junior pathologist in doubt or difficulty should always be able to get the help of an experienced pathologist

The technician and the pathologist should be treated fairly by the clinicians, and, as Dr Discombe stresses, they should also be supplied with the essential informa tion about the patient without which the laboratory worker may be seriously handicapped

Pathology Department,
Worthing Hospital

R AIDN

SIR,—In your leading article you quote me (p 1376) as having uncompromisingly said[6] "that junior residents should not be called upon to perform cro matching tests, and that if necessary 'the pathologist must be got out of bed to perform this heavy and responsible task'" The article proceeds "We wonder

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1 Discombe G Blood Transfusion a Guide to the Practice o Transfusion in Hospitals London 1955
2 Discombe G *Lancet* 1952 1 734
3 Zeitlin R A *Nursing Mirror* Nov 19 1954
4 Dunsford, I Bowley C C Techniques in Blood Groupin London 1955, p 161
5 Dunsford I Bowley C C *Ibid* p 177
6 French A *Med leg J, Lond* 1955 23 93

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Special Articles

BIOLOGICAL EFFECTS OF ATOMIC RADIATION

A REPORT published in Washington last week is the American counterpart of the Medical Research Council's report on Hazards of Nuclear and Allied Radiations, which is the subject of a leading article on p 999 The report is based on a survey by six committees of the National Academy of Sciences The recommendations of the genetics committee include the following

(1) Records should be kept for every individual, showing his total accumulated lifetime exposure to radiation

(2) The medical use of X rays should be reduced as much as is consistent with medical necessity

(3) The average exposure of the population's reproductive cells to radiation above the natural background should be limited to 10 roentgens from conception to age 30

(4) The 10-roentgen limit should be reconsidered periodically with a view to keeping the reproductive cell exposure at the lowest practicable level

(5) Individual persons should not receive a total accumulated dose to the reproductive cells of more than 50 roentgens up to age 30 years, and not more than 50 roentgens additional up to age 40

(6) Techniques for monitoring world-wide fall-out should be further improved

(7) Measurements of the storage of radiation in the stratosphere should be continued and extended

(8) A national agency should control and keep records of all dumping of radioactive material in the ocean

Speaking of contamination by strontium 90 from fall-out after atomic explosions, the report says that already detectable but biologically insignificant traces of strontium 90 have been found in milk supplies thousands of miles from the site of atomic explosions At present contamination of food is negligible "But the maximum tolerable level is not known There is not nearly enough information about the long-term biological effects on man or animals from eating radiation contaminated food Research in this area is urgently needed" The fall-out dose is at present small compared with background radiation and with the average exposure to medical X rays in the United States

CENTRAL HEALTH SERVICES COUNCIL

THE Minister of Health has appointed or reappointed the following doctors to the council and standing advisory committees for the period ending March 31, 1959

Central Health Services Council

Janet Aitken, *H J B Atkins, Prof Robert Cruickshank, *E J Rees, *A Talbot Rogers

Standing Advisory Committees

Medical—Janet Aitken, *H J B Atkins Professor Cruickshank, *S Whately Davidson, *E J Rees, *A Talbot Rogers

Dental—Sir William Kelsey Fry, *A M Horsnell (until March 31, 1957)

Pharmaceutical—Prof Andrew Wilson

Ophthalmic—Janet Aitken, *J W Tudor Thomas, Oscar Williams

Nursing—Janet Aitken *G C Kelly

Maternity and Midwifery—*Sir Arthur Gemmell Jean M Mackintosh, *E J Rees *A Talbot Rogers, J Forest Smith

Mental Health—Desmond Curran, J R Rees, C A H Watts

Tuberculosis—James Grant, N R Barrett, *F. A H Simmonds

Cancer and Radiotherapy—Janet Aitken, J R K Paterson *E J Rees, *Prof R W Scarff

* New appointment

Symposia

VENEREAL DISEASES AND TREPONEMATOSES

THE First International Symposium on Venereal Diseases and Treponematoses, sponsored jointly by the World Health Organisation and the Public Health Service of the U S Department of Health, Education and Welfare, was held in Washington, D C from May 28 to June 1

Syphilis

Incidence

It was repeatedly emphasised that, although modern methods of syphilis control based on contact tracing and penicillin therapy, can effectively bring down the incidence of early syphilis, some permanent organisation is required to keep it down In the U S A the incidence of early syphilis has declined progressively from 75 6 per *100,000 in 1947 to a provisional figure of 4 1 per 100 000* in 1955 In consequence there has been a considerable relaxation of effort, and case-finding has been less intensive About a year ago the numbers of new cases of primary and secondary syphilis rose in several major American cities Today the significance of this warning is more apparent, and the numbers of cases of early syphilis are increasing in many of the smaller cities with populations of 20,000–200,000 In 1955, of 127 such cities concerning which figures are available, a rise over 1954 occurred in no less than 47 This despite diminished case-finding so the situation is probably even worse than the figures suggest

Serum Tests

With the declining incidence of syphilis some have queried whether the cost of routine serum tests (premarital, prenatal, on hospital patients, &c) is justified by the yield There is no doubt that it is justified, for only by such means can the reservoir of undetected syphilis be disclosed In December, 1954, there was an estimated number of 1 921,000 syphilitics requiring treatment in the U S A Today of all cardiac conditions in adults the only one which is really preventable is cardiovascular syphilis A serum test will reveal latent syphilis before cardiovascular changes have developed, and treatment with penicillin will prevent these from arising

Experience in Russia

From the papers of the three Russian speakers—Prof Boris Mikhailovich Pashkov, Prof Pyotr Vasilievich Kozhevnikov, and Prof Nikolai Sergeivich Smelov—it was evident that in Russia congenital syphilis is not uncommon, and that endemic syphilis exists in some areas There is not yet faith in penicillin as the sole curative agent, and, as was the practice in many European countries until a few years ago, arsphenamine and bismuth preparations are still used in addition

Treatment

Of the purely scientific papers one by A Hurtig (Ottawa), describing the successful combined use of cortisone and antibiotics in a large series of resistant pelvic infections, made a considerable impression In the U S Navy larger doses of penicillin have become necessary through the years in the treatment of gonorrhœa in the Far East Of the newer antibiotics 'PA 105' has been successfully used in the treatment of granuloma inguinale, and spiramycin in the treatment of gonorrhœa and non gonococcal urethritis

Future Action

That the venereal diseases and the treponematoses remain major public health hazards throughout the world, that they are not a hazard of any single nation

INTRAMUSCULAR IRON

Widespread Acceptance...

"The Iron given parenterally was absorbed from the intramuscular site and utilised "[1]

"Utilisation for haemoglobin production was extremely good "[2]

"In every patient a satisfactory rise in the haemoglobin took place "[3]

" all the patients in the series developed a vigorous sense of well-being which contrasted very strikingly with their previous chronic ill-health "[3]

"From the present series it appears that this new iron-dextran complex is a notable advance in the treatment of the iron deficiency of pregnancy "[4]

1 LANCET 1954 2 942.
2. B.M.J 1954 2 1257
3 B M J 1954 2 1255
4 LANCET 1954 2 1245

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(Lancet, 1954, 2, 1245)

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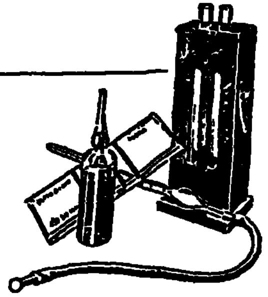

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and cannot be controlled on a world-wide basis by any nation independently, and that, so long as they exist in any nation, they constitute a menace to all nations, was the collective view of the American Venereal Disease Association, which met during the symposium The association's resolution, which was read to the meeting, urges the maintenance and close integration of a cooperative, international, long-range control programme against the venereal diseases and the treponematoses

An executive committee, of which Dr F W Reynolds (U S A) is chairman and Dr R R Willcox secretary, is to handle arrangements for the International treponematoses award

Medicine and the Law

Incurable Insanity as a Ground for Divorce

Two husbands sued for divorce on the ground that their respective wives had been of incurably unsound mind and continuously under care and treatment for a period of at least 5 years immediately preceding the presentation of their petitions Since 1940 medical evidence has been given at the hearing of insanity petitions by affidavit by the medical superintendent of the hospital where a person alleged to be of unsound mind has been under treatment during the relevant period, and such affidavit, according to a direction of the President of the Probate, Divorce and Admiralty Division,[1] has to state, inter alia, that the patient has been continuously under his care and treatment during the 5 year period and to give his opinion that the patient is of incurably unsound mind In the present cases the treatment of each of the wives had been delegated to consultants on the hospital staffs (under the Ministry of Health ruling of 1950) and the medical superintendents felt themselves unable to swear to all the matters required by the direction of 1940 Additional affidavits dealing with treatment and the incurable nature of the insanity had been sworn in both cases by all the consultants concerned with the treatment of the wives during the 5 year period

The President, Lord MERRIMAN, said that, owing to delegation to consultants of responsibility for the clinical treatment of patients (as distinct from the general care which remained vested in the medical superintendent), the medical superintendent was sometimes unable to give first hand evidence about the diagnosis of the patient's mental illness and the nature of the treatment Accordingly, in addition to the usual matters, the medical superintendent should state that he had delegated responsibility to a consultant, giving the full name of the consultant and the date of delegation In such cases an affidavit would be required from the consultant giving the diagnosis, the nature of the treatment prescribed, any special treatment, and the effect thereof, also, if it were the fact, that in the opinion of the consultant and in the light of the medical knowledge of the day, the patient was of incurably unsound mind and the reasons for that opinion, and whether the patient was able to appreciate extra comforts and if so to what amount If the period of delegation to the last consultant was, on the face of it, insufficient to enable him to depose with certainty, the deponent would be the consultant who had treated the patient for an earlier period of sufficient duration, but, in that case, the evidence would have to be brought up to the date of the presentation of the petition either by the present consultant or the medical superintendent, and the date of the assumption of responsibility by each and any consultant and its duration ought to be specifically stated

His Lordship then granted decrees to each of the two petitioners

Usher v Usher and Abley v Abley—*Probate, Divorce and Admiralty Division*, June 11, 1956 C Lawson (Jacques & Co) R Ormrod (Official Solicitor) R L Bayne Powell (The Law Society), H T Walker (Official Solicitor)

ELAINE JONES
Barrister at Law

Parliament

Danger of Children Riding on Farm Tractors

ON the second reading in the House of Lords on June 11 of the Agriculture (Safety, Health and Welfare Provisions) Bill, Earl ST ALDWYN, joint parliamentary secretary to the Ministry of Agriculture, said that every year between five and ten children were killed by falling off tractors There was a real danger here which must be prevented if possible The Bill was read a second time

QUESTION TIME

Fortified White Flour

Last Monday Mr D H AMORY, the Minister of Agriculture, was asked by several members why in face of the evidence of the Medical Research Council and the British Medical Association in favour of National flour he had accepted the Cohen Panel's recommendation in favour of fortified low extraction flour In his replies he said It was because of the conflict of scientific opinion regarding the nutritive value of flour of varying extraction rates that the Government in May of last year invited the President of the Royal Society to nominate a panel of independent persons of accepted authority representative of scientific and medical opinion The whole object of what the Government did was to enable the Government to remain perfectly neutral in this matter as between two strongly expressed medical points of view I should like it to be absolutely clear that we are not proposing to prohibit anybody from eating bread made with flour of any particular extraction rate at all The only prohibition we are imposing is on the use of flour which does not contain a certain minimum quantity of these three token nutrients

Mr F T WILLEY Whilst recognising the right hon gentleman's endeavours to resolve this conflict may I ask him whether he will not admit that he has failed? Has he seen the opinions recently expressed in medical journals, and is he aware that it appears that the weight of medical evidence is against him, in view of this, would he at any rate look at the matter again?—Mr AMORY I think this may well be one of the controversies which will continue until the end of time In the meantime, the consumer will in the future be able to choose the kind of loaf he or she wishes to eat I feel that the Government are not entitled to prevent the consumer from exercising such choice, unless there is incontrovertible evidence that it would be to the detriment of his or her health

Later he added As regards wholemeal bread, of course, everybody will be entirely free to buy it—[An hon member If they can afford it]—and I shall be among them

Dr EDITH SUMMERSKILL While the Minister says that he believes people should have freedom of choice, does he not feel that he has a duty to the poorest in the community, who understand nothing about extraction rates, as we do in this House, and that it is his duty to see that they get, and he helps them to buy, what is best for the nutrition of the family?—Mr AMORY Again, that is precisely why the Government decided to ask this panel of distinguished scientists and medical experts to resolve the conflict of evidence

Expenditure Cuts and the N H S

When Mr HAROLD MACMILLAN, Chancellor of the Exchequer, said he hoped to make a statement shortly about the way in which the Government intends to save £100 million, Mr A W J LEWIS asked Will the Chancellor see that there is no cut in the National Health Service, such as is being rumoured or suggested, particularly in view of the fact that we have had an independent report which stated that the health service should not be cut but that there should be some extension of financial support to it? Is the Chancellor aware that the depreciation in the value of the pound is affecting the health service just as it is affecting everyone? In view of that should there not be increased financial support for the health service?

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[1] *Times* Nov 29 1940

[1] See *Lancet* Feb 11 1956 p 280

THE LANCET

LONDON SATURDAY, JUNE, 23, 1956

Radiation Hazards

OF the grave questions which faced the Medical Research Council's committee on radiation hazards, two stand out Are X rays as used in medicine today, harmful to the patient or his progeny ? And what are the possible effects both on the race and on the individual of the continued explosion of thermonuclear weapons ? Inevitably the committee had often to base their conclusions on incomplete evidence, and much remains uncertain But by presenting their findings (and their reservations) so plainly, they have made it much easier to see how things stand

The report published last week[1] gives a reasoned and informed assessment of the risks to individuals and to populations Though information on human and mammalian genetic effects is scarce, the committee have tried to place the genetic risks in reasonable perspective In estimating the contribution of the various man-made sources of radiation to the population gonad dose, they have taken as their base-line the natural or background radiation, which has been relatively constant during man s evolution The dose to the gonads from all natural sources has been put at 0 1r per year or about 3 0r per generation of thirty years[2] and in this country man has probably increased this dose by at least 25% in the past fifty years by his use of ionising radiations Genetic damage is irreparable and cumulative, and, since it is the frequency of gene mutation which is increased by radiation the rise in the mutation-rate is directly proportional to the radiation dose received by the gonads Radiation has, of course, no genetic effect after the age of reproduction, but all radiation received by the germ-cells and their ancestors before conception is effective and cumulative The committee find nothing to suggest that radiation-induced mutations will be in any way novel—or beneficial In all probability the mutations to be expected in man as the result of this increased exposure will be qualitatively the same as those already arising spontaneously

The committee were unable to give a figure for the population gonad dose from radiotherapy, it is believed to be considerably less than that from diagnostic radiology, but greater than from any other source Diagnostic radiology contributes to the population as a whole a radiation dose not less than 22% of that from background sources Mr OSBORN and Mr SMITH reported in our columns last week the results of their preliminary survey in England and Wales on which this disturbing figure is based Their survey shows that the annual total of diagnostic X-ray examinations is much higher than had previously been supposed and the American committee which has been examining the situation in the United States have been likewise startled by their own findings (Some extracts from the American report appear on p 1007) On an average, 1 examination is performed every two and a half years on everyone in England and Wales The survey was designed to estimate the minimum contribution of diagnostic radiology to gonad dose in the "genetically alive population"—that part of the population who may become parents This period of risk extends from the conception of the parent to the conception of his or her last child Diagnostic radiology s contribution of not less than 22% of the background dose is several times larger than that from any other source of artificial radiation And this is a minimum estimate Mr OSBORN and Mr SMITH emphasise that the actual dose to the gonads of the "genetically alive" population is greater than their estimate, though whether it is two or five or ten times greater they cannot yet say Whatever the true figure is, it is clearly formidable. Nearly three-quarters of this dose, it seems, comes from a few types of X-ray examination which make up only 7% of the total number of examinations This potentially dangerous group consists in examinations of the hip, femur, lower abdomen, and lumbar spine, and pyelography and pelvimetry The committee recommend that the time has now come for a review of present practice in diagnostic radiology, "both from the point of view of the dose distribution over the population as a whole and from the point of view of the special risks to individuals associated with examinations involving heavy exposure As the report says, a great deal can be done The number of X-ray examinations can be reduced, particularly in young people, and the dose can be cut by more careful radiography, stricter definition of the beam, and the rapid introduction of modern techniques, such as image intensification

Fall-out from test explosions of nuclear weapons adds, at the moment, less than 1% to the background level of radiation, and this source is not, the report says, an appreciable genetic hazard—at the present rate of firing The American report reaches the same conclusion But a very few thermonuclear explosions have made an appreciable addition to the dose, and, if the rate of firing increases, the dose will rise in proportion In dealing with the effects of fall-out on individuals (as opposed to the genetic hazards), the M R C report rightly emphasises that we know very little about the possibilities We have some evidence that patients with ankylosing spondylitis who have had radiotherapy are more liable to leukæmia than those not irradiated But we are particularly ignorant of the consequences of long-continued irradiation by low doses, whether from external sources or from radioactive substances that have been swallowed or inhaled and then incorporated in the body tissues From this point of view, the most sinister constituent of fall out from hydrogen bombs is the radioactive isotope, strontium 90 Since strontium is soluble and behaves rather like calcium, it will be absorbed by mouth and retained in bone Strontium 90's long half-life of twenty-eight years will then ensure a high radiation dose to bone Measurements of the strontium content of human bone have been made in this country to see what the bombs so far exploded have done In an appendix to the M R C. report Dr W G MARLEY records that the maximum activity so far found in Britain was in the skeleton of a one year-old child, which contained 1 2 micromicrocuries per g of calcium Adult bones which have been measured showed lower activities, ranging from

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[1] The Hazards to Man of Nuclear and Allied Radiations Cmd 9780 H M Stationery Office Pp 128 5s 6d

[2] Spiers F W See *Lancet* June 2 1956 p 839

Mr MACMILLAN Of course I shall take carefully into account all that the hon gentleman has said

Medical Aspects of Nuclear Radiation

Replying to a question, the PRIME MINISTER said that the complex matters dealt with by the Medical Research Council Committee on the Medical Aspects of Nuclear Radiation would require careful study by all concerned The findings about radiation from such sources as the diagnostic use of X rays needed much detailed consideration with the appropriate scientific, medical, and industrial bodies To the extent that Government departments were concerned, arrangements were being made for the necessary studies to be made as soon as possible

In reply to Mr WALTER ELLIOT, who asked whether a popular summary of the results could be issued, the PRIME MINISTER said that this would be difficult "Of course, this is not a Government publication, in the sense that it is done by a body entirely free from Government control or influence" But if, after study of the report, the House felt a need for further elucidation, "we will then consider what we can do to help"

Public Health

Poliomyelitis Vaccination

THE first phase of the poliomyelitis vaccination programme due to end by June 30 will now be confined to the 200,000 children in Great Britain who were first selected This is because the safety tests successfully passed by all previous batches cannot be completed on any further batch in time to enable local health authorities to arrange for the inoculation of more children by June 30 In a letter to local health authorities explaining the position, the Ministry of Health has stated that priority will be given to children now registered when vaccination is resumed in the autumn

Antibiotics in Preservation of Fish

Most of the fish eaten in this country is caught between the Faroe Islands and the Arctic Circle and reaches us at the speed of a steam trawler or even slower Even those who sell it will admit that its taste is not that of fish eaten within a few hours of leaving the sea The change is due in some part to the growth of bacteria present on the scales, and the traditional methods of preservation depend on cooling or the action of salt to check bacterial multiplication These were of course devised without any knowledge of bacteriology, and it may well be that the optimum temperature for the growth of the bacteria which cause spoilage is quite low

The Torry Research Station at Aberdeen has recently been making trial of a new method of preservation first suggested in Canada It is found that the addition of 5 p p m chlortetracycline (aureomycin) to the salt in which the fish is packed in the trawler improves considerably the appearance, taste, and smell of the fish on landing The process may add 7–10 days to the "life" of the fish Trawlers would make longer voyages and customers be better satisfied As the law stands, such treatment is illegal; but if the trials are successful there will be strong arguments for adopting this method of preservation It would be foolish to adopt or condemn it in our present state of ignorance

Stewing for 30 minutes destroys the chlortetracycline in fish preserved in chlortetracycline-ice, but frying leaves minute traces There is little information about the effects on man of small and intermittent doses of antibiotics Some animals thrive better and fatten quicker when given a small daily dose of chlortetracycline, but their lives are brutish and short, and long-term effects on them are of no concern It has, however, been suggested recently that pathogenic strains of *Escherichia coli* are liable to appear in herds where the calves receive a diet supplemented by chlortetracycline[1] The Torry Institute is seeking some other antibiotic which will be as effective as a preservative but will be more easily destroyed when its usefulness is over It is to be hoped that the search is successful, for the method as a whole has much to recommend it

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[1] Smith H W Crabb W E *Vet Rec* 1956 68 274

In England Now

A Running Commentary by Peripatetic Correspondents

IN medicine, as in the world at large, there is U and non-U

A U doctor is self-revealing in any discussion It is more than being on terms of easy formality with the "right" diseases Your U man knows that the collagen diseases are acceptable nowadays, and could not be caught mentioning such things as "Adaptation Syndrome" or worse still "Stress" But more than that, it is his speech which sets him apart from his non-U fellows—and Fellows "Systemic lupus erythematosus" is U It is non-U to talk of "disseminated lupus," and worse of "D L E" It is non-U to say "periarteritis nodosa", but so very U to talk of "polyarteritis nodosum" In the specialties the schism is more obvious When one hears a neurologist speaking of the "pupillary reactions to light and accommodation" it is certain that he is non-U The U phrase is, of course, "light and convergence" Cardiologists tend in the main to be U, but if they talk of "lifting outflow tracts" you may be sure of it Only the non-U would say "parasternal heave" U rheumatologists speak of "spondylitis ankylopoietica," the non-U ones of "ankylosing spondylitis", and One-up Men call it "Strumpell-Marie disease"

Candidates for consultant appointments may derive some help from the following list though it is incomplete

U	Non U
Endocarditis lenta	Infective endocarditis Subacute bacterial endocarditis
Type 1 nephritis	Acute nephritis
Myelomatosis	Multiple myelomatosis
Addisonian anæmia	Pernicious anæmia P A
Corticotrophin	A C T H
Gall stones	Cholelithiasis
Valvotomy	Valvulotomy
Phthisis	Pulmonary tuberculosis T B
Lymphoma	Reticulosis
Physical medicine	Physiotherapy
Dystrophia myotonica	Myotonia dystrophica
Atrium	Auricle
m eq per litre	Mg %
Hypokalæmia	Hypopotassæmia
E S R	B.S R
Icterus	Jaundice

* * *

To deceive evil spirits (who have very astute hearing) the sickly son in a Chinese household may not be given a name until he has survived the perils of the first year The laws of the Colony previously permitted the addition of the name of the child up to seven years after the registration of the birth, but recently this period of grace has been reduced to one year Full advantage is taken of this privilege by the more conservative Chinese, who have to have time to agree to a name which will be auspicious, will be in harmony with his horoscope, and will not displease his ancestors In the meantime the little fellow may be referred to as "the dog" or even "the buffalo"

It might have been with the idea of fooling the spirits that the Tong-Kang labourer arranged for his wife to be admitted to the tuberculosis hospital under the name of an obliging lady-friend who also supplied the necessary identity card But the subterfuge did not succeed Unfortunately the wife died and the death certificate and burial permit were issued in the name on the identity card Then the trouble started The spirit of the dead wife appeared to the Tong-Kang labourer in a dream and pleaded with him to have these mistakes rectified so that her soul could rest in peace

His first attempt at appeasement was to erect a tombstone with the correct name and a very loving epitaph on it This palliative had no lasting effect In no time the husband suffered painful reminders that the records had not been changed Supernatural dogs scratched his back while he slept Mysterious bruises and swellings appeared on his body Worst of all, the obliging lady-friend (who was legally dead and buried but was in fact hale and hearty although minus an identity card) was threatened with tuberculosis if the necessary corrections were not made in the official records before the moon waned After some confusing Statutory Declarations had sorted the quick from the dead the necessary changes were duly made in the official records

0 05 to 0 2 micromicrocuries per g of calcium It is not surprising that the highest activity was in a child, since growing bone, compared with adult bone, takes up more bone-seeking isotopes Samples of sheep bones contained 14 micromicrocuries per g but in a few mountain pastures figures were up to ten times greater

So far as we know, the M R C committee and the International Commission on Radiological Protection have no records of human damage attributable to strontium In making their recommendations, therefore, they have had to extrapolate from animal work and from the scanty records of human radium poisoning The International Commission recommended that the body burden of radium should not exceed 0 1 microcuries for persons exposed to radiation at work, and it is known that a large safety factor was not included in this figure Easily recognised radiographic bone changes have been recorded in patients with body burdens of from 0 4 microcuries of radium upwards, and radium produced a bone sarcoma in a person with a burden of 3 6 microcuries [3] These effects of radium usually appear after very long latent periods of ten or twenty years Larger body burdens may, of course, be associated with different and earlier changes, as in the American dial painters [4] who had massive bone necroses, infections, and aplastic anæmia (these "aplastic anæmias" might today have been diagnosed as acute aleukæmic leukæmias) Though damage by ingested radium in man has been known for many years, there are as yet no data on the ultimate results of long-continued low-level activity from ingested radium in a "closed population"—i e, one which has been followed up to extinction There is, therefore, no evidence about the possibility of premature ageing or chronic ill health in man as a result of irradiation Such changes have been observed in animals [5] It is hard to say how radium and strontium compare, but the biological effects in bone of alpha-particle emission from radium are probably greater than the beta-radiation from strontium-yttrium decay In view of this difference the International Commission recommended a higher maximum permissible body burden for strontium than for radium —namely, 1 0 microcuries for those occupationally exposed This corresponds to 1000 micromicrocuries of strontium per g of calcium in the skeleton, which is about a thousand times greater than the most heavily contaminated bones yet examined But the M R C committee declare that "immediate consideration would be required if the concentration of radioactive strontium in bone showed signs of rising greatly beyond that corresponding to one hundredth of the maximum permissible occupational level" In other words if it goes above 10 micromicrocuries per g

If, in fact, poisoning reaches that level it is likely to do so first in young people with growing bones It is also reasonable to suppose that, apart from this age difference, the whole population would be equally affected It seems that the fall out of thermonuclear explosions is deposited at the rate of 10–20% per year, so that strontium would continue to find its way into bone for years after the "alarm level" had been reached No doubt this is one of the reasons for the guarded words which the M R C committee uses about the hazards of fall out from test explosions They say that the hazards from external radiation due to fall-out are so far negligible, and no detectable increase in the incidence of ill effects is to be expected from internal radiation by radioactive strontium at its present level But if the rate of firing, particularly of thermonuclear weapons, increases, harm may be done in a small proportion of the population The report makes no estimate of how big an increase in the rate of firing would be required to produce the first detectable, and presumably gross, damage This question of poisoning by strontium 90 is one on which the medical profession, like the M R C committee, can only advise on the possible results of continued exposure It is the committee's view that, with proper safeguards, exposure from all sources in peace time can be maintained at levels which can be accepted by the citizen "without undue concern either for himself or his offspring" But unless the safeguards include the stopping of further thermonuclear tests, is this conclusion justified? By the time we have gathered sufficient evidence to assess more accurately the danger of strontium 90 poisoning, it may be too late to prevent disastrous consequences

Pyelonephritis

PYELONEPHRITIS is the commonest disease of the kidneys [1] In some forms, such as "pyelitis" of children, its course is relatively benign, and acute attacks in the adult can readily be controlled, after identification of the causal organism, by appropriate treatment Recurrent and chronic attacks, however, are very resistant to treatment On p 973 this week, Dr JAN BROD points out that, while chronic pyelonephritis is the commonest cause of deaths from renal failure in Prague, two-thirds of the cases had escaped clinical recognition In an attempt to improve this situation, Dr BROD compared the clinical features of 132 cases of chronic pyelonephritis, 54 of chronic glomerulonephritis, and 16 of vascular nephrosclerosis, and his inquiry throws welcome light on a confused subject The well-known diagnostic points were not always as helpful as expected pathogenic organisms were grown from the urine in 81% of cases of chronic pyelonephritis, but also from 50% of cases of chronic glomerulonephritis On the other hand, a large excess of white blood-cells was found in the urine of 76% of those with pyelonephritis, as opposed to only 14% in glomerulonephritis and vascular nephritis Otherwise, the most helpful and easily determined abnormality was a long-continued loss of renal concentrating power, quite out of proportion to the degree of impairment of the glomerular filtration rate This disorder of the distal tubules included decreased ability to save base (Na), and there was a tendency towards dehydration, decreased alkali reserve, and acidosis Another point of diagnostic importance was a striking difference in the function of the two kidneys in chronic pyelonephritis, as assessed by ureteric catheterisation, using the concentrating index of endogenous creatinine ($\frac{U}{P}$ ratio), the difference was insignificant in normal kidneys and in those affected by chronic glomerulonephritis

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[3] Looney W B Hasterlik, R J Brues A M, Skirmont E *Amer J Roentgenol* 1955 73 1006 See also Recommendations of the International Commission on Radiological Protection *Brit J Radiol* 1955 suppl no 6

[4] Martland, H S *Proc N Y Path Soc* 1926, 26, 65 *J Amer med Ass* 1929 92 466, 552 *Amer J Cancer*, 1931 15 2435

[5] Blair H A U S Atomic Energy Commission Report, 1953 p 227 *Ibid* 1954 p 312

[1] Weiss, S Parker F jun *Medicine Baltimore* 1939 18 221

So far the soul of the dead wife appears to have found peace The Tong-Kang labourer came to the Health Office yesterday looking a different man He has put on weight, is sleeping well, and no longer fears he is going mad And the obliging lady-friend's cough is quite better

* * *

Correcting an examination paper recently I came on this "Pyelitis Recognised by looking at the urine 1 gross—opalescence 2 microscop—pus cells de luxe" A week later, at the end of the oral examination, I asked the writer what "de luxe" meant For a moment he looked puzzled and then said with relief "Oh, dee lux Well it means plus plus, sir" "In what language?" "Slang" Nonplussed (pas de luxed), I let him go

He was a great linguist, that fellow He described the signs of umbilical sepsis as "calor, dolor, rubor, edema, læsio infunctio" (Omphalological papers please copy) Furthermore, he always wrote et instead of and "Home helps for the aged have been a terrific boon The G P can keep in touch c̄ the other health workers in the district by inviting them to tea every now et then et exchanging ideas et experiences for the mutual benefit of his panel patients"

I wonder why he emphasised tea as the collation Surely on a Sunday morning the health visitors, &c, would enjoy sherry et cake c̄ the dr

* * *

I have just obtained my second child's birth certificate There is nothing remarkable in that thousands of British fathers have shared the experience during the past year All I had to do was to drive into the sleepy afternoon streets of the nearby market town, walk up a flight of stairs, and recite *sotto voce* to the registrar the required particulars There was no-one in the waiting-room, no-one else in the office save the registrar's clerk 3*s* 9*d* changed hands in a somewhat furtive, uncommercial fashion, I was given a couple of N H S forms, and the birth certificate unostentatiously reached my private address the following morning

How different was my experience, two years ago, when my firstborn arrived! I met my two witnesses (one Italian, the other American) outside the vast, imposing Register Office in Rome, at 8 A M Unless one was there at opening time, there wasn't a hope of completing the formalities before the office closed at 2 P M Inside, the milling crowd divided itself roughly into two preliminary queues (easily recognisable by their respective demeanours), one to record births, the other deaths But this, which took perhaps twenty minutes, was only the beginning We next proceeded upstairs to sign the registration book, in the presence of one of a team of registrars, working three to a room and maintaining a steady output of one registration every two minutes or so A weighted handclasp with an attendant speeded our progress at this point, we had not waited more than a quarter of an hour before we were giving the usual particulars to a registrar, who wore the black gown of the Italian civil servant and had the little finger-nail of his right hand carefully tapered to an inch-long point

The birth was now duly registered, and my witnesses could leave, but I had to go through a fresh sequence of formalities in order to obtain the certificate I waited in another queue to apply for the certificate, and in yet another in order to pay the fee The certificate would be ready the following morning, and once more I appeared promptly at 8 A.M, and got the certificate after a relatively short wait Finally I went to the British consulate and registered the birth a second time The whole procedure cost about 1*s* 9*d* for the Italian certificate, 8*s* for the British one, but the Italian document is better value for money being gaily adorned with coloured stamps and impressed with the magic letters S P Q R I have only to look at it to see once more the mimosa blooming in the Roman gardens on that April day

Of course it's all a question of national temperament and I would not presume to say whether the Italian way of doing things is better for being a challenge to one's tenacity, or the English for being so much simpler

* * *

Overheard in the clinic "He's come on ever so well since I changed to ostrichmilk no 2"

Letters to the Editor

USE OF VITAMIN K IN THE NEWBORN

Sir,—The standing committee of the British Pædiatric Association on prematurity, in their letter last week,[1] have done well to emphasise the danger of overdosage of vitamin K This warning comes most opportunely closely following the account by Dr Bound and Dr Telfer (May 19) of the effect of large and small doses of 'Synkavit' on plasma-bilirubin levels in premature infants

This is yet another example of how easily valuable therapy in moderate dosage can become a menace when given in excess of requirements Such lessons are only learned by bitter experience They bring to mind other relatively new diseases, such as retrolental fibroplasia following the over enthusiastic use of oxygen, and "idiopathic" hypercalcæmia, probably the result of carrying prophylaxis against rickets too far in the current manufacture of infant foods in this country[2,3]

The Hospital for Sick Children
Great Ormond Street
London W C 1

BERNARD SCHLESINGER

Sir,—The findings of Dr Bound and Dr Telfer prove beyond all doubt that large doses of vitamin K administered to premature babies increase the hyperbilirubinæmia, thus contributing to the development of kernicterus The mechanism of this action—whether stimulation of hæmolysis or diminished excretion of bile-pigment by the liver—is regarded by the authors as undetermined

May I call attention to a paper published several years ago[4] in which my associates and I showed that in the active phase of epidemic hepatitis the hyperbilirubinæmia appreciably increases in the eight hours after intravenous injection of the same water soluble vitamin-K analogue (synkavit)? The dose of 70 mg we administered to adult patients is rather small, compared with 50 mg for premature infants, but the rise of plasma-bilirubin level amounted on average to 3 2 mg per 100 ml in thirty tests (minimum 1 8 mg, maximum 17 0 mg) This immediate effect, observed only in icteric hepatitis, was absent in obstructive jaundice and Laennec's cirrhosis Hæmolysis being out of the question, it was attributed to a temporary reduction, caused by functional overtaxing, of the liver's capacity to handle bilirubin The same mechanism probably accounts for the more protracted and dangerous action of considerably heavier doses (per lb body-weight) in premature infants

István Hospital
Budapest Hungary

G GOTTSEGEN

BREAD

Sir,—For anyone to show a reasonable interest in the nutritional value (rather than the preservation) of food often suggests beards and sandals as well, further it is probably not difficult to acquire a reputation as a food faddist even when the approach to the subject is quite objective But the problem of flour extraction rate so fully set out in your editorial of June 9, is not a matter of fads or fancies, it is a matter of fact to which the M R C Conference report gives as clear a basis from the scientific aspect as is yet possible to find Even so no claim is made that the data presented are by any means the last words on the subject, this alone would, one imagines, have caused the panel on flour to have paused before making too definite recommendations

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1 Capon N B Crosse V M Gaisford W Lightwood R Miller F W *Lancet* June 16 1956 p 966
2 Morgan H G Mitchell R G Stowers J M Thomson J *Ibid*, p 925
3 Stapleton T, Macdonald W B Lightwood R *Ibid* p 93[illegible]
4 Gottsegen G Horn Z Hárs M C *Acta med scand* 1951 140 127

or vascular nephrosclerosis X-ray examination, and especially serial examination, in chronic pyelonephritis, often showed differences in size and density of renal shadows and in spread and evacuation of contrast medium Consideration of these points would undoubtedly help towards more widespread recognition of the condition

The clinical picture has been correlated with the common pathological finding of irregular superficial depressions associated with wedge-shaped scars through the kidney parenchyma [1–6]—a type of lesion sometimes ascribed to ischæmia [7] or developmental dysplasia [8, 9] The possible relation of these scars, and therefore of pyelonephritis and the resulting vascular changes, to a type of hypertension [1, 3, 5, 10] is of the first importance Experimental evidence now provokes further thought on this subject De Navasquez [11, 12] found that when gram-negative bacilli were injected intravenously into animals with normal kidneys, the organisms did not leave the blood-vessels but passed through the organ harmlessly and never appeared in the urine But when coagulase-positive *Staphylococcus aureus* was injected pyelonephritis followed and renal scarring developed with the same features as the human disease localisation of the organisms was presumably due to diffusion of coagulase from the plasma to produce coagulative necrosis in the surrounding tissues, thus enabling the organisms to multiply in a presuppurative phase before the phagocytes could reach them In animals which had survived a staphylococcal infection and had presumed scars (later confirmed), intravenous injection of gram-negative bacilli of the coliform group invariably produced an acute pyelonephritis which was fatal within two weeks The kidneys showed asymmetrical contraction, with coarse stellate scars resulting in an intrarenal hydronephrosis In addition to these old scars, there were linear abscesses in their immediate vicinity, the purulent exudate being confined to the distended tubules, and the pelvis showed patchy inflammation It seemed that the intrarenal hydronephrosis resulting from the first infection had slowed the blood-stream sufficiently for the second infecting organisms to multiply and produce suppurative lesions This was further evidence that, in kidneys without mechanical defects, infarctions or atheroma, these stellate scars were the result of hæmatogenous pyelonephritis De Navasquez pointed out that the primary staphylococcal infection in the rabbit, with appropriate dosage of organisms, was self-limiting and left no clinical evidence, but it enabled the gram-negative bacilli to settle out in the kidney when they would not otherwise have done so But we must not conclude from these animal experiments that in man a previous infection must be staphylococcal before a coliform infection can take hold Moreover, the way in which these animals were infected (20–100 million bacilli were injected into an ear vein) is artificial and gives no clue to the method of infection in man The secondary infection in the rabbit led to death from progressive uræmia and anuria, but, as De Navasquez explained, this is because the rabbit's kidney is monopyramidal, and obstruction at the single papilla by a small lesion can affect all the collecting tubules, whereas the multilobular human kidney has a much greater margin of safety

The development of these scars was also examined by Heptinstall and Gorrill,[13] who injected *Staph aureus* into rabbits, some of which were kept alive with penicillin They then examined the kidneys at intervals up to four months Again, the naked-eye and microscopic appearances were very similar to the scars attributed to pyelonephritis in man Heptinstall and Gorrill then produced a unilateral pyelonephritis with a coliform organism by temporary occlusion of one ureter [14, 15]—a procedure which localised the infection to the affected kidney while the other remained normal After three days the ureter was released and either then or at periods up to four months, the normal kidney was removed In this group of animals, the blood-pressure was measured at least twice weekly It was found that there was no elevation of blood-pressure with a unilateral infection when the opposite kidney was intact and even when it was removed the blood-pressure rose only when there was considerable scarring in the affected kidney In the scarred areas in all kidneys infected for over forty days, arteries and arterioles seemed to have increased in numbers, merely because of the disappearance of tubules The only structural change in the vessels was an increased cellularity of the media in the older infections and nothing significant was found in animals with high blood-pressure It may well be that the design of the experiment did not allow the high pressure to continue long enough for changes to develop Thus, in the animals, a rise in blood-pressure was due, not to vascular changes, but to extensive scarring in a remaining single kidney

Patients with chronic pyelonephritis do not necessarily develop hypertension Of Longcope's [16] patients with chronic pyelonephritis, those without hypertension had normal vessels and some with severe hypertension had vessels with slight changes Weiss and Parker [1] formed a more definite view from their cases of chronic pyelonephritis, mild proliferative vascular changes were associated with normal blood-pressure, and severe changes were almost always associated with severe hypertension On the other hand, Goldring and Chasis [10] found evidence that pyelonephritis did not cause hypertension, for hypertension was not more frequent in their patients with pyelonephritis than in those without From their study of 11 kidneys removed for hypertension and found to show scars of chronic pyelonephritis, Pickering and Heptinstall [5] concluded that the renal lesion was sometimes the cause of the hypertension but the evidence regarding the separate responsibility of the pyelonephritis and the vascular changes was too conflicting for either to be held

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[2] Gibson A G *Lancet* 1928 ii 903

[3] Longcope W T Winkenwerder W L *Bull Johns Hopk Hosp* 1933 53 255

[4] Platt R Dawson J *Quart J Med* 1950 19 33

[5] Pickering G W, Heptinstall R H *Ibid* 1953 22 1

[6] Enticknap J B Joiner C L *Brit med J* 1953 i 1016

[7] Gaskell J F *J Path Bact* 1911–12 16 287

[8] Ask Upmark E *Acta Path microbiol scand* 1929 6 383

[9] Marshall A G *J Path Bact* 1956 71 95

[10] Goldring W Chasis H Hypertension and Hypertensive Diseases New York and London 1944

[11] De Navasquez S *J Path Bact* 1950, 62 429

[12] De Navasquez S *Ibid* 1956 71 27

[13] Heptinstall R H Gorrill R H *Ibid* 1955 69, 191

[14] Lepper E H *Ibid* 1921, 24 192

[15] Mallory G K Crane A R. Edwards J E *Arch Path* 1940 30 330

[16] Longcope W T *Ann intern Med* 1937 11 149

A pause would have been desirable if only because bread, itself a staple article of diet and likely to be increasingly used as such, is not the only food which is nowadays tampered with, preserved, or even misrepresented, despite legislation to prevent at least some of these happenings. As a profession we are inclined to take short-term views of cause and effect, and a sentence in the M.R.C. Conference report should be drummed into everybody: "the absence of recognisable illness in an individual is not a sufficient criterion that his diet is nutritionally sound."

I have got myself into trouble in the past because of my objections, for quite clear reasons, to the pasteurising of milk as an end in itself; amongst these objections is that we know from experimental work and simple observation that heat-treated milk loses something more than part of its ascorbic acid content. The usual reply to this is that deficiencies are made up by other articles of food. If one by one the principal articles of food are going to be denatured with official connivance, where shall we finish up? Everybody agrees that all sorts of what are called metabolic or constitutional diseases are on the increase; while it would be stupid to assign their basic pathology necessarily to nutritional causes, at least it makes some of us wonder. There is plenty of evidence from nutrition experiments on laboratory animals that queer things can happen; even clearer is the evidence on a long-term basis from experience in feeding livestock generally in which changes are more readily observed than in man. But the human animal, for better or for worse, is so resistant to abuses of its economy, whether nutritional or other, that lots of things which must be there to be seen are missed because we do not know what to look for. Since food is the most important of the triad governing life—food, warmth, and shelter—it ill behoves us to monkey about with food too much until we are more sure of our ground.

A recent experience emphasises how much remains to be learnt about nutrition of quite a simple kind. For a number of years I have bred and reared cattle, and in a national show just a fortnight ago I won amongst other prizes one for a sixteen-month-old heifer. This rather surprised me as her nutritional state in the ring was not so good as it had been a few weeks before the show when she was brought in from the herd and given, with a companion, special scientific(?) feeding, as is usual preparatory to such an event. On returning from the show she was turned out with others into an old orchard carpeted with rough old herbage and within a fortnight she has found for herself a diet which has filled all the hollows that special attention did little to correct. So much for thinking one knows anything about feeding animals. What about human dietary—so easily influenced by Authority?

London, W.1 W. R. THROWER

TUBAL OCCLUSION

SIR,—Last week Mr Green-Armytage stated that there is danger in the doctrine that "among patients attending infertility clinics who are found to have blocked tubes, spasm, irritability, anæsthesia, nerves, or even frailty in deductions and methods, are the causes of tubal occlusion in all but 6–7% of cases." After reading this, it is instructive to turn to what Professor Polanyi says in the same issue:

> "Science is said to describe *facts* which are there whether you like them or not. . . . The function which I attribute here to scientific passion is that of distinguishing between demonstrable facts which are of scientific interest, and those which are not."

For many years now, I have taught and written that a *minimal* criterion for tubal occlusion should be two negative tubal insufflations at 250 mm. Hg plus a confirmatory hysterosalpingogram, on separate occasions. Even this criterion is not proof-positive of non-patency of the tubes. For too many years a single insufflation finding of non-patency at 200 mm. Hg, or a single hysterosalpingogram which shows apparent non-patency, has been accepted by many gynæcologists as denoting tubal blockage. The importance of tubal spasm, simulating tubal blockage, can be easily demonstrated: every case which shows apparent non-patency at 250 mm. Hg under anæsthesia, should have a repeat insufflation a few days later without anæsthesia, when normal tubal patency and function is seen in two out of every three such cases. This result has been obtained by me in more than 300 such tests and without the preliminary use of amyl nitrite or any antispasmodic.

I am interested in Mr Green-Armytage's statement that tuberculosis alone accounts for 5–6% of all occlusions. In a paper presented before the Royal Society of Medicine in 1943, I propounded the view, for the first time, that tubal blockage may in a considerable proportion of cases, be due to subclinical tuberculous salpingitis.

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DIAGNOSIS OF THYROTOXICOSIS

SIR,—I was interested to read last week's letter by Dr Freeman and Dr Mattingly on the diagnosis of doubtful cases of thyrotoxicosis.

The differentiation of thyrotoxicosis from an anxiety state is one of the common problems of general practice, and one which often involves referral to hospital with expensive and time consuming investigations. The measurement of sleeping pulse-rate would be a very simple investigation in general practice if it were possible to use a fairly short-acting hypnotic such as intramuscular paraldehyde; and I would be interested to know whether a true resting pulse rate is obtainable in this way. If so admission to hospital for three days, as suggested by your correspondents, would seem unnecessary and extravagant.

London, W.11. J. TUDOR-HART

A SHORT SMALL INTESTINE ASSOCIATED WITH FIBROSIS OF THE LIVER

SIR,—The article by Dr Raeburn and Dr Brafield (June 9) calls attention to the association of a short small intestine with fibrosis of the liver. This association does not seem to be always present, as the following case shows.

A woman, aged 55, had had intermittent vomiting for the past six months. A barium meal investigation revealed partial obstruction at the duodenojejunal flexure. The proximal 4 inches of the jejunum showed constant narrowing of the lumen with rigidity of the walls and complete loss of the mucosal pattern. The small gut appeared to be short but was otherwise normal. A diagnosis of malignant neoplasm of the jejunum was suggested.

At necropsy (Dr W. I. Leslie) a congenitally short jejunum and ileum, measuring 8 feet together, was found. The proximal part of the jejunum was bound by firm adhesions to the tail of the pancreas; its lumen appeared to be narrowed and somewhat kinked, but its wall was not infiltrated by growth. There was a scirrhous carcinoma in the distal half of the pancreas. The spleen showed nothing abnormal apart from intense congestion. The liver was firm and was not enlarged; on section numerous metastatic tumour nodules were found widely distributed throughout the parenchyma.

In this case of congenitally short small intestine no evidence of fibrosis of the liver was present. Possibly the short jejunum, being in closer contact with the tail of the pancreas than is usual, caused chronic irritation by intermittent pressure, thus contributing to the development of cancer in this region.

London, W.1. A. ELKELES

responsible Dr Brod's findings are that hypertension develops with increasing frequency as the pyelonephritis progresses, to the same degree as in chronic glomerulonephritis, though four times more often than in chronic cholecystitis (taken as a control for other chronic infections), his biopsy studies rebut the idea of a vascular cause, since vascular lesions were absent in 5 patients with grave hypertension Malignant hypertension developed at an earlier age in pyelonephritis with hypertension than in essential hypertension, but only when the renal disease was far advanced His results are in line with the experimental findings in suggesting that the onset of hypertension is determined by the lack of sufficient healthy renal tissue (or the presence of sufficient diseased renal tissue) Whatever the ultimate answer to these unsettled questions may be, all cases of pyelonephritis must be treated seriously and every resource must be used to eradicate the infection as completely as possible at the earliest opportunity

Steroids in Anæsthesia

Some years ago Selye[1 2] demonstrated in rats the anæsthetic properties of 75 steroids with various structures He noted that some compounds were potent anæsthetics but had little hormonal activity Subsequently, hydroxydione (21-hydroxy pregnane 3, 20-dione sodium succinate), a water soluble steroid, was shown experimentally to have a wide margin of safety and to be a likely drug for clinical use[3] Indeed, work on various animals indicated that it has a therapeutic index considerably greater than that of thiopentone[4], hydroxydione has no hormonal activity[5] Under the name of 'Viadril,' it was first described in use as a clinical intravenous anæsthetic last year[6] Although it is not a barbiturate, it lends itself to comparison with thiopentone, and other thiobarbiturates, because of its similar effects and method of administration The early reports suggested that it had some advantages over these drugs both in its ability to produce greater relaxation without correspondingly increased medullary depression and in its seemingly specific action on the reflexes of the respiratory tract But some later findings have been less encouraging, and the disadvantages of the new anæsthetic have become more apparent

On another page this week Dr Galley and Dr Rooms describe their experiences with hydroxydione, and pharmacological and other clinical investigations have lately been reported elsewhere[5 7] From the start, it was realised that hydroxydione was an irritant, and in one series venous thrombosis followed in 15 out of 70 patients who received dilutions as low as 0 5% given as part of a freely running infusion Dr Galley and Dr Rooms find that 2 5 g dissolved in a 540 ml bottle of saline solution gives no trouble These dilutions, however, necessitate the use of large volumes of fluid to get even a small quantity of the drug into the patient—a cumbersome method of inducing anæsthesia More concentrated solutions cause pain (unless injected very slowly) and, commonly thromboses With the dilute solutions, loss of consciousness is slow, very closely resembling the onset of natural sleep but depending on the concentration rate of injection, and state of the patient Drowsiness may take as long as five minutes to appear, and sleep a further five minutes The full anæsthetic effect is often not attained until fifteen or twenty five minutes after the initial injection A slightly quicker result can be achieved by speeding up the rate of injection, but hypotension may result Experimental work on cats[7] suggests that the hypotension is caused by inhibition of the vasoconstrictor centres in the brain, coupled with a direct vasodilator action on the peripheral vessels themselves But hydroxydione also depresses the ventricular muscle, though not so much *nor for so long as an equivalent dose of thiopentone* Dr Galley and Dr Rooms have observed hypotension, even in young patients, and an increased pulse-rate irrespective of a fall in blood pressure *Respiration is seldom greatly influenced, but* the volume may be reduced slightly and the rate increased[7] Apnœa, such as is often caused by thiopentone, is very unusual Investigation of the duration of action suggests *that 1 g* lasts for about two and a half hours[8]

There is little evidence that hydroxydione is an analgesic, and, under apparently deep anæsthesia with hydroxydione alone, sensory stimulation produces immediate reflex activity This response is very similar to the reaction of patients under thiobarbiturates, such as thiopentone, and indeed electroencephalography has failed to show any difference between hydroxydione and these ultra short acting drugs[5 9] These facts are substantially in favour of its classification as a hypnotic rather than as an analgesic On the other hand, all reports have remarked on its selective depression of laryngeal and pharyngeal reflexes, without medullary depression This action is the opposite of what may be expected under barbiturate anæsthesia, when many reflexes in this area are often exaggerated, and it is a big advantage for some operations A further difference seems to be the remarkable sense of well being and lack of fatigue during the first twenty-four hours after operation in patients anæsthetised with hydroxydione

It is too early to assess the value of steroids in anæsthesia Despite the valuable evidence given by Dr Galley and Dr Rooms, many anæsthetists will not yet be convinced that hydroxydione has much to offer that cannot already be achieved with fewer disadvantages by existing drugs Unless the anæsthetist takes the chance of venous thrombosis and hypotension by giving a more concentrated or more rapid injection, induction takes too long for all but major operations Moreover the selective depression of respiratory-tract reflexes, when continued into the postoperative stage, may well increase the ever present dangers of this period Nevertheless the investigation of hydroxydione has opened up possibilities in a new line of anæsthesia which may well culminate in valuable additions to those drugs which have stood the test of time

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[1] Selye H *J Pharmacol* 1941 73 127

[2] Selye H *Endocrinology* 1942 30 437

[3] Laubach G D Pan S Y, Rudel H W *Science* 1955 122 78

[4] Pan, S Y Gardocki J F Hutcheon D E Rudel H Kodet M J, Laubach G D *J Pharmacol* 1955 115 432

[5] Howland W S Boyan C P Kuo Chen Wang *Anesthesiology* 1956 17 1

[6] Murphy F J Guadagni N P DeBon F *J Amer med Ass* 1955 158 1412

[7] Taylor N Shearer W M *Brit J Anaesth* 1956 28 67

[8] Harbord, R P Wild W N *Proc R Soc Med* 1956 (to be published)

[9] Bellville J W Howland, W S Boyan C P *Brit J Anaesth* 1956 28 50

GIANT HYPERTROPHIC GASTRITIS

SIR,—Giant hypertrophic gastritis is generally considered a benign condition Dr Williams (April 7) suggests that an extensive resection through healthy tissue, as for carcinoma, is unnecessary, and Mr Park (May 19) advocates resection of part of the affected mucosa

Penetration of the muscularis mucosæ by epithelial elements was not mentioned by Menetrier [1] or by Spriggs [2] but has been described as occurring in giant hypertrophic gastritis by a number of subsequent writers including Dr Williams Grime and Whitehead's [3] case is cited as evidence that giant hypertrophic gastritis is a benign condition, since their patient was well 13 months after incomplete removal of the affected stomach, but this stomach showed no submucosal penetration Maimon et al [4] describe submucosal penetration in three of their six cases, stating that "it does not suggest neoplasm, it is equivalent to the type of herniation commonly seen in the secondarily contracted gall bladder producing the gland spaces which are called crypts of Rokitansky"

On the other hand Brunn and Pearl [5] say that the only certain sign of malignancy is the invasion by the epithelium through the muscularis mucosæ, describing cases of the allied and often associated condition of multiple gastric polyposis, they found evidence of carcinoma in 12% and, in a later paper,[6] in 19 out of 37 cases

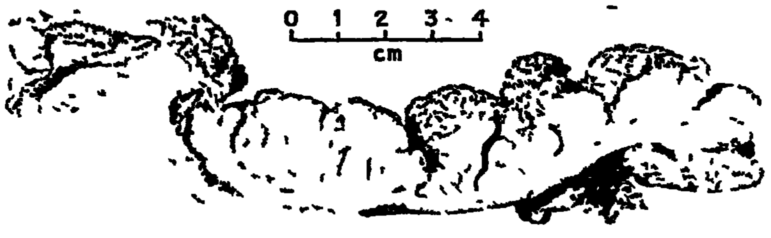

Fig 1—Stomach wall Compare hypertrophied portion with normal on left

Histologists are accustomed to regard invasion of the submucosal stroma by epithelial elements as a major criterion of malignancy in the large intestine The following case raises the question of whether it should not be so regarded in the stomach

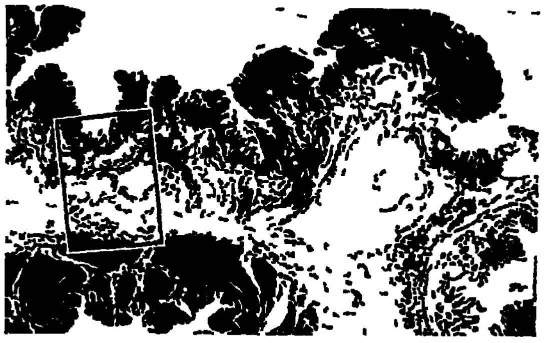
Fig 2—Section of hypertrophied stomach wall (× 5)

A man of 57 years came to hospital with epigastric and left subcostal pain, of 4 months' duration, unrelated to meals, posture, or exercise but relieved by milk Each night he had severe pain lasting 15 minutes, and all day he had an ache He had nausea but had not vomited, and he had been constipated for 7 weeks Hæmoglobin 113% Histamine test meal free acid, mucus, but no blood Barium meal suggestive of gastric carcinoma

At laparotomy, by Mr G O Jolly, the stomach wall was found to be greatly thickened, and was recognised as an example of giant hypertrophic gastritis, but at the cœliac axis there was what appeared to be a carcinomatous lymph node No other site of primary carcinoma could be found, so a total gastrectomy was performed

The mucosa, over an area 16 × 13 cm in the fundus was much hypertrophied and thrown into rugæ 1 5 cm across and 2 5 cm high, resembling cerebral convolutions (fig 1) The mucosa was everywhere freely mobile over the muscle No polypi were present There was no evidence of past or present ulceration

On histological examination the affected mucosa is greatly thickened but maintains the normal architecture and cytology (fig 2) Dilated, irregularly shaped acini, lined by regular well differentiated mucus secreting columnar epithelium, are present in the lower levels of the mucosa and penetrate extensively through the muscularis mucosæ into the sub mucosal layer (fig 3) Everywhere the epithelium remains regular and cytologically benign (fig 4) There is a chronic inflammatory infiltrate by plasma cells, lymphocytes and some eosinophils in the lamina propria and submucosal layer

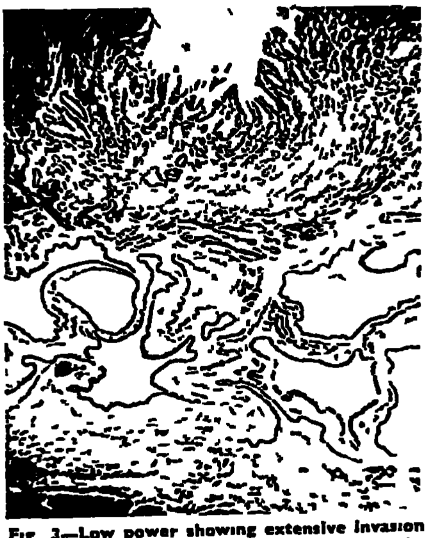
Fig 3—Low power showing extensive invasion of submucosal layer without invasion of muscle wall (× 20)

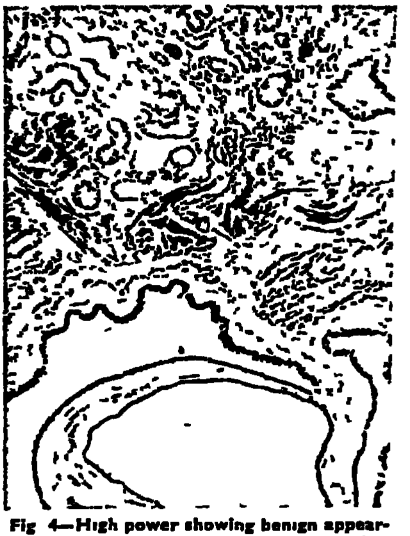
Fig 4—High power showing benign appearance of invading epithelial elements (× 70)

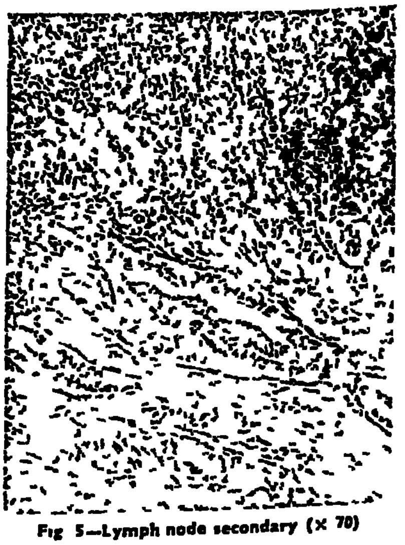
Fig 5—Lymph node secondary (× 70)

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1 Menetrier P *Arch Physiol norm path* 1888, 1, 32, 236
2 Spriggs F I *Quart J med* 1943, 12 1
3 Grime, R T Whitehead R *Brit J Surg* 1951 39 244
4 Maimon, S N Bartlett J P Humphreys E M, Palmer W L *Gastroenterology*, 1947 8 397
5 Brunn, H Pearl F *Surg Gynec Obstet* 1926, 43, 559
6 Pearl F L Brunn, H *Ibid* 1943 76 257

Annotations

UPPER ALIMENTARY BLEEDING

BLEEDING from the upper alimentary tract is a problem which taunts us, sometimes diagnostically and always therapeutically. During the decade 1923–32 the mortality at the Massachusetts General Hospital due to massive hæmorrhage from acute ulcer was 13%, and it remained so during the years 1938–47: in 1948–53 it had risen to 17%.[1] Methods of blood replacement have improved immeasurably since 1932 and surgery has entered the therapeutic field as an emergency measure—all to no good, it seems. In the first memorial lecture before the American Gastroenterological Association, Dr F. Avery Jones reported 39 deaths in 563 patients with bleeding from peptic ulcer during 1941–46 and 57 in 744 during 1951–54,[2] a mortality of approximately 7% in each group; and this has remained unaltered although operation was advised during the latter period for patients with recurrent bleeding, for those between 40 and 70 years old, and for those with chronic ulcers. Welch et al.[1] have shown that, in the Massachusetts series, only 8 patients were operated on in an emergency during 1923–32 and all 8 died, compared with 45 operations during 1938–47 with 22% mortality, and 100 operations during 1948–53 with 25% mortality. If the best that surgery can achieve gives a higher rate than the over-all mortality and does not reduce it, why switch to surgery? Brandon[3] is convinced that immediate gastrectomy is not the solution in the late stages of hæmorrhage, and he has had very encouraging results with adrenaline and Russell's viper venom given through a stomach tube. If excessive bleeding recurs after this treatment, Brandon repeats it as a preparation for operation.

But the results of treatment of acute hæmorrhage are confused by the increasing age of the population. The proportion of Avery Jones's patients over 60 has risen from 33% in 1941–46 to 40% in 1951–54; and Welch et al. encounter massive bleeding in patients over 70 fifteen times more often now than was the case in 1932. Moreover, ulcer associated with hæmorrhage has been twice as common as a cause for admission in all patients in their sixth decade as in their fifth; and the mortality from bleeding increases steeply with age, being almost doubled (13–25%) from the sixth to the seventh decade. Thus, increasing age has spoilt the figures and at the same time has necessitated more operations, since in the view of Welch and his colleagues the elderly tolerate operation better than expectant treatment. Though Avery Jones's surgical policy has not reduced over-all mortality, there has been an improvement in patients under 60 and in those with chronic gastric ulcer.

If operation is to be performed, it is important to determine the site of bleeding before operation; and this may be by no means easy. Common sense and a knowledge of the probabilities are a fair guide: in the Boston series œsophageal varices accounted for 32% and duodenal ulcer for 38%. It is understandable therefore that Nachlas[4] should have found it a help in diagnosis to compare gastric and œsophageal aspirations after occluding the œsophagus at the level of the diaphragm by an inflatable balloon. But his apparatus would have little application in this country; in Avery Jones's series whereas 32% of admissions were due to duodenal ulcer only 2·7% arose from portal hypertension. Avery Jones uses gastroscopy to try to find the source of bleeding and he prefers this method to X-ray investigation. Should these measures fail and the source of blood is still not revealed by a proper examination at laparotomy of the cardia, the fundus, and the mucosa through an incision into the stomach, most surgeons perform partial gastrectomy since the undetectable lesion is commonly due to small erosions hidden within the folds of the stomach so *that* no *tell tale induration* can be *felt* by the exploring fingers. But that is the kind of bleeding which Brandon has successfully treated with adrenaline and viper venom; and further experience with this method may reduce the indications for operation.

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[1] Welch, C. E., Allen, A. W., Donaldson, G. A. *New Engl. J. Med.* 1955, 252, 921.
[2] Avery Jones, F. *Gastroenterology*, 1956, 30, 166.
[3] Brandon, W. J. M. *Lancet*, April 7, 1956, p. 360.
[4] Nachlas, M. M. *Surgery*, 1955, 38, 667.

HELP FOR THE PSYCHIATRIST

DOCTORS and the community continue to learn more and more of the serious impact of mental illness on marital, social, industrial, and educational relations. As a result, an ever wider range of patients and conditions are referred to the psychiatrists, who are unable to deal adequately with all the patients sent to them. Nor are they equipped to meet the additional demands of society for guidance in the prevention and treatment of minor mental disturbance. Hopes have therefore been raised that much might be done on the spot by non-specialists if they commanded better knowledge of the working of the mind and simple psychotherapy. In this way social services would be greatly improved and a considerable burden might be lifted from psychiatric clinics.

At a meeting of the Tavistock Institute of Human Relations on June 15, Dr J. D. Sutherland described the work of a group of psychiatrists specially trained in psychotherapy and interested in the application of their work to the problems of the community. He emphasised that one of the most pressing matters facing the National Health Service was how to deal with the vast amount of illness and unhappiness caused by psychological disorders. Anyone connected with a psychiatric clinic knew only too well the depressing situation created by the gap between the available therapeutic resources and the needs for treatment. There was also the great mass of psychological ill health which did not reach the psychiatrist. In psychiatric clinics, the need for more psychotherapy was paramount: the great difficulty, as Dr Sutherland saw it, was that psychiatrists were often quite inadequately trained in psychotherapeutic skill. He did not think that increased opportunities for and training in psycho-analysis was the solution: "the therapeutic results of this form of treatment do not warrant such an expansion." At the Tavistock Clinic, therefore, attempts have been made to devise more economical psychotherapies, and group analytic methods are now offered as the main treatment to adult patients.

While general practitioners and doctors in maternity and child-welfare clinics can refer patients to psychiatric clinics for treatment, the hope of treatment there all too often proved vain. They were therefore forced to give rough and ready psychological help themselves, realising at the same time how much more they could do if only they knew how. Social workers, probation officers, social and industrial psychologists, and educationists found themselves in much the same situation. With more knowledge of psychology, they could greatly increase the efficiency of their work and often avoid sending patients to psychiatric clinics. Like general practitioners, Dr Sutherland remarked, "they too know that if they cannot do it, there is little or no chance of it being done in the overburdened psychiatric clinics."

From the number of applications received for courses at the Tavistock Clinic, it was clear, Dr Sutherland said, that many members of professional and non-professional groups were eager to increase their psychological skill. Two years of part-time training had been found to be the minimum for reasonable efficiency.

Three lymph nodes from the lesser curvature show sinus catarrh but no evidence of malignancy The cœliac lymph-node and adjacent connective and adipose tissue contain mucus secreting carcinoma, some of which is similar to, but less well differentiated than the submucosal elements in the stomach and some of which is poorly differentiated (fig 5)

The patient was well when last seen two months after the operation

I hope to follow this case in order to verify that there is no other primary from which this secondary deposit could have been derived Meanwhile, in view of the histological similarity between the better-differentiated elements in the lymph node secondary and the submucosal elements, and the fact that no other primary was noted at the time of operation it must be assumed that the carcinoma originated in the stomach

This case suggests that giant hypertrophic gastritis may not always be as benign as it is assumed to be, and that penetration of the submucosa by epithelial elements, however benign in appearance, should be regarded with grave suspicion

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Manchester 4

ROGER GILLETT

ANTENATAL IDENTIFICATION OF HEREDITARY DISORDERS

SIR,—Since amniotic fluid cells can be obtained from the 12th week of pregnancy [1,2] and the fluid has been shown to contain well-preserved cells from the 12th week and possibly even earlier,[3–5] the most obvious clinical value of using these cells for antenatal diagnosis would be in certain cases of sex-linked abnormalities Dr Edwards's comments (April 28) on antenatal detection of hereditary disorders raise the interesting point of using amniotic fluid cells for other purposes, such as the detection of fœtal antigens

The actual detection of fœtal antigens can lead directly to early identification of incompatibility during pregnancy, and this may be especially valuable in certain cases where the father is heterozygous It may also be useful in the field of preventive medicine, in cases of hereditary abnormalities that are genetically linked to an antigen For this latter purpose it is insufficient to have the type of linkage that has been found with the nail-patella genes,[6] since this is a linkage with the ABO group as a whole It is necessary to have a close linkage, preferably without any crossing over, between a hereditary abnormality and a particular antigen—e g, the antigen for B within the ABO group The type of linkage to seek is that found between elliptocytosis and a specific Rh combination, where in one family [7] the gene for oval cells always goes with the antigen constitution cDE In this case there is complete linkage and no crossing-over

In a list compiled in 1954,[8] of 28 characters that had been examined for linkage with blood-group genes, only 1 shows positive evidence for linkage But, as Race and Sanger pointed out,[8] this should not discourage further investigation since there are now available many more antigenic markers than could be used in most of the earlier studies It is therefore desirable that anyone collecting material on human genetics should specifically test for this type of evidence

It may be predicted that, with an increase in our knowledge of the genetics of man, there will be an increase in the use of amniotic fluid cells, and possibly even of other constituents of the fluid

Weizmann Institute of Science
Rehovoth Israel

LEO SACHS
MATHILDE DANON

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1 Dieckmann W J Davies M E *Amer J Obstet Gynec* 1933 25 623
2 Alvarez H Caldeyro R *Surg Gynec Obstet* 1950 91 1
3 Serr D M Sachs L Danon M *Bull Res Coun Israel* 1955 5B 137
4 Sachs, L Serr D M Danon M *Science* 1956 123 548
5 Sachs L Serr D M Danon M *Brit med J* (in the press)
6 Renwick J H Lawler S D *Ann Eugen Lond* 1955 19 312
7 Goodall H B Hendry D W W Lawler, S D Stephen S A *Ibid* 1953 17 272
8 Race R R Sanger R Blood Groups in Man Oxford 1954

HORMONES AND BREAST CANCER

SIR,—In his provocative letter last week Dr Loeser states that seaweed was used in Ancient Egypt as a therapeutic agent but wrongly makes the implicit assumption that this was a rational measure

It is now generally appreciated that Egyptian medicine comprised a curious admixture of largely empirical therapy and a strong element of magic, employing not only oral and written formulæ but amulets and similar talismanic objects The materia medica of Egypt included rather extraordinary substances and it is not surprising that seaweed should have been included

It has also been suggested that in Classical Greece burnt seaweed was administered in the treatment of goitre It cannot seriously be claimed, however, that either in Egypt or in Greece was iodine deliberately used as a rational therapeutic agent, any more than it can be said that Leucippus Democritus or Lucretius really anticipated the modern atomic theory based on experimental evidence

Edible seaweed or dulse has been utilised as a food in Scotland and Ireland, and it would be interesting to know whether there is folk-lore belief in its therapeutic application A small breed of Orkney sheep is said to subsist largely on seaweed and is claimed to have a high mutton-iodine content It would be of further interest to know whether this diet has any effect on endocrine relationship in these animals

Glasgow S 1

A T SANDISON

SIR,—Dr Loeser is to be congratulated on his letter In view of your leading article of May 12, there can be no doubt that there is urgent need for reappraisal of the treatment of advanced cancer The surgical procedures have become so radical that in many cases the cure, or palliation, must be considered far worse than the disease Adrenalectomy and hypophysectomy, the latest arrivals in the field, offer magnificent opportunities for the exercise of a high degree of surgical skill, but it would be a brave family doctor who would actually advise a patient to undergo such operations More and more, attention must turn to the endocrine control of advanced carcinoma, in preference to mutilating surgical procedures, and some attempt must be made to collect the observations and work of independent observers, such as Dr Loeser, in this field

All work on the endocrinotherapy of cancer is based on an attempt to modify the hormone environment of the tumour by injection or ingestion of hormones, or by deprivation of hormones by thyroidectomy, oöphorectomy, adrenalectomy, castration, or hypophysectomy It would appear that the success or otherwise of such methods of endocrinotherapy depends on the effect of the technique employed on the internal balance of the pituitary There is considerable evidence to show that the cause of cancer is a hypophyseal dysfunction, or hyperfunction of the thyrotrophic centre (the eosinophil cells) with a relative hypofunction of the gonadotrophic centre (the basophil cells) This hypothesis explains the success of Dr Loeser's treatment by thyroid just as it explains the success or failure of other hormone treatments

The administration of small doses of thyroid extract over a long period will diminish the thyroid secretion and the secretion of thyrotrophic hormones, and so enable the pituitary-dysfunction to be temporarily corrected There is a danger, however that the effect of this administration of thyroid will wear off, and that the original imbalance will be restored, as happens in massive testosterone therapy We all have experience of the patient with carcinoma of the breast whose secondaries disappear completely with testosterone for two or three years and then return with speedily fatal results

As well as attempting to modify the pituitary state by exogenous hormones, attention must be turned to modifying the production of endogenous hormones This can best be done by the application of short waves to the pituitary and gonads, although it is possible that future methods of treatment will be by radioactive isotopes A combination of the administration of exogenous hormones and short wave irradiations on some inoperable cases, in my practice, has

"The basic task during this period is for the trainee to learn to make adaptations in his or her own personality, in other words to get to know himself" Nothing approaching a personal analysis was envisaged—or indeed necessary After training, "an essential feature of continuing practical work is the maintenance of an easily accessible personal relationship between the various groups and the consultants at the clinic With such a permanent integration the case worker's skill has increased to a quite remarkable level, and provides a safety net for all parties, the patient, the case-worker, and the consultant" Such contact need never be more intensive than once weekly, and often much less

Dr Sutherland felt that a few specially trained consultants working in the main centres would suffice to improve local services He pictured close contact extending from the psychiatric clinic through general practitioners, public-health workers, health visitors, probation officers, social workers, marriage guidance counsellors, educationists, and teachers—to fields far removed from clinical psychiatry proper *It is to developments of this kind that the Tavistock Clinic and the Tavistock Institute of Human Relations are planning to devote* a substantial part of their efforts

FINCHDEN MANOR

IN a new book[1] with a deceptive title more appropriate to an Edwardian novel, there is a serious contribution to the literature of psychological maladjustment, and its diagnosis and treatment Written by a journalist in non-technical language, it is none the less of interest to teachers and psychiatrists as a remarkably clear and interesting account of the pioneer work of a *residential establishment* where Mr G *Lyward* has for many years been engaged on the rehabilitation of maladjusted adolescent boys Finchden Manor is designed so that boys sent away from their schools "for delinquency, or for obvious mental sickness, should have a chance of being put right, instead of being left to the further mercy of their inward conflicts and compulsions" The atmosphere of the Manor is permissive, pressures are released and a boy is allowed, often for the first time in his life, to relax and for a period of respite go his own way and do what he wants Those labouring under excessive demands laid upon them by ambitious parents, or enduring other emotional strains, find this non-demanding restful atmosphere the first stage to their complete recovery of health, spontaneity, and zest for life Guidance is offered when required, advice given when sought There is no psychotherapy as such, no elaborate individual treatment The highly unusual but largely untrained staff are always there to give emotional support, to offer a challenge or interpret behaviour, and to supply the general background of disinterested affection necessary for a boy's natural development Such a system puts severe strains upon the staff and demands unusual patience and insight The boys, too, have to be of superior intelligence if they are to be able to understand what is taking place and be able to discuss themselves and their problems objectively It is not surprising that few boys with intelligence quotients under 115 are accepted into residence

Mr Lyward's method of treatment is extremely personal, based more upon intuition and experience than upon scientific analysis Yet it does not conflict with orthodox psychiatric methods, and it illustrates the way in which therapeutic communities can be set up without highly trained or professionally qualified staff "Casualness" characterises the Lyward touch—and individual treatment (which he calls "unfairness," by which is implied not treating boys alike for the sake of superficial conformity but dealing with each according to his personal needs) So each boy sets out on a voyage of discovery of himself and of the community in which he lives, under the piloting touch of a man of genius and unusual devotion For Lyward is something of a genius and it is doubtful if the work could survive his departure

This book is a valuable companion to the recent *Ministry of Education* report on maladjusted children[2] filling in the human material on the bare bones of fact It is written from the standpoint of a convinced believer and is naturally uncritical and over enthusiastic Inevitably it will be compared with David Wills's *The Barns Experiment*, although his school at Ancrum received boys of a much lower intellectual level and generally from a poorer social background Their methods are rather similar, but Wills does not claim so high a proportion of successes as Michael Burn does for Finchden Manor Wills's book is by comparison a more balanced and objective piece of writing, and as a contribution to sociology will certainly outlive the newer book What *would have been equally valuable would have been* a book written by Lyward himself setting forth *the principles underlying his treatment, together with* a deeper analysis of his successes and failures For failures in such remedial work are as significant as the successes in that they reveal the limits of such treatment and identify the types of children unlikely to respond to it Lyward's so called "answer" to maladjustment is only one possible answer and only succeeds with some children Once that is understood, his work can be viewed in its proper perspective, as a sensitive and skilled exploration of the possibilities of the human personality's power for self healing in a secure and *loving* human environment

CIGARETTE SMOKE

IN 1936 Bogen[3] reported that during the burning of the first quarter of a cigarette the temperature of the inhaled smoke was little different from room temperature it reached body temperature only when half the cigarette had been consumed, and it did not exceed body temperature until the cigarette had burnt down to a length of about 1 cm More precise data were given by McNally[4] using thermometers placed in the smoke stream He found that smoke temperatures remained at 27°C for the first 3 5 cm and rose to 52°C when the cigarette was *smoked to* within 0 5 cm of the end He pointed out that the rapidity of smoking was important, since cigarettes smoked quickly gave a much hotter smoke, particularly when the cigarette was short

Experiments conducted by Harlow[5] in the research laboratories of the American Tobacco Co gave figures for the "coal" temperature (temperature at the burning point) of cigarettes and certain types of pipe tobacco The coal temperature of cigarettes was 774°C during puffing and 746°C during free burning The smoke *temperature 3 5 mm* from the burning end was 103 C, which means a change in temperature of more than 600°C in the 0 01 sec taken to travel the 3 5 mm As Greene[6] has pointed out, these results indicate that, in smoking, tobacco is very rapidly heated to high temperatures, and, in fact, the conditions in burning tobacco are those of thermal cracking whereby free radicles are produced and organic substances break down and recombine Greene asserts that there is overwhelming evidence that organic compounds readily yielding free radicles are carcinogenic Harlow found that the temperature of cigarette smoke entering the mouth did not exceed body temperature until the cigarette was smoked to a shorter length than 23 mm, and only 1 produced remarkable short term improvement at least equal to that from drastic surgical procedures

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[1] *Mr Lyward's Answer* By MICHAEL BURN London Hamish Hamilton 1956 Pp 286 21s

[2] See *Lancet*, 1955, ii, 1328

[3] Bogen E *Calif Med* 1936 45 342

[4] McNally W D *Amer J Cancer*, 1932 16 1502

[5] Harlow F S *Science* 1956 123 226

[6] Greene C R *Ibid*, p 227

In July, 1938, the late Mr James Joyce, addressing the Reading Pathological Society, said

' It is my firm opinion that until cancer can be treated from a new angle such as endocrinology may provide, we cannot hope to obtain the results which will satisfy us in any field of cancer therapy "

Eighteen years later it would appear that we can but re echo his words, and hope that this branch of endocrinology will be raised to the status its importance merits

Reading W G TAIT

INTERMITTENT POSITIVE-PRESSURE RESPIRATION

SIR,—The very interesting case of respiratory paralysis described by Dr Lawes and Dr Harries (May 26) will be carefully studied by all who might have charge of such a case The methods used are known to have been inadequate and so the problem becomes twofold (1) What treatment was more likely to have succeeded ? (2) Is all the necessary equipment at hand to treat a similar case should it be admitted to our own respiratory unit ? We would like to comment on some details of the treatment used and to put forward alternative suggestions

The tracheotomy tube was probably of too small a diameter, and the shape was a major cause of death

We feel that the tube designed on this unit [1] would have given better results The metal linings are now made by Thackray, and Magill s tubes in good condition are readily available, so there is no question of special rubber tubes having perished before being wanted We have not seen any tracheal ulceration develop whilst using these tubes, and have had the added pleasure of seeing an established ulcer heal in a few days when the first of our tubes was put into service

The following tests probably explain why the infant had increasing carbon-dioxide tension even though the correct ventilation was apparently taking place as shown by measuring the air leaving the expiratory port of the Stott valve

A Stott valve was connected to a Radcliffe machine which had a gas meter recording the air intake The patient was represented by a spirometer with variable weights on the bell Expired air was measured by another spirometer, unidirectional valves and a pressure gauge were also used at times Results were variable not only when using different valves but also when repeating the same test on the same valve, but the over all picture was consistent Our conclusions were that air can pass from the inlet to the outlet without going to the patient The volume leaving the Stott valve will equal that entering the machine but will be quite different from that which reaches the patient The following are two average examples of 600 ml entering the machine and eventually leaving the valve, only 400 ml reached the " patient " Similarly of 450 ml only 300 reached the " patient " The " lost " air is thought to be compressed in the tubing during inspiration and released during expiration In clinical use we repeatedly found that the apparent tidal volume had to be maintained in the region of 50% above the figure given on the Radford nomogram, and any reduction in this volume was quickly followed by protests from the patient

When a B O C flutter valve was submitted to the same test this discrepancy did not occur We have found that the B O C valve, being made of softer rubber, produces a 2 5 cm water pressure between the machine and the valve and less than 0 5 cm water pressure in the airway whilst the Stott valve produces 6–8 cm pressure between the machine and the valve and a sustained pressure of 1 5–2 cm water pressure in the airway This may interfere with the gaseous exchange in the lungs It was found, however, *almost at the cost of a life*, that the diaphragm of the B O C valve can be inserted reversed and this should be appreciated by all who use them

Because the percentage of dead space rises as the tidal volume falls a slower rate of ventilation with increased tidal volume should have helped to reduce the carbon dioxide tension in the infant Had this not resulted, the temporary use of an efficient absorber could have been tried Whilst a circle absorber is likely to have been effective, Sandiford's [2] to and fro one is almost without dead space and so should be better With a circle absorber in use, minute volumes can be read on a gas meter

We are in full agreement that the inflationary pattern of the Radcliffe is too prolonged By redesigning the escapement mechanism we can now vary the wave pattern at will

To summarise, we suggest that the infant was receiving a deficient volume of air through too narrow a tube, and from the many tests which we have done on the Stott valve during recent months we consider the *performance* to be very variable and that it is not reasonably possible to measure the tidal volume being delivered One is left to control the patient largely on clinical observations

There is still room for considerable improvement in our knowledge of techniques and machinery Is all possible being done to pool existing experience and knowledge which is being gained *on a few isolated units* which are treating in all comparatively few patients each year ?

H B C SANDIFORD
Portsmouth Poliomyelitis Unit I MCDONALD

A CALCIUM-INFUSION TEST

SIR,—Dr Nordin and Dr Fraser, in your issue of June 2, record an experiment in which 98 patients, including " 21 patients in whom there was no reason to suspect metabolic bone disease " and " 30 patients with miscellaneous conditions in which bone disease might be suspected " were subjected to a four hour intravenous infusion

Would it not be a good principle to state clearly in all accounts of experiments utilising human controls that the human *controls* are volunteers and to record the means by which their cooperation was achieved ?

London N W 5 ANTHONY RYLE

***Dr Ryle's letter has been shown to Dr Russell Fraser whose reply follows —ED L

SIR,—Both the preliminary and other subsequent tests of the intravenous procedure described were performed on volunteers amongst the research team With all patients, agreement to the performance of the test procedure was of course obtained Those not initially suspected of bone disease willingly *gave their* consent We had every reason to believe, from personal experience, that the test was devoid of any risk, and in fact no untoward symptoms or effects followed the test in any instance

Postgraduate Medical School,
London W 12 RUSSELL FRASER

ANTENATAL CARE

SIR,—" A concerted effort against toxæmia of pregnancy " need not involve " the chairmen of boards of governors, and of hospital management *committees*," as implied by the Ministry memorandum to which you referred last week

It must involve the careful study of the prevention of Eclampsia and Pre Eclampsia [3] wherein R H J Hamlin sets out the " seven steps " by means of which he eradicated eclampsia at the Women's Hospital, Crown Street, Sydney, together with *acceptance* of his two points (*a*) early detection by weight increase between 20th and 30th weeks, and (*b*) institution of a high protein, high vitamin, and low carbohydrate diet at that stage

The Ministry's memorandum pays lip service to Hamlin (" in Australia the practice of the Women's *Hospital*, Crown Street, Sydney, described by Hamlin "), but further on states " *a routine designed to detect the* smallest deviation from the normal, for example, a rising blood pressure slight œdema or unduly rapid weight smoker in 1000, he estimated, smokes cigarettes to that length Though Greene gave figures for the coal temperature of pipe tobacco 200°–300° lower than that of cigarettes, Harlow maintains that the coal temperature of pipe tobacco can be even higher than that of cigarettes because of the pipe-smokers' habit of taking several small puffs in a very short period

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[1] Hodges R J H Morley R O Driscoll W B McDonald I *Lancet* Jan 7 1956, p 26

[2] Sandiford H B C *Anæsthesia*, 1953 8, 122

[3] *Lancet* 1952 i 64

BREATH-HOLDING ATTACKS

PARENTS usually agree that their children are most "difficult" during the toddling and preschool years Negativism, temper tantrums, sleep disturbances, and sphincter troubles are at a peak, and there is little reassurance in being told that all children have behaviour problems No doubt the child is also finding his parents difficult too and he will hardly be consoled by the fact that his parents' intolerable and inexplicable attitudes are normal Breath-holding attacks are one of the most alarming manifestations of inter-personal tensions during this period Although they are by no means rare they are often correctly diagnosed only after much anxiety and unnecessary investigations Perhaps it is their rarity outside the home which has made many doctors unfamiliar with them

Hippocrates[1] was apparently familiar with breath-holding and there have been many excellent clinical descriptions since One of the best is quoted by Sir Robert Hutchison[2] from a letter written to him by an observant grandmother

> "The boy seems a thoroughly healthy little fellow, is just two, but he has a kind of choking fit The doctor has never happened to see him in one (as he does not choke to order), and I do not think understands the cause of them The symptoms are these sometimes when he is thwarted he draws in his breath to cry, but no sound comes, and he gradually turns blue about the lips, his throat seems closed Cold water is dashed on him sometimes for quite a long time At last he gasps, then goes limp and unconscious, after a short time he revives, has a good cry, and gets better"

The more detached observer, while not attaining her vividness, might have amplified and slightly amended this description Fear and fury, as well as frustration precipitate attacks But the stimulus may not always be psychic, sharp pain, a fall, or any sudden trauma set off attacks After a few cries the breath is held in expiration, cyanosis ensues and later gives way to pallor and unconsciousness If the attack is further prolonged before it is relieved by inspiration, a typical epileptic convulsion occurs This is usually quite brief and is seldom followed by postictal confusion or sleep

Current ideas about breath-holding attacks have lately been well reviewed by Zellweger[3] and by Hinman and Dickey[4] The confusion that existed in the past between breath holding attacks, idiopathic epilepsy, and laryngismus stridulus has been clarified Zellweger stresses the "neurovegetative instability" of these children and their parents—a presumably constitutional state which is not widely accepted in this country Hinman and Dickey believe that breath holding attacks are a primarily emotional disorder symptomatic of profound insecurity in the child Most of the children are between six months and five years and it is generally agreed that the disorder is self-limiting A history of pertussis is not uncommon, the paroxysmal cough and laryngospasm of that disease may in some way condition an abnormal respiratory response, as Bridge et al[5] suggested

Diagnosis is not difficult from a detailed history. The attacks are always preceded by a typical stimulus, and the sequence of events and brief duration are characteristic Some confusion with epilepsy is understandable, but the breath-holding infant who has an epileptic fit due to self induced cerebral anoxæmia[6] is no more likely to suffer from epilepsy than the adult whose fits are induced by electroconvulsive therapy or convulsive drugs While the doctor must recognise the identity of the fit in severe breath-holding attacks, there is no indication whatsoever for the prescription of anticonvulsants nor should the word "epilepsy" be mentioned to the parents Electro encephalography is not helpful except in the rare case in which both epilepsy and breath-holding occur in the same child

The management of the condition may be difficult The parents are usually relieved to know that the attacks are not dangerous, nor symptomatic of grave nervous disease Neither they nor the child are helped by giving in to every demand of the child nor by trying to stop the attacks by slapping the child or pouring cold water on him Reassurance and a sympathetic regard for the whole emotional background will do most good in preventing attacks Provided that the child receives security and affection in proper measure the attacks themselves are best treated with apparent unconcern When security and love are clearly lacking, the whole family needs guidance As Culpeper[7] wrote, "There is a disease in children from anger or grief, when the Spirits are much stirred and run from the Heart to the Diaphragm forceably, and hinder or stop the breath Sometimes they have a shrill voice the Spirits suddenly breaking forth, but when the passion ceaseth, this Symptom ceaseth"

PRELUDE TO RESEARCH

Dr William B Bean[8] offers salutary advice on how to embark on research The first necessity is that there should be an idea He has no use for "the dragnet and grappling hook approach which hopes to bring up from the murky waters whatever body may be floating about, if there is one" but which too often brings forth only a monstrous array of papers without ancestors or descendants Rather should the aim be to produce, after a piece of thoughtful work a paper which adds a sound brick to the growing edifice of knowledge

Ideas cannot be generated at will they come from wide general information and intense and thoughtful observation, with meditative rumination often at inaccessible levels They tend, moreover, to be fleeting, and they should therefore be committed at once, briefly but intelligibly, to a notebook, from which, at the first opportunity, they are transferred more elaborately to a commonplace book Before starting an investigation the worker should demand of himself a clear statement (broad in aspect but narrow in detail) of its purpose The construction and subsequent study of such a statement may show the idea to be unsound, the method unsatisfactory or the work not worth doing—conclusions far better reached now than later All data should ultimately be recorded in a bound recording book, or at any rate the folder, drawer, or cabinet number of the original crude data should be recorded Bean favours Hale Ham's procedure of making an experimental protocol—a clear, brief, permanent record permitting exact duplication in the future, and containing data sufficient for publication *Biological material*, reagents, and apparatus—especially any departure from standard equipment—should be fully described *Actual procedure* is the crux of the experiment, the details of which should be set down so precisely that it can be repeated readily by anyone conversant with the subject "A compulsive neurosis, conditioned by active and critical thought, seems to be the occupational prerequisite of the investigator" gain" One realises, as no mention is made of what action he took when the 'smallest deviation from the normal" was detected that his vital point—dietetic control—has been missed In 1952 Hamlin outlined the progressive stages to eclampsia

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[1] Quoted by Still G F The History of Paediatrics *London* 1931

[2] Hutchison R Lectures on Diseases of Children London, 1936 p 247

[3] Zellweger von H *Helv paediat Acta* suppl v 1948 3 35

[4] Hinman A Dickey, L B *Amer J Dis Child* 1956 91 23

[5] Bridge E M, Livingston S, Tietze J *Pediat* 1943 23 539

[6] Sharpey Schafer E P Howard P, Leathart G L Dornhorst A C *Brit med J* 1951 ii 382

[7] Culpeper, N Tractate of the Cure of Infants 1684 Quoted by Still G F (ref. 1)

[8] Bean, W B *Circulation Res* 1955, 3, 317

> Weight gain of over 8 lb during the 20th to 30th weeks
>
> Digital œdema appearing at the 31st to 32nd week
>
> The slight, almost imperceptible, rise of diastolic pressure between the 34th and 37th weeks
>
> A slight rise in systolic pressure about the 37th week
>
> A swift sudden deterioration through albuminuria (or even without albuminuria) to severe pre eclampsia or eclampsia '

It would appear Sir that the Ministry has heard of Hamlin but has not read him or they would know that a set of weighing-scales and an appropriate diet sheet in mandatory terms would abolish eclampsia, as Hamlin has

Since Feb 6 1952, I have followed Hamlin's methods in 110 cases a very small series, and have had 1 case of albuminuria This patient had persistent albuminuria after I had performed a surgical induction at the 36th week but was subsequently proved to have a tuberculous abscess discharging via a fistula into the bladder

Hildenborough Kent C GLAISHER

ANÆSTHESIA IN OBSTETRICS

SIR —Anæsthesia for the application of forceps, in addition to the danger of inhaled vomit diminishes the mother's expulsive forces and also impairs fœtal vitality Why therefore, should these disadvantages be courted when analgesia is sufficient ?

Devonport,
Plymouth O LL LANDER

DEADLY SWEETS

SIR,—In your annotation of June 9, referring to a further case of ferrous sulphate poisoning, there is an unfortunate contradiction in advice In one place you state "The problem of accidental poisoning will not be solved by reproaching the manufacturer" But further on one reads -

> 'The replacement of all attractively coloured and flavoured drugs of potential danger by something less deceptively decorated is long overdue, and is the most effective single step we can take towards preventing these tragedies"

There is hope that this further case of iron poisoning may stimulate the manufacturers to issue these tablets in 'Cellophane' envelope strips but your statement that the manufacturers should not be reproached may reduce the likelihood of their coöperation Surely this further tragedy should force us all to redouble our efforts with the manufacturers, as well as to increase the knowledge of the general public on the subject

Plymouth HUGH JOLLY

SIR,—In your annotation you say The replacement of all attractively coloured and flavoured drugs of potential danger by something less deceptively decorated is long overdue " Influenced by similar earlier comments in your own and contemporary journals, and by a resolution of the Pharmaceutical Society, my company issued and made widely known to the profession a white and virtually tasteless form of tab ferr sulph co *N.F* I understand we were not alone in such action The continuing demand, however, is for the coloured sugar-coated tablets the white ones are not wanted I cannot feel that so many thousands of prescribers are without sound reasons for their preference

Evans Medical Supplies Ltd
Speke Liverpool C W ROBINSON
Director

RUPTURE OF THE SPLEEN

SIR —Your annotation last week refers to various diagnostic radiological features In a case recently admitted to this hospital, Howell-Jolly bodies appeared in the peripheral blood, and before laparotomy I strongly suspected a lesion of the spleen

A woman, aged 57, was admitted for observation following a car accident not at that time having any definite evidence of injury Three days later she collapsed and complained of abdominal pain Examination of the blood showed numerous large polychromatic red cells many of which contained Howell-Jolly bodies At laparotomy the same day a ruptured spleen weighing 300 g, together with blood-clot was removed, there having been a hæmoperitoneum There were subcapsular and intrasplenic hæmorrhages Histological examination failed to reveal any evidence of glandular fever or of any other lesion likely to lead to rupture

Howell-Jolly bodies are known to appear after splenectomy and in certain diseases but I had not previously been aware that their appearance might precede splenectomy in cases of injury In the present case a possible explanation is that a form of 'auto-splenectomy' took place owing to pressure of the various hæmatomata on the splenic vein and interference with venous return from the spleen

I suggest that examination of the blood for Howell-Jolly bodies may be useful in cases of injury in which abdominal and particularly splenic lesions are suspected, but in which laparotomy is not immediately desirable

Llanelly Hospital
Glamorganshire A L WELLS

PARAPLEGIA FOLLOWING SPINAL ANÆSTHESIA

SIR,—It becomes almost embarrassing when a university professor of anæsthetics persists determinedly in appearing completely simple in this problem of the unexplained perils inherent in spinal anæsthesia, and ignores the issue raised by the two propositions (1) that the only known common factor in cases of neurological complications ensuing upon spinal anæsthesia is the intrathecal introduction of an anæsthetic substance, and (2) that the immersion of ampoules of such substances before use in toxic solutions is not such a common factor

It may be taken for granted that in an important university department such as Sir Robert Macintosh's at Oxford there is an adequate bibliography of the very numerous instances of neurological disaster ensuing upon spinal anæsthesia Nothing less could be expected of a department the head of which has felt himself able to publish a monograph upon this technique for the instruction of his colleagues

He must have at hand the information needed either to lend some cogency, if this were possible, to his umbrella hypothesis of the cracked ampoule or, alternatively, to reveal its large irrelevance

Can we not persuade him of the expediency, if not of initiating some fruitful research upon this question, at least of providing a comprehensive and dispassionate review of all the known facts and hypotheses up to date ?

Surely it is not unreasonable to ask of a university department responsible for research, for teaching and for setting an example of practice in its own field, something more academic and serious than the collection of three out-of date anecdotes about cracked pots

London W 1 F M R WALSHE

SIR,—In the early days of my 'chemical sympathectomy," produced by paravertebral injection of a 10% aqueous solution of phenol I had one case which is of interest in connection with this subject

An obese woman was given a paravertebral injection of 10 ml of 10% aqueous phenol solution at the level of L3

The Casualty Department

II SHORTCOMINGS AND DIFFICULTIES *

T G LOWDEN
B M Oxfd, F R C S
CONSULTING SURGEON, SUNDERLAND GROUP HOSPITALS

THE work of the casualty department has been outlined Some of the difficulties facing its medical and administrative staff can now be considered

Medical Problems

Lack of Continuity

Where a junior medical officer, a rota of such, or a rota of general practitioners is responsible for the care or disposal of casualty cases, one of the greatest disadvantages is lack of continuity of medical care An unsupervised appointment lasting six months or a year, or an attendance at the clinic once or twice a week, gives little opportunity for the doctor to acquire skill, to explore new methods, or to assess late results There have been great improvements in the treatment of many types of casualty case in recent years, and under the present system these changes have little chance of affecting many of the patients

Shortage of Staff

In a health service already seriously understaffed with junior medical men the relative unattractiveness of an appointment to the casualty department has resulted in a great shortage of casualty officers

Before the establishment of a nationally controlled health service criticism was restrained by an appreciation that much of the hospital system was provided by voluntary effort Since this establishment there has been no such restraint, and although the increase of complaint and attack has done a certain amount of good, it has often been unjust and irresponsible Casualty departments are particularly liable to suffer from complaints Most of these are about delay in attention to minor cases, and this is often unavoidable in an ill designed department where, during certain parts of the day, the speed of arrivals far exceeds the speed with which attention can be given The more serious ones refer to occasions when major injuries or urgent medical conditions have to wait The usual reason for this is lack of medical cover, sometimes because the establishment does not allow of a doctor being constantly in the department, and sometimes because, although the establishment is adequate, it has been impossible to find doctors to complete it

Fear of Legal Action

The increase in litigation against the hospital services, and in the amounts awarded in damages, are making all doctors careful about exposing themselves to legal action , and because casualty departments are particularly liable to such actions, appointments to them have become even less popular than before Those who accept such appointments find that their clinical decisions are increasingly modified by this situation Consequently many patients are admitted for observation and are investigated unnecessarily

Some administrative bodies, with this in mind, tend to appoint officers of more seniority and aim to make consultant surgeons ' responsible " for the work of the casualty department What this " responsibility " entails is at present obscure If a consultant is to have any practical effect on casualty work it will take a great deal of his time To make him merely " responsible on paper " may relieve the anxieties of administrative authorities for a time, but it will confer little benefit on the patients, and will do little to reduce the margin of error in the clinical work Nobody can be " responsible " in the medical sense, when engaged elsewhere

Clinical Standards

Clinical results can be vastly improved by applying to the minor surgical problems of the casualty department principles which are generally applied in inpatient surgery Clinical response partly depends on starting treatment as soon after the injury or the onset of the disease as possible Two days' delay for a septic hand may mean an extra two weeks' incapacity Holding a weekly consultant clinic does little to combat this

Economy of Staff and Money

With the establishment of routine consultation and dressing techniques the long queues of repeat attendances which begin the day's work in most casualty departments can be reduced , and if some assembly line system is adopted, in which all ambulant patients pass successively through records, medical, and nursing stations, each one can be dealt with more quickly Such a casualty service needs at least one doctor and corresponding nursing and clerical assistance Bacteriological and radiological services are essential, and so is adequate space designed to allow transit through entrances, waiting and treatment rooms, and exits without congestion

It is neither an economic proposition nor would it be possible at present to establish such a department in every hospital in the country For this to be justified a turnover of about 10,000 patients per annum would be needed 20,000 patients would require at least two doctors, but considerably less than twice the other facilities, and from this point of view a concentration of casualty work might appear to be a simple solution However, any attempt to merge a number of smaller units into a single large one has inherent disadvantages

1 Some of their functions, especially those of reception and disposal, cannot be divorced from the other functions of the individual hospitals

2 Where a local department is absorbed into a central, patients have to travel further , and because many of them suffer from trivial complaints, they are less likely to go to this extra trouble It is useless trying to encourage early attention and at the same time making it harder for patients to get it

Pilot investigations on the economic impact of minor injuries and sepsis indicate that a working man may cost the Exchequer £5–6 a week when he is incapacitated, and that his loss of earnings amounts to £3 more[3] The global sum cannot at present be estimated, but must be counted in millions It is possible, by improving medical and nursing cover, to reduce this by a significant amount From the point of view of national expenditure, therefore a nation-wide improvement in the casualty service would repay the outlay of a large sum It would, for instance, pay the Ministry of National Insurance and Pensions, were they to hand over to the Ministry of Health £1 million a year, earmarked for this purpose alone Their own payments in benefits would come down by more than this It would pay the big industrial undertakings to finance improvement in the casualty departments of their own areas, and many of them did so generously before the " appointed day " It is another occasion for that popular rhetorical question " We may not be able to afford it, but can we afford *not* to have it ? "

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* Second of three articles dealing with some of the difficulties facing casualty departments of non teaching hospitals, and outlining a scheme for a more comprehensive accident service

[3] Wilkes R *Brit J industr Med* 1954 11 260

vertebra Within a few minutes paraplegia developed with sensory loss up to T6 segment Lumbar puncture was carried out and a clear fluid smelling strongly of phenol was obtained Chemical tests confirmed the presence of phenol The paraplegia wore off in three hours, but the patient had weakness of the quadriceps femoris on the side of injection which took three months to disappear

It would seem that the needle must have entered an intervertebral foramen and pierced the dura, although no cerebrospinal fluid dripped from it and test aspirations were negative The weakness of the quadriceps is explained by the high concentration of the phenol round the spinal nerve roots emerging at the site of injection

This case has been the only one with neurological complications out of several hundred treated personally by such injections, and it certainly emphasises the need for great care when carrying out paravertebral injections of potent fluids In addition, it indicates that a considerable amount of phenol can be introduced intrathecally without lasting damage to the spinal cord In the light of this evidence it seems most unlikely that an ampoule of spinal-anæsthetic fluid immersed in 5% phenol solution could absorb, through microscopic cracks, enough phenol to cause a permanent paraplegia when injected intrathecally As Sir Francis Walshe indicates (June 2), the only common factor in the reported cases of paraplegia after spinal anæsthesia is the use of a spinal anæsthetic, and it seems clear that the risk of such a tragic complication is inherent in the injection, no matter how perfect the technique of its administration

Manchester HERBERT HAXTON

CAUSE OF HYPOGLYCÆMIC SYMPTOMS

SIR,—In your interesting annotation of June 9 you state that it is hard to estimate the significance of our finding that sweating still occurs in response to hypoglycæmia in patients after thoracolumbar sympathectomy It should be made clear that sweating was only seen in the regions such as the face and upper limbs, not affected by the sympathectomy No sweating was seen in the regions denervated by the operation However, the point at issue is whether sweating still occurs when, owing to adrenal denervation, adrenaline is not liberated The persistence of sweating in these patients is thus further evidence that adrenaline plays no part in sweating due to hypoglycæmia

The lack of correlation between adrenaline release and occurrence of sweating is demonstrated in several other observations You mention the fact that intravenous infusions of adrenaline do not produce sweating It is also of interest that the sweating which is a conspicuous feature in a patient with a phæochromocytoma may persist for several days after removal of the tumour,[1] and clearly it cannot be due primarily to the excessive liberation of adrenaline

Edinburgh E B FRENCH
Sheffield R KILPATRICK

BUTALITHONE SODIUM IN ELECTROCONVULSIVE THERAPY

SIR,—It may be of interest to mention our preliminary experience with butalithone sodium ('Transithal,' 'Ulbreval') as a substitute for thiopentone sodium in anæsthesia for electroconvulsive therapy

We have found that butalithone sodium, in a dose of 0 25–0 5 g given intravenously over half a minute, depresses respiration less than does thiopentone, so that usually inflation is unnecessary The patient speedily returns to a safe state of consciousness, so that a junior nurse may be left in charge, and the interval before full recovery is very considerably shorter, so that less time is wasted in waiting both by patients and staff in a busy outpatient department

In our experience, extending over several hundred cases, side effects, such as hiccup and retching, have been no commoner than with thiopentone

A F M LITTLE
Plymouth A ARNAUD REID

APPENDICECTOMY DURING GYNÆCOLOGICAL OPERATIONS

SIR,—British gynæcologists have always been somewhat doubtful about the advisability of routine appendicectomy when performing hysterectomy or other abdominal gynæcological operations Some British surgeons, however, and many Americans[1] include appendicectomy as a routine The late Victor Bonney always advised against routine appendicectomy, and obedience to the principles of this great master has caused me regret on only 3 occasions in which acute appendicitis followed within one week of hysterectomy, involving the patient in a further emergency operation I have seen a similar complication twice after vaginal hysterectomy In 1 of these patients a gangrenous appendix with peritonitis was removed forty eight hours after operation, and in another a chronic pelvic abscess involving the right fallopian tube and ovary developed and was operated upon three month after the original procedure

The great argument against routine appendicectomy has been the danger of disseminating infection from the bowel wound in the cæcum into the recently exposed cellular planes of the retroperitoneal space It is certainly true that the pelvic peritoneum recently traumatised by the operation of hysterectomy has not the same ability to resist infection as when the pelvis is intact It is possible, too, that the pelvic peritoneum is already fully occupied in dealing with the contamination from the vagina inherent in total hysterectomy and that the two portals of infection may, in certain instances, prove overwhelming

Although it is interesting to speculate on these possible sources of infection, I felt that, if exact information could be obtained from a representative number of British gynæcological surgeons, the results might be helpful to those who, like myself, wonder what is the best and safest procedure A questionnaire was, therefore addressed to 31 surgeons, and their replies are summarised below

(1) Do you remove the appendix as a routine when performing hysterectomy ?
No 26, *Yes* 5

(2) Have you seen any complications as a result of this operation, such as peritonitis, intestinal obstruction &c ?
No 25, *Yes* 6 (burst abdomen 1, peritonitis 7, intestinal obstruction 1, *Escherichia coli* infection of wound 6) (Of the 6 replying 'yes," some had seen more than 1 complication—hence the discrepancy in the figures)

(3) Have you encountered any complications from not removing the appendix ?
No 30, *Yes* 1 (a case of appendicectomy after myomectomy followed by fatal peritonitis)
Of these 'noes," 7 recalled patients in whom appendicectomy was necessary within a few months of the hysterectomy There is no evidence to connect the hysterectomy directly with the appendicitis—i e, it did not occur within one month of the operation, as in my cases

(4) Can you give me any references to any published work on this subject ?
The replies to this question were an almost universal blank, apart from the figures published by the Royal Society of Medicine in 1949 from the Samaritan Hospital, London

(5) Any other observations ?
Of the 26 surgeons who do not routinely remove the appendix, 16 made the observation that they would

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[1] Swan H J C *Brit med J* 1951, i 440

[1] Taniguchi T, Kilkenny G S *Amer J Obstet Gynec* 1950 60 1359

what he would say to the practice which some hospitals have to adopt, of sending for a technician to perform this work after hours "

It is true that I used similar words during the debate following Dr Loutit's address to the Medico Legal Society last May, but I should like to amplify that by quoting further from the report in the *Medico Legal Journal*[6]

> I asked the lecturer if he agreed that " cross matching and grouping should never be undertaken by any doctor unless he had had adequate training and experience in this highly technical and potentially dangerous procedure " Dr Loutit replied that " he would say that cross matching should be done by the most expert man available and if he was in bed he was available " This would appear to include a competent technician who might well, as Dr Shillitoe says (Jan 7), have more expert knowledge and experience than a junior house officer of the hazards involved
>
> Dr Loutit also said that " he could see that under certain circumstances it might be right that a house physician, even although technically unskilled, should make the best possible attempt to do the grouping and cross matching It is a case of balancing the hazards, when in the absence of a transfusion the patient would die "

Dr Discombe's book[1] will be invaluable to resident doctors confronted with this difficult decision, and I hope it will be made freely available to them by all hospitals where such cases may arise

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ALISTAIR FRENCH
Secretary

DISTURBANCES OF CARBOHYDRATE METABOLISM CAUSED BY ALCOHOL

SIR,—The observation by Dr Hunter, Dr Merivale, and Dr Smith (Dec 31) that " disturbances of carbohydrate metabolism, shown by the two dose glucose-tolerance and the pyruvate metabolism tests, were found in 7 alcoholic patients " confirms the results reported by K C Murfitt and myself to the Association of Clinical Pathologists in October, 1954 Our results were based on investigation of 47 male and 17 female alcoholics in 1953 (group I) and 42 male and 12 female alcoholics in 1954 (group II), all under the care of Dr M M Glatt at Warlingham Park Hospital In our paper we said

> " The patients of group I of both sexes had had vitamin-B_1 treatment when their blood was examined Of the men, 42 were tested and none showed an abnormally low value Indeed, a number showed abnormally high values—evidence of more than adequate medication Of 15 group I women examined, 4 had abnormally low cocarboxylase values In 1 case thiamine deficiency was confirmed by an abnormal response of the blood pyruvate to glucose administration In spite of an adequate cocarboxylase level, 14 of 46 group I men had high blood pyruvate levels, suggesting that the mild exercise they had taken to reach the laboratory had overtaxed their not fully recovered cocarboxylase mechanism Similarly, 5 of 16 women of group I had high pyruvate values
>
> " The patients of group II had not had vitamin B_1 treatment and were all bled fasting and in bed All had normal pyruvates 2 men and 5 women had abnormally low cocarboxylase values
>
> " These results indicate that this type of alcoholic is prone to add thiamine deficiency to his liver dysfunction "

Our methods of conducting the pyruvate-metabolism test and of estimating blood-pyruvate were the same as those of Dr Hunter and his co-workers We estimated blood cocarboxylase, which is a measure of the body's thiamine status, by the method of Kay and Murfitt[7]

Mental Hospitals' Group Laboratory
West Park Hospital, Epsom, Surrey

W W KAY

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[7] *Biochem J* (in the press)

IN THE MENTAL HOSPITAL

SIR —One imagines that our predecessors in psychiatry of a hundred years and more ago would have been encouraged and perhaps amazed to see that some of their beneficial ideas even today required emphasis, and perhaps re discovery, in the pages of your journal May I quote, for example, from the case notes of Frederick Needham, describing his treatment of one Susan Appleyard

> This girl was admitted to this hospital in 1853, when she was 20 She was described then as restless and laughing unmeaningly, and by 1858 she had sunk, it is stated, into a state of the most complete dementia , wherein she lay coiled up, moaning dismally Needham wrote on March 28, 1859 " This case is unchanged She still pulls her dress over her head, and lies coiled up in corners of the room "
>
> On April 12, 1859, Needham wrote " I this morning went into the gallery and made her—opposed a good deal at first—allow herself to be washed, her hair to be brushed, and then took her with me at first by main force into the gallery and garden I walked her about for about half an hour in the garden, had her dressed in new petticoats, a new dress, new boots and new stockings, and placed her in a superior gallery in a chair, before a table on which there was dinner, and put a knife and fork into her hand, telling her that I should insist upon her doing everything she was told, and should if need be make her do so I also said that she had to come amongst ladies and into a better gallery, and that therefore she must behave herself as she should in better society and in better apartments She ate her dinner quietly, spoke sensibly evincing much more intellectual power than one would have supposed her to possess, and then as soon as the meal was concluded she proceeded, and with much dexterity, to wash up the plates etc There was no more drawing up of the dress, no more lying down, but she conducted herself to the surprise of everyone well and correctly Her treatment thus commenced, I purpose continuing, and have ordered the attendants to never let her lie down or have her dress up, to give her a good bed , to take her each night to the water closet before bed time , to take her into the garden and greenhouse daily, and to get her to work as much as possible , to call her Miss Appleyard and to treat her as if she were quite changed Should the treatment in this case succeed it will be one of the best instances of humane and kind moral treatment as successful in cases even of the most confirmed and degraded dementia, and will indeed endorse the old *motto*, applicable also to insanity, nil desperandum "
>
> A year later Needham referred to this patient as " clean, quiet and orderly in her habits , looks well and is cheerful, happy and contented "

Needham was an unusual man, and one might take many examples from his notes and his reports of practices which have been more recently regarded as modern for example, the use of water-colours as an adjunct to occupational therapy, and the establishment of a patients' discussion club, which met fortnightly in the hospital, and which indeed published abstracts of its meetings in the hospital periodical called *The York Star* Needham, who pointed out that this printed publication owed its origin to the earlier issues of a patients' journal both at Morningside and at Dumfries Asylum, commented

> " Literary efforts of this kind, which now form so important a feature in the moral treatment of the insane, are useful not only as a means of employment and mental exertion, leading to the evolution of coherent ideas and the interruption or repression of morbid trends of thought , but because they furnish subject matter for general conversation and in this way beneficially influence a wider circle than that immediately engaged in them "

All was grist to Needham's mill, from his contemplations on the possible use of powdered charcoal as a deodorant in the long-stay wards to his more general reflections on the hospital and lunacy policy

There is, however, one short sentence of his, taken from his 1871 report, which may perhaps sum up both our current conceptions of the " therapeutic community " in a mental hospital and former ideas of the "moral treatment" of insanity This sentence reads "The insane man is too often a sane man decivilised, and to him the various processes of civilisation have again to be applied"

Bootham Park, York ARTHUR BOWEN

PULMONARY EMBOLISM

SIR,—In your leader of Dec 31 there are statements which are at variance with experience in this hospital and which I fear may be misleading

You state "that most lethal emboli strike with dramatic suddenness, bringing vicious chest pain and hæmoptysis before any diagnosis of limb thrombosis has been made" It is true that many fatal embolisms occur without recognised warning, but surely chest pain and hæmoptysis are not signs of the rapidly fatal embolism but rather of the embolism which the patient survives, and depend on the development of local congestion and pleurisy Although many embolisms, as you say, are almost instantaneously fatal, there are others in which death is delayed for a few hours and may be averted by treatment If anything useful is to be done for these patients the diagnosis should be made and treatment started at once In my experience neither pain nor hæmoptysis is to be expected in the early stages after a large embolism The important features of such a case are sudden collapse and signs of obstruction in the right side of the heart

Of more importance is your statement that there is statistical evidence for the view that "as it is the first embolism that kills, if the patient survives he has little to fear from later ones" You do not give the source of this evidence, but in an investigation which was undertaken in this hospital and reported in your journal before the introduction of current methods of treatment,[1] out of a total of 157 pulmonary embolisms only 34 were fatal in the first attack Of the 123 survivors of an attack of embolism 10 died of subsequent attacks A mortality-rate of 8% in the survivors of the first embolism can hardly be regarded with equanimity

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R S PILCHER

HEALTH CENTRE OR GROUP PRACTICE?

SIR,—The main point we wish to make appears to have been missed by Dr Stephen Taylor (Dec 31) The provision of premises for group practices is being hindered by such persuasive statements on what constitutes the needs for "efficient general practice" as Dr Stephen Taylor has put forward He says that anything less costly than the Harlow centres can be got only by making "real sacrifices in efficiency"—which implies that health-centre practice on the Harlow scale is in fact the cheapest efficient way of conducting general practice As a group of some years' experience we beg to differ

We omitted to say in our first letter (Dec 17) that about 60% of our finance was required for new building The remaining 40% comprised the purchase and the rebuilding and adaptation of an existing house Had a suitable central site been available for new building, our cost per patient at risk would have come down further by three or four shillings

We have no intention of criticising the Harlow centres, but Dr Taylor's arguments are liable to make general practitioners and planners believe that nothing less will do, and that much which is inessential has received the stamp of approval and therefore must be essential

In our earlier letter we showed that the widely publicised de luxe standards in premises for general medical practice can be stripped down to basic and economically achievable proportions—to 13*s* 3*d* as against £1 per patient at risk We know that just like us, there are groups of doctors up and down the country working without sluice or specimen examination rooms, and without a hall for a waiting-room or pram shelter —and working in excellent harmony with local authority services without special rooms for antenatal and baby clinics

Let the Nuffield Trust carry on its wonderful work, but it should not be thought that less costly ways are necessarily less efficient

C E MUNRO
E V KUENSSBERG
A R LAURENCE
G MACNAUGHTAN
A H D LARGE
Edinburgh G IRVINE

MENTAL HEALTH SERVICES

SIR,—In your note on a New Occupation Centre in Leeds for Mentally Handicapped (Dec 31), Dr Z P Fernandez, chairman of the Leeds mental health services subcommittee, is quoted as saying that Leeds spent more in the mental-health field than any other local authority in the country, averaging £103 per 1000 of population as against £7 or £8 in other areas All credit to Leeds for its fine record in mental health—but the statement does scant justice to other local health authorities The average annual expenditure on mental health services for county boroughs in England and Wales is £44 12*s* per 1000 population, and the only authorities with an expenditure as low as £7 or £8 are a few Welsh counties and one Welsh county borough

Dr Fernandez also states that Leeds has the highest ascertainment record in the country Leeds has 3 8 known mental defectives per 1000 population, of whom 3 5 per 1000 are "ascertained" cases In Bristol the figures are 4 15 per 1000 and 3 8 per 1000 respectively Is mental deficiency really more prevalent in Bristol, or have we a higher ascertainment-rate? I wonder!

H TEMPLE PHILLIPS
Chief assistant medical officer of health

Department of Public Health,
Tower Hill, Bristol, 2

MYXOMATOSIS

SIR,—Your annotation of Jan 7 calls for certain criticism It suggests that the immediate result of the deliberate spread of this plague is an increase in the yield in rabbit-free areas and that the eventual gains could be much more striking But surely these figures are drawn from the returns last year when the weather conditions were abnormally favourable, while certain farmers may have profited in this way, others, to whom the rabbit was their livestock, have lost heavily

When to the balance sheet is added the price of inferior dead rabbits imported for food at a very much enhanced price as a substitute for the good rabbits wantonly destroyed by disease, when our merchants are paying 22*s* per dozen for foreign rabbit pelts which they formerly bought for 6*s*, when we realise that the rabbit was a plentiful, cheap, and wholesome supply of meat for farm workers and others throughout the land, competing with the high prices for other meat, surely we must think again before we put an undue assessment on the value of myxomatosis

Recently a scientific farmer, the gist of whose paper is in favour of myxomatosis,[1] has stated that as the result of it we see farms, where the rabbits were the livestock and livelihood of the farmers, "now empty warrens, whose ill fenced and ill watered lands are poorly adapted to sheep and inhospitable to cattle—sheep and cattle which many of these farmers cannot afford to buy", while your annotation admits that "our wild rabbit has qualities that will almost certainly ensure its survival both myxomatosis and hordes of rabbits may be permanently with us"

We then read that "To avoid this and to increase food supplies, the Minister of Agriculture is pressing on with the designation of rabbit clearance areas in which occupiers of the land must destroy the rabbits or, if this is impossible, prevent their causing damage" The Ministry of Agriculture has

remove it if, on inspection, they found it to be diseased, to look unhealthy, to be kinked, to be adherent retrocæcally, or to contain fæcoliths A few commented that appendicectomy undoubtedly increased the risk of postoperative pyrexia and infection and that it was a complicating factor in the convalescence after hysterectomy

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[1] Pilcher R S *Lancet*, 1939 ii, 629

[1] *Birmingham Post*, Dec 17 1955

As a result, the following suggestions can be made

(1) That British gynæcologists by a majority, do not advise routine appendicectomy when performing hysterectomy

(2) That this rule should not be followed unreasonably and the appendix if obviously diseased or unhealthy, or if containing fæcoliths, is probably best removed

(3) That there is a real danger of local and general peritonitis, and that simultaneous appendicectomy and hysterectomy should be covered by a course of postoperative antibiotics

I acknowledge the kind coöperation of the members of the Gynæcological Travellers' Club and other colleagues who kindly answered my questionnaire

St Bartholomew's Hospital,
London, E C 1 JOHN HOWKINS

FATS AND DISEASE

SIR,—Dr Sinclair's letter (April 7) intrigues me In 1952 and subsequently we reported studies, begun in 1950, which showed a profound decrease in plasma cholesterol and phospholipids, in patients maintained on diets containing large amounts of unsaturated vegetable fats[1 2] Among the possible reasons for such an effect were considered (1) absence of cholesterol, per se, (2) a positive effect of some vegetable sterol, (3) a positive effect of vegetable phospholipid, (4) a positive effect of one or more fatty acids present in the vegetable fat

Over the intervening years, by a process of exclusion, all except the last have been essentially eliminated Studies in which fats of vegetable origin, but of very different iodine number, have been alternated in the diet have shown that the decrease in plasma cholesterol and phospholipid levels is directly related to the amount of unsaturated fat present in the diet[3] A very recent study, in which 100 g of a synthetic triglyceride, containing approximately 2 g of linoleic acid, has been administered daily,[4] further implements this conclusion

Dr Sinclair's observations regarding abnormal deposition of lipids in the skin under conditions of essential-fatty-acid deficiency are of considerable interest, as are his speculations regarding the very possible rôle of essential fatty acid and/or pyridoxine deficiency in the pathogenesis of degenerative vascular disease. His observations regarding increased requirement for essential fatty acid in male animals may be particularly pertinent in this regard

The work of Shapiro and Freedman[5] on the relation of essential-fatty acid and methionine deficiencies to hypercholesteræmia may help to clarify some of the observations of Best et al.[6] and of Stare et al[7] on the atherogenic effects of deficiency of choline, of methionine and of cystine

If one accepts as a working hypothesis the concept that transport of fatty acid is the major function of cholesterol[8] and recalls that the "normal" fatty acid, which is esterified with cholesterol, is an unsaturated acid,[8] it would seem not improbable that relative or absolute unavailability of essential fatty acids may result in "jamming" of cholesterol metabolism, with resultant increase in production and abnormal deposition of cholesterol If this concept be even partly correct, it is obvious that experimental efforts designed to evaluate the specific metabolic functions of essential fatty acids per se, are important Such studies are under way in this laboratory

Dr Keys (April 28) is less than enthusiastic regarding the concept of the importance of essential-fatty-acid deficiency in the pathogenesis of atheromatosis Dr Keys says "We have observed this [i e, differential effects of different fats upon cholesterogenesis] as well as others, including Kinsell in California, Ahrens in New York and, recently, Bronte Stewart in South Africa" Dr Keys until recently felt that fats were fats, and all were equally bad in regard to cholesterogenesis Since he appears to have accepted the weight of evidence for the profound differences in "cholesterogenic effects" between some animal and vegetable fats, we may expect that before too long he will decide that deficiency of essential fatty acids plays an important role in the pathogenesis of degenerative vascular disease

Institute for Metabolic Research
Highland Alameda County
Hospital Oakland 6 California LAURANCE W KINSELL

SIR,—May I add my humble voice to the recent flurry of interest engendered by Dr Sinclair's letter on the possible multitudinous rôles of essential fatty acids in disease? Perhaps this series of letters should be entitled "Hard Fats and Hard Arteries"! Although we are living in an age of rapid advances and as rapidly crystallising opinions, the healthy controversy let loose may well mark the initial break-through in one aspect of the problem of atherosclerosis While I may be accused of speaking upon a subject to which I am a relative newcomer, my attention in the past three years has been devoted to orienting myself through the slough of fats, lipoprotein carriers (alpha and beta), S_f and S-negative particles, Cohn fractions, phospholipids, lipid phosphorus, free and esterified fractions of cholesterol and their ratios, neutral fats and triglycerides, choline and methionine effects and the relative incidences of arterial diseases in countries torn by war and altered by peace The purpose of this attempt at orientation was to find what approaches might lead to therapy, for our formerly hypertensive patients are no longer dying of their disease but of atherosclerosis and its manifestations

Out of these contemplations came a regression (because of confusion) to non-ultracentrifugal simples and to Aschoff's statement 'From plasma of low cholesterol content no deposition of lipoids will occur even though the mechanical conditions are favourable"[9] Added to this might be "It may matter little how cholesterol and its esters are carried in blood, what is important is the blood level and the nature of the ester" Schonheimer's old but careful analyses of aortic plaques showed clearly that esters of cholesterol increased with severity of the lesions[10], several fatty acids were demonstrated, but the principal ones were saturated or monoethenoid (stearate, palmitate, oleate) The solubilities of cholesterol esters of unsaturated fatty acids are greater than are those of saturated acids with chains of equal lengths[11]

To my knowledge, Snapper was the first to suggest that deficiency of unsaturated acids might lead to atherosclerosis,[12] by pointing out the low incidence of the

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1 Kinsell L W Partridge J Boling L A Margen S Michaels G D *J clin Endocrin* 1952 12 909

2 Kinsell L W Michaels G D Partridge J W Boling L A Balch H E Cochrane G C *J clin Nutr* 1953 1 224

3 Kinsell L W Michaels G D *Fed Proc* 1955 14 661 Friskey R W Michaels G D Kinsell L W *Circulation* 1955 12 492

4 Kinsell L W Friskey R W Michaels G D Brown F R *J clin Nutr* (in the press)

5 Shapiro S L Freedman L *Amer J Physiol* 1955 181 441

6 Wilgram G F Hartroft W S Best C H *Brit med J* 1954 ii 1

7 Mann G V Andrus S B McNally A Stare F J *J exp Med* 1953 98 195

8 Kelsey F E Longenecker H E *J biol Chem* 1941 139 727

9 Aschoff, L Lectures on Pathology New York 1924 p 131

10 Schönheimer R *Z physiol Chem* 1926 160 61

11 Deuel H J jun The Lipids New York 1951 vol 1

12 Snapper I Chinese Lessons to Western Medicine New York 1941

cases discussed above Furthermore, spontaneous movements, though sometimes few, were never entirely absent Of the children with cerebral palsy 4 had a history of possible birth injury, and as they grew older, abnormal postures, stiffness and clumsiness of the limbs, or involuntary movements appeared, while there was no muscular wasting, in these cases, too, the tendon reflexes were present throughout and sometimes exaggerated In the mentally defective children it gradually became apparent that their delay in physical development was accompanied by a parallel deficit in emotional and intellectual attainments The diagnosis of mental defect in infancy is never easy, but in these children the true state of affairs was generally apparent by the end of the first year of life In the cases of scurvy, arachnodactyly, and the other conditions listed above, it also became clear with the passage of time that the moderate degree of muscular weakness and hypotonia shown by the patient was not due to a primary neuromuscular disorder The same will usually be true in cases of malnutrition or in endocrine or metabolic disorders, usually signs of the primary disease, of which the hypotonia is but a symptom, will be evident In glycogen-storage disease, for instance, hepatic enlargement will often be found Furthermore, in patients with hypermobile joints due to congenital laxity of the ligaments there is no impairment of spontaneous movements or of muscular development, and often the condition affects more than one member of the family

It is thus apparent that, in most cases diagnosed as amyotonia congenita, the nature of the underlying disease will be revealed as a result of repeated clinical observations, particularly during the first year of life Cases of spinal muscular atrophy will deteriorate during this time, unlike benign congenital hypotonia, while in brain-injured or mentally defective children signs of the central nervous disorder, or a failure of intellectual development, may come to light It is natural that an anxious parent will press for an answer at a first interview, but it is surely far wiser to temporise in any case of doubt than to give a gloomy prognosis which may not be justified by subsequent events If doubt persists, as it may, after two or three interviews, it will often be necessary to admit the patient to hospital for observation and for investigations, including electromyography and muscle biopsy, which, if done with care, will always either confirm or refute a diagnosis of spinal muscular atrophy If these studies and metabolic investigations are normal, it may still be necessary to await the appearance of involuntary movements—e g, in cases of cerebral palsy—or signs of spontaneous improvement (suggesting a diagnosis of benign hypotonia) before making a final diagnosis

The findings in this series of cases have led to the conclusion that the term " amyotonia congenita " should be discarded, unless it is used with the clear understanding that it refers to the syndrome of infantile hypotonia and is not taken to designate a specific disease It is surely more satisfactory to call all cases of spinal atrophy, whether beginning at birth or subsequently, " infantile spinal muscular atrophy " or " Werdnig Hoffmann disease " " Amyotonia congenita " should not be used to denote such cases, because in the minds of many physicians this diagnosis raises the possibility of spontaneous improvement Furthermore, although the cases of " benign congenital hypotonia " referred to in this paper correspond most closely to Oppenheim's original description of amyotonia, it is preferable that these too should be identified by a new descriptive term such as the one given, in view of the many varied meanings which have become attached to " amyotonia " over the years Clearly, all hypotonic babies require meticulous observation until the nature of the disease responsible for the muscular manifestations becomes apparent, only then may it be possible to offer an accurate prognosis

Summary

The results are reported of a follow-up study of 109 cases which had been diagnosed as amyotonia congenita, usually in infancy, 2–25 years before

In 67 patients the disease giving rise to generalised hypotonia and hypermobility had been progressive, and 55 of them had died between the ages of 5 weeks and 12 years The 12 survivors were severely disabled and were aged 4–20 years at the time of follow up In these 67 cases the disease was clearly spinal muscular atrophy, whether the condition was present at birth or began late in the first year of life made little difference to the subsequent history of the illness

Of the remaining 42 patients, 8 had recovered completely 9 other patients had improved considerably but had remained moderately disabled throughout life, with general weakness and decrease in bulk of the skeletal musculature, the condition of these patients corresponded to descriptions of " benign congenital myopathy," but reasons are given for supposing that they did not have a true muscular dystrophy It is suggested that the entire syndrome, embracing the cases which recover completely and those in which recovery is incomplete, may reasonably be called " benign congenital hypotonia " The two forms of this syndrome may be the different end-results of a similar neuromuscular abnormality present at birth, in some cases the condition may be entirely overcome by the processes of postnatal development, but in others some muscular disability persists Another 5 patients were found to have muscle disease, 1 had a picture like that of benign congenital hypotonia but with myasthenic features, 3 eventually showed the characteristic features of progressive muscular dystrophy, and 1 was a case of polymyositis (chronic myositis fibrosa)

6 other patients were found on follow-up to have some form of " cerebral palsy," and 8 others were mentally defective and showed no sign of neuromuscular disease In the remaining 6 cases it was apparent that the muscular hypotonia observed in infancy had been due to scurvy (2 cases), arachnodactyly, multiple congenital defects, congenital dislocation of the hip, and spinal ganglioneuroma

The differential diagnosis of the many conditions which may give rise to the syndrome of amyotonia congenita (the limp floppy baby) is discussed Many clinical observations at intervals may be required before the underlying disease can be accurately diagnosed In difficult cases investigations such as muscle biopsy may be helpful The term " *amyotonia congenita* " should be discarded, unless it is taken to mean the clinical syndrome of infantile hypotonia without any prognostic implications Spinal atrophy should be called " infantile spinal muscular atrophy " or " Werdnig-Hoffmann disease," whatever the age of onset, and the name " amyotonia congenita " should not be used to denote cases of this type

I wish to thank the physicians and surgeons of the National Hospital and of the Hospital for Sick Children for permission to consult their records and to follow up their cases, Dr E A Carmichael and Prof A A Moncrieff for encouragement and advice, the medical committee of the National Hospital and the research committee of the Hospital for Sick Children for their support, Dr B Kiernander and the staff of the department of physical medicine in the Hospital for Sick Children for making available many of the facilities necessary for this work, Miss M Mayfield, the almoner, for assistance in tracing some of the cases, and Mrs B Wilson for valuable assistance in this survey

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vertebra Within a few minutes paraplegia developed with sensory loss up to T6 segment Lumbar puncture was carried out and a clear fluid smelling strongly of phenol was obtained Chemical tests confirmed the presence of phenol The paraplegia wore off in three hours, but the patient had weakness of the quadriceps femoris on the side of injection which took three months to disappear

It would seem that the needle must have entered an intervertebral foramen and pierced the dura, although no cerebrospinal fluid dripped from it and test aspirations were negative The weakness of the quadriceps is explained by the high concentration of the phenol round the spinal nerve roots emerging at the site of injection

This case has been the only one with neurological complications out of several hundred treated personally by such injections, and it certainly emphasises the need for great care when carrying out paravertebral injections of potent fluids In addition, it indicates that a considerable amount of phenol can be introduced intrathecally without lasting damage to the spinal cord In the light of this evidence it seems most unlikely that an ampoule of spinal-anæsthetic fluid immersed in 5% phenol solution could absorb, through microscopic cracks, enough phenol to cause a permanent paraplegia when injected intrathecally As Sir Francis Walshe indicates (June 2), the only common factor in the reported cases of paraplegia after spinal anæsthesia is the use of a spinal anæsthetic, and it seems clear that the risk of such a tragic complication is inherent in the injection, no matter how perfect the technique of its administration

Manchester **HERBERT HAXTON**

CAUSE OF HYPOGLYCÆMIC SYMPTOMS

SIR,—In your interesting annotation of June 9 you state that it is hard to estimate the significance of our finding that sweating still occurs in response to hypoglycæmia in patients after thoracolumbar sympathectomy It should be made clear that sweating was only seen in the regions, such as the face and upper limbs, not affected by the sympathectomy No sweating was seen in the regions denervated by the operation However, the point at issue is whether sweating still occurs when, owing to adrenal denervation, adrenaline is not liberated The persistence of sweating in these patients is thus further evidence that adrenaline plays no part in sweating due to hypoglycæmia

The lack of correlation between adrenaline release and occurrence of sweating is demonstrated in several other observations You mention the fact that intravenous infusions of adrenaline do not produce sweating It is also of interest that the sweating which is a conspicuous feature in a patient with a phæochromocytoma may persist for several days after removal of the tumour,[1] and clearly it cannot be due primarily to the excessive liberation of adrenaline

Edinburgh **E B FRENCH**
Sheffield **R KILPATRICK**

BUTALITHONE SODIUM IN ELECTROCONVULSIVE THERAPY

SIR,—It may be of interest to mention our preliminary experience with butalithone sodium ('Transithal,' 'Ulbreval') as a substitute for thiopentone sodium in anæsthesia for electroconvulsive therapy

We have found that butalithone sodium, in a dose of 0 25–0 5 g given intravenously over half a minute, depresses respiration less than does thiopentone, so that usually inflation is unnecessary The patient speedily returns to a safe state of consciousness, so that a junior nurse may be left in charge and the interval before full recovery is very considerably shorter, so that less time is wasted in waiting both by patients and staff in a busy outpatient department

In our experience, extending over several hundred cases, side effects, such as hiccup and retching, have been no commoner than with thiopentone

A F M LITTLE
Plymouth A ARNAUD REID

APPENDICECTOMY DURING GYNÆCOLOGICAL OPERATIONS

SIR,—British gynæcologists have always been somewhat doubtful about the advisability of routine appendicectomy when performing hysterectomy or other abdominal gynæcological operations Some British surgeons, however, and many Americans[1] include appendicectomy as a routine The late Victor Bonney always advised against routine appendicectomy, and obedience to the principles of this great master has caused me regret on only 3 occasions in which acute appendicitis followed within one week of hysterectomy, involving the patient in a further emergency operation I have seen a similar complication twice after vaginal hysterectomy In 1 of these patients a gangrenous appendix with peritonitis was removed forty eight hours after operation, and in another a chronic pelvic abscess involving the right fallopian tube and ovary developed and was operated upon three months after the original procedure

The great argument against routine appendicectomy has been the danger of disseminating infection from the bowel wound in the cæcum into the recently exposed cellular planes of the retroperitoneal space It is certainly true that the pelvic peritoneum recently traumatised by the operation of hysterectomy has not the same ability to resist infection as when the pelvis is intact It is possible, too, that the pelvic peritoneum is already *fully* occupied in dealing with the contamination from the vagina inherent in total hysterectomy and that the two portals of *infection* may, in certain instances, prove overwhelming

Although it is interesting to speculate on these possible sources of infection, I felt that, if exact information could be obtained from a representative number of British gynæcological surgeons, the results might be helpful to those who, like myself, wonder what is the best and safest procedure A questionnaire was, therefore addressed to 31 surgeons, and their replies are summarised below

(1) Do you remove the appendix as a routine when per*forming hysterectomy ?*

No 26, *Yes* 5

(2) Have you seen any complications as a result of this operation, such as peritonitis, intestinal obstruction, &c ?

No 25, *Yes* 6 (burst abdomen 1, peritonitis 7, intestinal obstruction 1, *Escherichia coli* infection of wound 6) (Of the 6 replying "yes," some had seen more than 1 complication—hence the discrepancy in the figures)

(3) Have you encountered any complications from not removing the appendix ?

No 30, *Yes* 1 (a case of appendicectomy after myomectomy followed by fatal peritonitis)

Of these "noes," 7 recalled patients in whom appendicectomy was necessary within a few months of the hysterectomy There is no evidence to connect the hysterectomy directly with the appendicitis—i e it did not occur within one month of the operation, as in my cases

(4) Can you give me any *references to any* published work on this subject ?

The replies to this question were an almost universal blank apart from the figures published by the Royal Society of Medicine in 1949 from the Samaritan Hospital London

(5) Any other observations ?

Of the 26 surgeons who do not routinely remove the appendix, 16 made the observation that they would

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IDIOPATHIC HYPERCALCÆMIA OF INFANTS

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IDIOPATHIC hypercalcæmia of infants is of two types (Lightwood and Stapleton 1953 Lowe et al 1954) benign or simple, with a good prognosis , and severe, with a bad prognosis and associated with mental retardation, a peculiar facial appearance, and osteosclerosis In both types calcium metabolism is deranged apparently exactly as in vitamin D intoxication (Creery and Neill 1954, Bonham Carter et al 1955)

Four infants with so called benign hypercalcæmia died in Dundee Three studied at necropsy are reported here , all had gross nephrocalcinosis and one had metastatic arterial calcification in the brain The clinical features and pathology were compared with those of other diseases causing renal calcification In particular, through the kindness of Dr Agnes R Macgregor, we have studied sections from the two cases of renal calcification which she described in the papers by Thatcher (1931, 1936) on hypervitaminosis D

Case-reports

FIRST CASE

A girl, born spontaneously on May 6, 1955 (birth weight 6 lb 2 oz), made good progress until the age of 6 months, when she weighed 17 lb 4 oz About then she suddenly became limp and pale for about 15 minutes but recovered rapidly She had similar attacks at the ages of 8 and $8^1/_2$ months She developed anorexia and constipation, began to lose weight, and vomited occasionally At the age of 9 months she was admitted to hospital on Feb 8, 1956 She had been fed on National dried milk from the age of 2 weeks and on admission she was receiving 30 oz of full cream National dried milk and about $1^1/_2$ oz of 'Farex' daily She was given half a teaspoonful of cod liver oil compound (400 I U of vitamin D) occasionally and a teaspoonful of 'Milk of Magnesia' every second day Her parents and a sister were healthy

On admission she was alert and of normal facial appearance weighed 16 lb 14 oz , was not dehydrated, and had no muscular hypotonia No cardiac murmur was heard, and an electrocardiogram was normal , her blood pressure was 120/70 mm Hg Radiography of her chest, abdomen, long bones, and skull showed no abnormality Three estimations of the plasma calcium level gave values of 12 7, 12 2, and 14 5 mg per 100 ml The blood urea level was 48 mg per 100 ml , plasma phosphate level 4 5 mg per 100 ml , plasma chloride level 98 m eq per litre, plasma bicarbonate level 20 1 m eq per litre, plasma cholesterol level 375 mg per 100 ml plasma albumin level 4 8 g per 100 ml plasma globulin level 1 7 g per 100 ml , plasma alkaline phosphatase level 16 3 King Armstrong units, hæmoglobin 12 4 g per 100 ml and leucocyte count 20 500 per c mm A catheter specimen of urine (pH 4) contained a trace of protein and a few leucocytes and was sterile on culture

Treatment and Course

The baby was treated with 'Locasol' (Trufood)—a dried milk low in calcium content—and oxytetracycline 250 mg daily by mouth , the leucocytes disappeared from the urine, and she gained weight despite anorexia and occasional vomiting *On Feb 28 she began to vomit more frequently and* passed a loose stool from which no pathogenic organisms were isolated Dehydration developed and was corrected with intravenous fluid Oxytetracycline was added to the infusion but despite this irregular pyrexia developed On March 3 the plasma calcium level was 11 4 mg per 100 ml , plasma phosphate level 3 6 mg per 100 ml , plasma alkaline phosphatase level 12 King Armstrong units, blood urea level 17 mg per 100 ml , plasma sodium level 139 m eq per litre, plasma potassium level 4 2 m eq per litre, and plasma chloride level 89 m eq per litre Intravenous therapy was discontinued, and locasol was given but was vomited , several loose stools were passed, but again no pathogenic bacteria were isolated At this stage the administration of cortisone 25 mg six hourly, potassium chloride, and locasol by intragastric drip improved her condition and stopped the vomiting Because the pyrexia continued, chloramphenicol was substituted for oxytetracycline On March 5, however, vomiting recurred, and the infant again became dehydrated An intravenous drip was started, but her condition deteriorated and she died next day, at the age of 10 months

Necropsy Findings

The body was that of a dehydrated infant weighing 14 lb 6 oz The *kidneys* were of average size (rt 25 g , lt 21 g) firm, and pale The capsule was healthy and the cortical surface smooth On section there were numerous foci of calcification in the outer medulla, forming radial white streaks, 1–2 mm long, parallel with the line of the tubules No deposits were seen in the apical half of the pyramids or in the cortex The *ribs* showed sclerosis of the cortex near the costochondral junctions Skull, lumbar vertebræ, femur, skeletal muscles, cardiovascular system (heart 30 g), respiratory, alimentary, endocrine lymphatic, hæmopoietic systems and central nervous system (brain 925 g) appeared normal

Histology

The appearance of the kidneys is described in detail below *Ribs* the cortex was much thickened but the trabeculæ were less affected The bony architecture was normal There was severe focal calcification of the media of a branch of the *middle cerebral artery* within the basal ganglia No pathological changes were found in the brain and spinal cord *Heart* a minute thrombus on the posterior wall of the left atrium was undergoing organisation , no calcification was seen *Liver* showed slight centrilobular atrophy *Œsophagus* showed slight ulceration immediately above the cardia Three *parathyroid glands* were found, of normal size and appearance Lungs tongue, submandibular salivary gland stomach and intestines, pituitary, thyroid, and adrenal glands pancreas, spleen, thymus muscles, skin internal genital organs ureters and bladder, arteries vertebræ and femur appeared normal

SECOND CASE

A report of this boy's illness has already been published (Morgan et al 1956 case 2) He was admitted on Sept 2 1954, at the age of 8 months because of anorexia, vomiting, and constipation

On admission his facial appearance was normal and no cardiac murmur was heard His plasma calcium level was 14 8 *mg per 100 ml* blood urea level 50 mg per 100 ml plasma bicarbonate level 23 3 m eq per litre and plasma chloride level 97 4 m eq per litre His urine (pH 7 5) contained

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remove it if, on inspection, they found it to be diseased, to look unhealthy, to be kinked, to be adherent retrocæcally, or to contain fæcoliths A few commented that appendicectomy undoubtedly increased the risk of postoperative pyrexia and infection and that it was a complicating factor in the convalescence after hysterectomy

As a result, the following suggestions can be made

(1) That British gynæcologists, by a majority, do not advise routine appendicectomy when performing hysterectomy

(2) That this rule should not be followed unreasonably and the appendix, if obviously diseased or unhealthy, or if containing fæcoliths, is probably best removed

(3) That there is a real danger of local and general peritonitis, and that simultaneous appendicectomy and hysterectomy should be covered by a course of postoperative antibiotics

I acknowledge the kind coöperation of the members of the Gynæcological Travellers' Club and other colleagues who kindly answered my questionnaire

St Bartholomew's Hospital
London E C 1   JOHN HOWKINS

FATS AND DISEASE

SIR,—Dr Sinclair's letter (April 7) intrigues me

In 1952 and subsequently we reported studies, begun in 1950, which showed a profound decrease in plasma cholesterol and phospholipids, in patients maintained on diets containing large amounts of unsaturated vegetable fats[1 2] Among the possible reasons for such an effect were considered (1) absence of cholesterol, per se, (2) a positive effect of some vegetable sterol, (3) a positive effect of vegetable phospholipid, (4) a positive effect of one or more fatty acids present in the vegetable fat

Over the intervening years, by a process of exclusion, all except the last have been essentially eliminated Studies in which fats of vegetable origin, but of very different iodine number, have been alternated in the diet have shown that the decrease in plasma cholesterol and phospholipid levels is directly related to the amount of unsaturated fat present in the diet[3] A very recent study, in which 100 g of a synthetic triglyceride, containing approximately 2 g of linoleic acid, has been administered daily,[4] further implements this conclusion

Dr Sinclair's observations regarding abnormal deposition of lipids in the skin under conditions of essential-fatty acid deficiency are of considerable interest, as are his speculations regarding the very possible rôle of essential fatty acid and/or pyridoxine deficiency in the pathogenesis of degenerative vascular disease His observations regarding increased requirement for essential fatty acid in male animals may be particularly pertinent in this regard

The work of Shapiro and Freedman[5] on the relation of essential fatty acid and methionine deficiencies to hypercholesteræmia may help to clarify some of the observations of Best et al[6] and of Stare et al[7] on the atherogenic effects of deficiency of choline, of methionine, and of cystine

If one accepts as a working hypothesis the concept that transport of fatty acid is the major function of cholesterol[4] and recalls that the "normal" fatty acid, which is esterified with cholesterol, is an unsaturated acid,[8] it would seem not improbable that relative or absolute unavailability of essential fatty acids may result in "jamming" of cholesterol metabolism, with resultant increase in production and abnormal deposition of cholesterol If this concept be even partly correct, it is obvious that experimental efforts designed to evaluate the specific metabolic functions of essential fatty acids, per se, are important Such studies are under way in this laboratory

Dr Keys (April 28) is less than enthusiastic regarding the concept of the importance of essential-fatty-acid deficiency in the pathogenesis of atheromatosis Dr Keys says "We have observed this [i e, differential effects of different fats upon cholesterogenesis] as well as others, including Kinsell in California, Ahrens in New York, and, recently, Bronte Stewart in South Africa" Dr Keys until recently felt that fats were fats and all were equally bad in regard to cholesterogenesis Since he appears to have accepted the weight of evidence for the profound differences in "cholesterogenic effects" between some animal and vegetable fats, we may expect that before too long he will decide that deficiency of essential fatty acids plays an important role in the pathogenesis of degenerative vascular disease

Institute for Metabolic Research
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SIR,—May I add my humble voice to the recent flurry of interest engendered by Dr Sinclair's letter on the possible multitudinous rôles of essential fatty acids in disease? Perhaps this series of letters should be entitled "Hard Fats and Hard Arteries"! Although we are living in an age of rapid advances and as rapidly crystallising opinions the healthy controversy let loose may well mark the initial break-through in one aspect of the problem of atherosclerosis While I may be accused of speaking upon a subject to which I am a relative newcomer my attention in the past three years has been devoted to orienting myself through the slough of fats, lipoprotein carriers (alpha and beta), S_f and *S-negative particles, Cohn fractions, phospholipids, lipid* phosphorus, free and esterified fractions of cholesterol and their ratios, neutral fats and triglycerides, choline and methionine effects, and the relative incidences of arterial diseases in countries torn by war and altered by peace The purpose of this attempt at orientation was to find what approaches might lead to therapy, for our formerly hypertensive patients are no longer dying of their disease but of atherosclerosis and its manifestations

Out of these contemplations came a regression (because of confusion) to non ultracentrifugal samples and to Aschoff's statement "From plasma of low cholesterol content no deposition of lipoids will occur even though the mechanical conditions are favourable"[9] Added to this might be "It may matter little how cholesterol and its esters are carried in blood, what is important is the blood level and the nature of the ester" Schönheimer's old but careful analyses of aortic plaques showed clearly that esters of cholesterol increased with severity of the lesions[10], several fatty acids were demonstrated, but the principal ones were saturated or monoethenoid (stearate, palmitate, oleate) The solubilities of cholesterol esters of unsaturated fatty acids are greater than are those of saturated acids with chains of equal lengths[11]

To my knowledge, Snapper was the first to suggest that deficiency of unsaturated acids might lead to atherosclerosis,[12] by pointing out the low incidence of the

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a few pus cells but no protein Radiographs of his skull and long bones were normal

Treatment and Course

His condition improved on treatment with cortisone and a low calcium diet, but on Dec 29, 1954, diarrhœa and vomiting developed, his urine contained protein and pus, and culture of a mid stream specimen yielded a growth of proteus No pathogenic organisms were grown from his stools He became dehydrated and was given intravenous fluid and intramuscular streptomycin 300 mg daily On Dec 31, 1954, he had a small hæmatemesis, and his plasma calcium level was 10 1 mg per 100 ml, plasma phosphorus level 6 4 mg per 100 ml, and blood urea level 95 mg per 100 ml By next day his condition had improved, and further improvement followed blood transfusion In spite of this improvement, however, he continued to vomit a little, and during the night of Jan 3, 1955, he became restless, had another small hæmatemesis, and died in coma within an hour (age 1 year)

Necropsy Findings

The body was that of an ill nourished infant weighing 13 lb The right leg was slightly œdematous proximal to the site of an intravenous drip (permission to examine the leg veins was withheld) The *kidneys* (rt 26 g, lt 31 g) were like those of case 1 (see below), but contained even greater deposits of calcium in the outer medulla, chiefly in the boundary zone *Ureters* and *bladder* were normal The *heart* weighed 35 g Many branches of the *pulmonary arteries* within the lungs were almost occluded by old and recent thrombus Both *lungs* were congested and contained small foci of early infarction at the bases The *œsophagus* contained a little blood apparently derived from superficial erosions immediately proximal to the cardia The *liver* (215 g) had a nutmeg appearance Examination of the central nervous system was not permitted Skeletal and muscular systems and endocrine, lymphatic, and hæmopoietic systems appeared normal

Histology

Kidneys see below *Lungs* showed early bronchopneumonia hæmorrhage, and small foci of early infarction The thrombus in the pulmonary arteries was undergoing organisation, and some was almost superseded by fibrous tissue *Liver* showed severe fatty change *Œsophagus* showed superficial ulceration and inflammation Two *parathyroid glands* were found, both were normal Arteries, stomach and intestines, thyroid pancreas, adrenals, muscles ribs vertebræ, thymus. and spleen appeared normal

THIRD CASE

A girl, born spontaneously on Dec 2 1954 (birth-weight 8 lb 9 oz), progressed satisfactorily until the age of 6 months, when she weighed *15 lb 5 oz*, but thereafter she became pale and listless and began to refuse her feeds Once she appeared to inhale some milk and a slight cough developed There was no vomiting but anorexia and listlessness persisted, and she was admitted at the age of 7½ months on July 23, 1955 She had been breast fed for a week after birth but thereafter given National dried milk Half a teaspoonful of cod liver oil compound (400 I U of vitamin D) was given daily from the age of 3 weeks, cereal foods were introduced at the age of 4 months She was given fluid magnesia or milk of magnesia almost every night Her parents and two brothers were healthy

On admission she was pale, flabby, and of normal facial appearance, and smiled readily She weighed only 13 lb 3 oz but was not dehydrated No cardiac murmur was heard Radiographs of her chest and long bones were normal Her plasma calcium level was 16 3 mg per 100 ml blood urea level 63 mg per 100 ml, plasma sodium level 150 m eq per litre, plasma chloride level 103 m eq per litre, and plasma bicarbonate level 17 m eq per litre, Hb 11 9 g per 100 ml, and leucocyte count 20,500 per c mm Her urine was acid (pH not recorded) and contained no protein, a catheter specimen showed 1–2 leucocytes per high power field, and *Escherichia coli* was isolated on culture

Treatment and Course

Sulphadimidine 0 25 g four hourly was given for four days, the high level of plasma calcium then became known, and intramuscular streptomycin 150 mg twice daily was substituted On this day the baby's temperature rose to 100 4°F and she vomited several times By next day (Aug 1, 1955) she was dehydrated although she had no diarrhœa, and her temperature had risen to 104 6°F, she then had a slight convulsion Her urine contained only a few leucocytes and was sterile on culture Intravenous fluid containing oxytetracycline was given, and by next morning her temperature had fallen to 99°F and she was less dehydrated Her plasma calcium level was now 9 6 mg per 100 ml, blood urea level 70 mg per 100 ml, plasma sodium level 139 m eq per litre, plasma potassium level 3 1 m eq per litre, plasma chloride level 109 m eq per litre, plasma bicarbonate level 18 m eq per litre, plasma phosphorus level 3 3 mg per 100 ml, plasma albumin level 3 3 g per 100 ml, plasma globulin level 2 2 g per 100 ml, and plasma alkaline phosphatase level 10 King-Armstrong units Her Hb was only 11 0 g per 100 ml, so a blood transfusion of 85 ml was given Throughout this day she improved she began to take interest in her surroundings and drank some milk, but she still vomited occasionally The intravenous drip was stopped and oxytetracycline continued by mouth She relapsed for no apparent reason during the following forty eight hours and died in coma on Aug 5, 1955, at the age of 8 months

Necropsy Findings

The body was that of a dehydrated female infant weighing 12 lb 14 oz The *kidneys* (rt 42 g, lt 30 g) were like those of cases 1 and 2, the only feature of note was the presence of heavy deposits of calcium confined to the outer medulla Ureters bladder, and internal *genitalia* were healthy Both *pleural sacs* contained a slight excess of serous fluid, and the *right lung* showed partial collapse posteriorly *Œsophagus*, *stomach*, and *intestines* contained a little blood apparently derived from superficial ulceration of the œsophagus immediately proximal to the cardia The cardiovascular system (heart 34 g), endocrine, skeletal and muscular systems, lymphatic and hæmopoietic systems, and central nervous system appeared normal

Histology

Kidneys see below *Lungs* showed slight chronic interstitial inflammation possibly resulting from aspiration *Œsophagus* was ulcerated and inflamed at the cardiac end Many nerve-cells in the *basal ganglia* and the Purkinje cells of the *cerebellum* showed terminal ischæmia One *parathyroid gland* was found it was histologically normal Heart and arteries, tongue, stomach, intestine, liver, thyroid, pancreas, adrenal glands, muscles, skin, internal genital organs, ureter, bladder, rib, ilium and vertebræ appeared normal

HISTOLOGY OF KIDNEYS

Case 1

Calcification was not confined to the medulla, but the few deposits in the cortex were extremely small Nearly all the medullary calcium was present in a granular amorphous form within foci of degeneration These foci were of different sizes and shapes Their numerical and anatomical distribution at different levels of the medulla suggested that they had developed in relation to the loops of Henle Thus, most of them were situated in the outer half of the medulla, where about seven eighths of the loops of Henle are said to turn back towards the cortex (Maximow and Bloom 1948), they were more sparse in the middle of the medulla and there occupied the position of the loops of Henle adjacent to and encircling the collecting tubules (fig 1), and the few foci in the apical region of the pyramids were surrounded by collecting tubules

Calcium had been deposited in the foci both in a finely granular form and in a coarser form The deposits contained abundant alkaline phosphatase and showed disintegration of the supporting stroma and basement membranes, and necrosis of the epithelium of adjacent tubules This latter change involved particularly those tubules in the position of loops of Henle and could be followed by their complete disappearance (fig 1, cf fig 6) The collecting tubules also showed segmental disintegration, although generally these tubules were less severely injured, involvement of their basement membrane and epithelium was occasionally followed by narrowing of the lumen, but most of the collecting tubules within these zones of disintegrating tissue were distinctly dilated

vertebra Within a few minutes paraplegia developed with sensory loss up to T6 segment Lumbar puncture was carried out and a clear fluid smelling strongly of phenol was obtained Chemical tests confirmed the presence of phenol The paraplegia wore off in three hours, but the patient had weakness of the quadriceps femoris on the side of injection which took three months to disappear

It would seem that the needle must have entered an intervertebral foramen and pierced the dura, although no cerebrospinal fluid dripped from it and test aspirations were negative The weakness of the quadriceps is explained by the high concentration of the phenol round the spinal nerve-roots emerging at the site of injection

This case has been the only one with neurological complications out of several hundred treated personally by such injections, and it certainly emphasises the need for great care when carrying out paravertebral injections of potent fluids In addition, it indicates that a considerable amount of phenol can be introduced intrathecally without lasting damage to the spinal cord In the light of this evidence it seems most unlikely that an ampoule of spinal-anæsthetic fluid immersed in 5% phenol solution could absorb, through microscopic cracks, enough phenol to cause a permanent paraplegia when injected intrathecally As Sir Francis Walshe indicates (June 2), the only common factor in the reported cases of paraplegia after spinal anæsthesia is the use of a spinal anæsthetic, and it seems clear that the risk of such a tragic complication is inherent in the injection, no matter how perfect the technique of its administration

Manchester HERBERT HAXTON

CAUSE OF HYPOGLYCÆMIC SYMPTOMS

SIR,—In your interesting annotation of June 9 you state that it is hard to estimate the significance of our finding that sweating still occurs in response to hypoglycæmia in patients after thoracolumbar sympathectomy It should be made clear that sweating was only seen in the regions such as the face and upper limbs, not affected by the sympathectomy No sweating was seen in the regions denervated by the operation However, the point at issue is whether sweating still occurs when, owing to adrenal denervation, adrenaline is not liberated The persistence of sweating in these patients is thus further evidence that adrenaline plays no part in sweating due to hypoglycæmia

The lack of correlation between adrenaline release and occurrence of sweating is demonstrated in several other observations You mention the fact that intravenous infusions of adrenaline do not produce sweating It is also of interest that the sweating which is a conspicuous feature in a patient with a phæochromocytoma may persist for several days after removal of the tumour,[1] and clearly it cannot be due primarily to the excessive liberation of adrenaline

Edinburgh E B FRENCH
Sheffield R KILPATRICK

BUTALITHONE SODIUM IN ELECTROCONVULSIVE THERAPY

SIR,—It may be of interest to mention our preliminary experience with butalithone sodium ('Transithal,' 'Ulbreval') as a substitute for thiopentone sodium in anæsthesia for electroconvulsive therapy

We have found that butalithone sodium, in a dose of 0 25–0 5 g given intravenously over half a minute, depresses respiration less than does thiopentone, so that usually inflation is unnecessary The patient speedily returns to a safe state of consciousness, so that a junior nurse may be left in charge, and the interval before full recovery is very considerably shorter, so that less time is wasted in waiting both by patients and staff in a busy outpatient department

In our experience, extending over several hundred cases, side effects, such as hiccup and retching, have been no commoner than with thiopentone

A F M LITTLE
Plymouth A ARNAUD REID

APPENDICECTOMY DURING GYNÆCOLOGICAL OPERATIONS

SIR,—British gynæcologists have always been somewhat doubtful about the advisability of routine appendicectomy when performing hysterectomy or other abdominal gynæcological operations Some British surgeons, however, and many Americans[1] include appendicectomy as a routine The late Victor Bonney always advised against routine appendicectomy, and obedience to the principles of this great master has caused me regret on only 3 occasions in which acute appendicitis followed within one week of hysterectomy, involving the patient in a further emergency operation I have seen a similar complication twice after vaginal hysterectomy In 1 of these patients a gangrenous appendix with peritonitis was removed forty-eight hours after operation, and in another a chronic pelvic abscess involving the right fallopian tube and ovary developed and was operated upon three months after the original procedure

The great argument against routine appendicectomy has been the danger of disseminating infection from the bowel wound in the cæcum into the recently exposed cellular planes of the retroperitoneal space It is certainly true that the pelvic peritoneum recently traumatised by the operation of hysterectomy has not the same ability to resist infection as when the pelvis is intact It is possible, too, that the pelvic peritoneum is already fully occupied in dealing with the contamination from the vagina inherent in total hysterectomy and that the two portals of infection may, in certain instances, prove overwhelming

Although it is interesting to speculate on these possible sources of infection, I felt that, if exact information could be obtained from a representative number of British gynæcological surgeons, the results might be helpful to those who, like myself, wonder what is the best and safest procedure A questionnaire was, therefore addressed to 31 surgeons, and their replies are summarised below

(1) *Do you remove the appendix as a routine when performing hysterectomy ?*
No 26, *Yes* 5

(2) Have you seen any complications as a result of this operation, such as peritonitis, intestinal obstruction &c ?
No 25, *Yes* 6 (burst abdomen 1, peritonitis 7, intestinal obstruction 1, *Escherichia coli* infection of wound 6) (Of the 6 replying 'yes," some had seen more than 1 complication—hence the discrepancy in the figures)

(3) Have you encountered any *complications from not* removing the appendix ?
No 30, *Yes* 1 (a case of appendicectomy after myomectomy followed by fatal peritonitis)

Of these 'noes," 7 recalled patients in whom appendicectomy was necessary within a few months of the hysterectomy There is no evidence to connect the hysterectomy directly with the appendicitis—i e it did not occur within one month of the operation, as in my cases

(4) Can you give me any *references to any* published work on this subject ?

The replies to this question were an almost universal blank, apart from the figures published by the Royal Society of Medicine in 1949 from the Samaritan Hospital London

(5) Any other observations ?

Of the 26 surgeons who do not routinely remove the appendix, 16 made the observation that they would

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[1] Swan H J C *Brit med J* 1951, i 440

[1] Taniguchi T Kilkenny G S *Amer J Obstet Gynec* 1950 60 1359

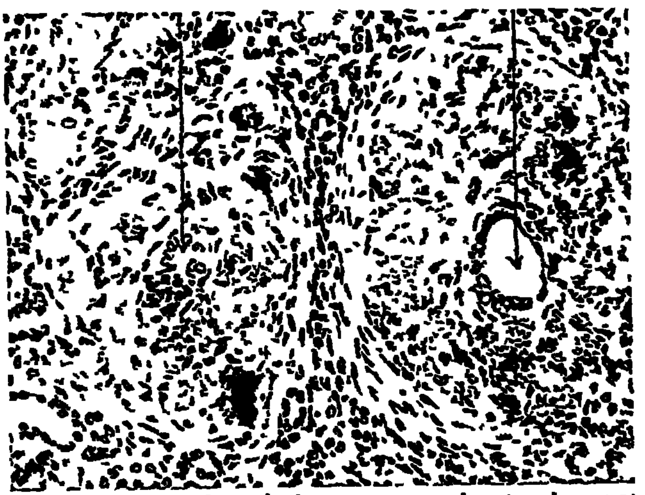

Fig. 1—Renal tissue of case 1, showing two granulomatous lesions at sites of amorphous deposits encircling damaged collecting tubules (arrowed). The histiocytic reaction is accompanied by giant cells, and fibrosis has developed at the periphery of each lesion. (Hæmatoxylin and eosin. × 220.)

These foci were infiltrated by histiocytic cells with twisted pyknotic nuclei; a few multinucleated giant cells were also present (fig. 1), but these were not all of foreign-body type, some apparently being shrivelled degenerating tubular epithelium. This granulomatous inflammation proceeded to fibrosis (fig. 1); hence, the presence of scar tissue round a dilated or a ruptured segment of a collecting tubule (cf. fig. 6 from case 3) probably indicated a former site of deposition of calcium and necrosis.

Some calcium had been deposited as concretions. Such deposits were rare in the medulla in comparison with the amorphous type, but the scanty minute cortical deposits were all of this nature and were similar to small deposits to be described in cases 2 and 3.

Signs of general tubular obstruction were slight—a few dilated collecting tubules, occasionally with non-calcified casts. The convoluted tubules were swollen and hydropic, as if filled with glycogen. A few glomeruli in the outer cortex were undergoing regression and obliteration, but most looked healthy. No vascular lesions were seen.

Cases 2 and 3

The changes in the kidneys were virtually identical in the two cases. There were massive deposits of calcium in the outer medulla, especially in the boundary zone (figs. 2 and 3). There were also a few minute deposits throughout both medulla and cortex.

Amorphous deposits of calcium, like those in case 1, were present throughout the medulla, but many of the granulomas were at a more advanced stage, with more fibrosis and much greater dilatation of the collecting tubules—weakened, presumably, by damage to their basement membrane and by disintegration of the surrounding tissue.

Most of the deposits of calcium in the medulla, however, consisted of concretions of various sizes, and these looked deceptively like calcified hyaline casts obstructing dilated tubules (figs. 2 and 3). This impression of an intratubular situation was strengthened by the flattened cells lining some of the spaces in which the concretion lay, but examination of an early lesion (fig. 7) showed that such cells were mesenchymal and not tubular epithelium. Most of the surviving tubules were dilated collecting tubules with flattened but distinctive epithelium. Many were distorted, and some were almost obliterated by deposits of calcium immediately outside their stretched out epithelium; but others were widely dilated, despite the proximity of large concretions, and some contained hyaline non-calcified casts.

Inflammation at the sites of these calcified concretions was slight; in some of the small deposits there was a mild cellular reaction of histiocytic type, and around the large lesions tubules were compressed and atrophied and there was mild fibrosis. Some of the dilated collecting tubules contained a few polymorphs, but there was no other evidence of pyogenic inflammation.

The mode of evolution of the large deposits of calcium—in all three cases—can only be inferred by analogy with smaller lesions. Thus, in one of the smallest granulomatous lesions (fig. 4) amorphous calcareous material had apparently been precipitated not in but between the medullary tubules. The tubules were damaged and compressed; their basement membrane had disappeared; and their epithelial lining, attenuated and necrotic, was invaginated by the interstitial calcium now in direct contact with its outer surface. In another small lesion (fig. 5) the calcareous material was again interstitial, but here irregular concretions of varied size and density surrounded and compressed the adjacent limbs of Henle. Not all the calcium in such lesions was extratubular, however, for (as this figure shows) calcification had transgressed the basement membrane of one of the tubules and involved its epithelial lining cells but not the hyaline cast in its lumen.

A few of the concretions invaginating the epithelial lining of collecting tubules (fig. 3) appeared to lie between

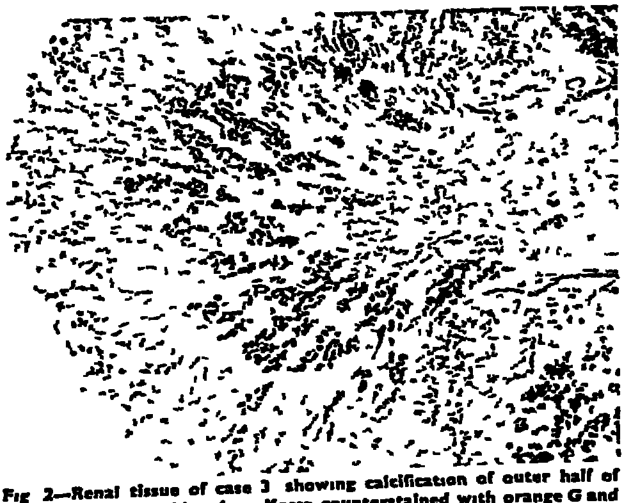

Fig. 2—Renal tissue of case 3, showing calcification of outer half of medullary pyramids. (von Kossa counterstained with orange G and neutral red. × 83.)

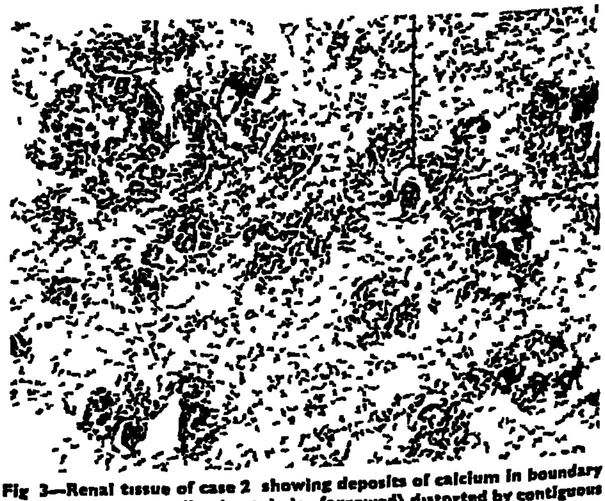

Fig. 3—Renal tissue of case 2, showing deposits of calcium in boundary zone, and cystic collecting tubules (arrowed) distorted by contiguous masses. (Hæmatoxylin and eosin. × 66.)

remove it if, on inspection, they found it to be diseased, to look unhealthy, to be kinked, to be adherent retrocæcally, or to contain fæcoliths A few commented that appendicectomy undoubtedly increased the risk of postoperative pyrexia and infection and that it was a complicating factor in the convalescence after hysterectomy

As a result, the following suggestions can be made

(1) *That British gynæcologists*, by a majority, do not advise routine appendicectomy when performing hysterectomy

(2) That this rule should not be followed unreasonably and the appendix, if obviously diseased or unhealthy, or if containing fæcoliths, is probably best removed

(3) That there is a real danger of local and general peritonitis, and that simultaneous appendicectomy and hysterectomy should be covered by a course of postoperative antibiotics

I acknowledge the kind coöperation of the members of the Gynæcological Travellers' Club and other colleagues who kindly, answered my questionnaire

St Bartholomew's Hospital
London, E C 1

JOHN HOWKINS

FATS AND DISEASE

SIR,—Dr Sinclair's letter (April 7) intrigues me

In 1952 and subsequently we reported studies, begun in 1950, which showed a profound decrease in plasma cholesterol and phospholipids, in patients maintained on diets containing large amounts of unsaturated vegetable fats[1][2] Among the possible reasons for such an effect were considered (1) absence of cholesterol, per se, (2) a positive effect of some vegetable sterol, (3) a positive effect of vegetable phospholipid, (4) a positive effect of one or more fatty acids present in the vegetable fat

Over the intervening years, by a process of exclusion, all except the last have been essentially eliminated Studies in which fats of vegetable origin, but of very different iodine number, have been alternated in the diet have shown that the decrease in plasma cholesterol and phospholipid levels is directly related to the amount of unsaturated fat present in the diet[3] A very recent study, in which 100 g of a synthetic triglyceride, containing approximately 2 g of linoleic acid, has been administered daily,[4] further implements this conclusion

Dr Sinclair's observations regarding abnormal deposition of lipids in the skin under conditions of essential-fatty-acid deficiency are of considerable interest, as are his speculations regarding the very possible rôle of essential fatty acid and/or pyridoxine deficiency in the pathogenesis of degenerative vascular disease His observations regarding increased requirement for essential fatty acid in male animals may be particularly pertinent in this regard

The work of Shapiro and Freedman[5] on the relation of essential-fatty acid and methionine deficiencies to hypercholesterolæmia may help to clarify some of the observations of Best et al[6] and of Stare et al[7] on the atherogenic effects of deficiency of choline, of methionine, and of cystine

If one accepts as a working hypothesis the concept that transport of fatty acid is the major function of cholesterol[4] and recalls that the "normal" fatty acid, which is esterified with cholesterol, is an unsaturated acid,[8] it would seem not improbable that relative or absolute unavailability of essential fatty acids may result in "jamming" of cholesterol metabolism, with resultant increase in production and abnormal deposition of cholesterol If this concept be even partly correct, it is obvious that experimental efforts designed to evaluate the specific metabolic functions of essential fatty acids, per se, are important Such studies are under way in this laboratory

Dr Keys (April 28) is less than enthusiastic regarding the concept of the importance of essential-fatty-acid deficiency in the pathogenesis of atheromatosis Dr Keys says "We have observed this [i e, differential effects of different fats upon cholesterogenesis] as well as others, including Kinsell in California, Ahrens in New York, and, recently, Bronte Stewart in South Africa" Dr Keys until recently felt that fats were fats, and all were equally bad in regard to cholesterogenesis Since he appears to have accepted the weight of evidence for the profound differences in "cholesterogenic effects" between some animal and vegetable fats, we may expect that before too long he will decide that deficiency of essential fatty acids plays an important role in the pathogenesis of degenerative vascular disease

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LAURANCE W KINSELL

SIR,—May I add my humble voice to the recent flurry of interest engendered by Dr Sinclair's letter on the possible multitudinous rôles of essential fatty acids in disease? Perhaps this series of letters should be entitled "Hard Fats and Hard Arteries"! Although we are living in an age of rapid advances and as rapidly crystallising opinions, the healthy controversy let loose may well mark the initial break-through in one aspect of the problem of atherosclerosis While I may be accused of speaking upon a subject to which I am a relative newcomer, my attention in the past three years has been devoted to orienting myself through the slough of fats, lipoprotein carriers (alpha and beta), S_f and S negative particles, Cohn fractions, phospholipids, lipid phosphorus, free and esterified fractions of cholesterol and their ratios, neutral fats and triglycerides, choline and methionine effects, and the relative incidences of arterial diseases in countries torn by war and altered by peace The purpose of this attempt at orientation was to find what approaches might lead to therapy, for our formerly hypertensive patients are no longer dying of their disease but of atherosclerosis and its manifestations

Out of these contemplations came a regression (because of confusion) to non-ultracentrifugal simples and to Aschoff's statement "From plasma of low cholesterol content no deposition of lipoids will occur even though the mechanical conditions are favourable"[9] Added to this might be "It may matter little how cholesterol and its esters are carried in blood, what is important is the blood level and the nature of the ester" Schonheimer's old but careful analyses of aortic plaques showed clearly that esters of cholesterol increased with severity of the lesions[10], several fatty acids were demonstrated, but the principal ones were saturated or monoethenoid (stearate, palmitate, oleate) The solubilities of cholesterol esters of unsaturated fatty acids are greater than are those of saturated acids with chains of equal lengths[11]

To my knowledge, Snapper was the first to suggest that deficiency of unsaturated acids might lead to atherosclerosis,[12] by pointing out the low incidence of the

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[1] Kinsell L W Partridge J Boling L A Margen S Michaels G D *J clin Endocrin* 1952 12 909

[2] Kinsell L W Michaels G D Partridge J W Boling L A Balch H E Cochrane G C *J clin Nutr* 1953 1 224

[3] Kinsell L W Michaels G D *Fed Proc* 1955 14 661 Friskey R W Michaels G D Kinsell L W *Circulation* 1955 12 492

[4] Kinsell L W Friskey R W Michaels G D Brown F R *J clin Nutr* (in the press)

[5] Shapiro S L Freedman L *Amer J Physiol* 1955 181 441

[6] Wilgram G F Hartroft, W S Best C H *Brit med J* 1954 ii 1

[7] Mann G V Andrus S B McNally A Stare F J *J exp Med* 1953 98 195

[8] Kelsey F E Longenecker H E *J biol Chem* 1941 139 727

[9] Aschoff L Lectures on Pathology New York 1924 p 131

[10] Schönheimer R *Z physiol Chem* 1926 160 61

[11] Deuel H J jun The Lipids New York 1951 vol 1

[12] Snapper I Chinese Lessons to Western Medicine New York 1941

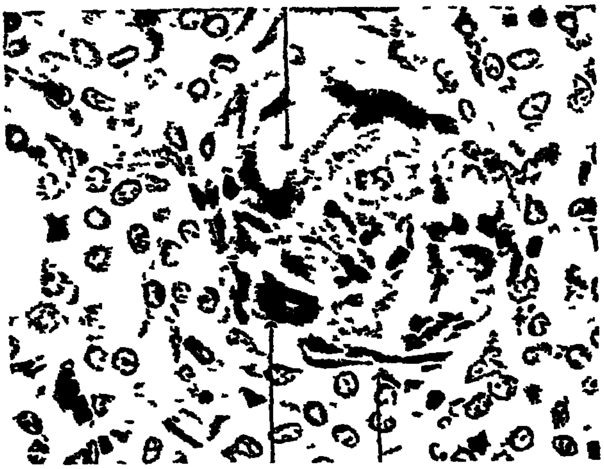

Fig 4.—Renal tissue of case 3, showing early and apparently intertubular lesion. Calcifying interstitial tissue is infiltrated with histiocytes. Tubules (arrowed) are compressed and show degeneration of epithelium and destruction of basement membrane. Top arrowhead lies on hyaline cast. (Hæmatoxylin and eosin × 535.)

the epithelium and the basement membrane. These concretions also are believed to have originated outside but up against the tubules, as in fig 7, for reticulin stains seem to show that the delicate intervening stroma may disappear and the once interstitial calcium now lies within the tubule, although still outside its epithelial lining. This illustration also shows how tubular distortion, comparable with that seen in the big deposits, can be produced from without by quite small interstitial concretions close to the basement membrane.

Cortical deposits of calcium were small and scanty. As in case 1, they appeared to be primarily interstitial, but in a few instances calcification had apparently involved some of the adjacent tubular epithelium. Signs of tubular obstruction within the cortex—dilatation of tubules and formation of hyaline casts—were less than would be expected from such gross medullary lesions, but the "bulk" of the convoluted tubules was considerably less than normal—the result, apparently, of atrophy or of failure of growth rather than of destruction. Most of the glomeruli were healthy, but some in the outer cortex were small and covered by prominent cuboidal epithelial cells and looked immature; a few of these superficial glomeruli also showed partial sclerosis, but there was no evidence of active glomerulitis. No vascular damage was seen.

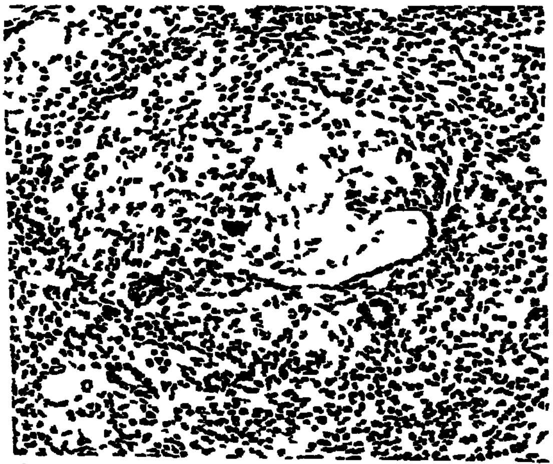

Fig 6.—Renal tissue of case 3, showing repair of focus of destruction in medulla. Cystic space in scar tissue is partially lined by epithelium and contains a large cast. Hardly any calcium can be seen. Giant cells, some possibly derived from tubular epithelium, are present in scar tissue. (Hæmatoxylin and eosin × 165.)

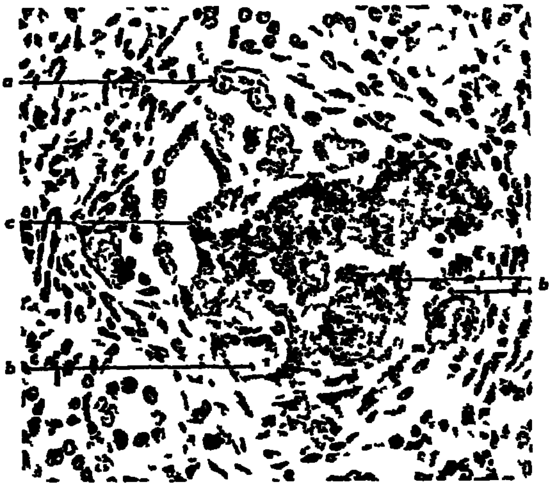

Fig 5.—Renal tissue of case 2, showing interstitial calcium concretions compressing tubules: *a*, laminated concretions; *b*, lumen of compressed tubules; *c*, calcification of epithelium of cast-containing tubule. (Hæmatoxylin and eosin × 275.)

DISCUSSION

The distinction between idiopathic hypercalcæmia of the simple type and infantile renal acidosis rests mainly on the biochemical findings. Thus, the normal values of the plasma bicarbonate level in cases 1 and 2 reasonably exclude renal acidosis. On the other hand, all the biochemical changes in case 3 could be found in either syndrome. Nevertheless, although the plasma-bicarbonate level is low, we accept the combination of a high plasma-calcium level, a normal plasma-chloride level, and an acid urine in the absence of dehydration as indicating idiopathic hypercalcæmia.

The two forms of idiopathic hypercalcæmia have been differentiated by clinical and radiological criteria since the biochemical changes do not provide a clear distinction. Despite their fatal outcome our cases conformed with the simple, so called benign, type. However, the validity of the criteria used is by no means certain, and gradations between the two forms are now being recognised (Russell et al. 1954). The peculiar facial appearance, believed by some to be distinctive (Schlesinger et al.

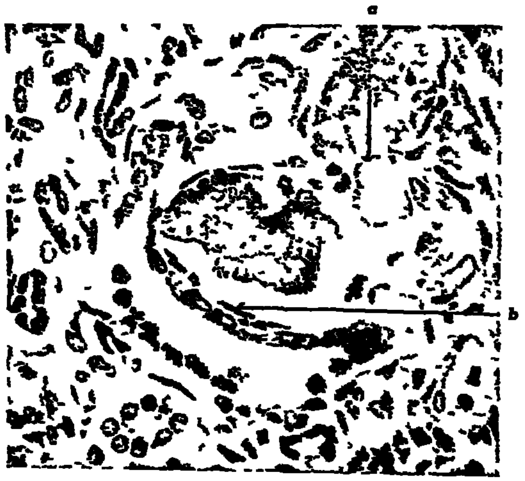

Fig 7.—Renal tissue of case 2, showing interstitial cast-like concretion distorting a collecting tubule. Another concretion, less intensely stained, is forming at *a*. Flattened cells (*b*) outside the tubular basement membrane line the interstitial "space" in which the concretion has formed. (Hæmatoxylin and eosin × 386.)

disease in Northern Chinese, their high dietary intakes of linoleate and particularly linolenate, and the high iodine number of their serum-lipids (mean 156.6, compared with about 110 for allergic individuals and 84 in our laboratories for atherosclerotic persons). He attempted to obtain a lipid chemist from this country for the purpose of measuring the degree of unsaturation in Chinese fat, when his work was interrupted by the Sino-Japanese war. Obviously, more studies on the iodine numbers of plasma lipids should be made. The fact that four groups of investigators (Ahrens et al.[13] in New York, Beveridge et al.[14] in Kingston, Ontario, Malmros and Wigand[15] in Lund, and Kinsell et al.[16] in San Francisco) and now a fifth (Bronte Stewart et al.[17] in South Africa) all have conclusively demonstrated marked decreases in total plasma cholesterol by feeding vegetable fats with high iodine numbers, leads one to the inescapable conclusion that synthesis, transport, or katabolism of this sterol is intimately affected by some constituent found in the oil and not in saturated animal fats. What is this substance?

Most of your respondents, as I did, have implicated linoleic acid. Dr. Sinclair himself suggests linoleic and arachidonic acids. There are discrepant experimental results inconsistent with this idea.

While the data is not complete, examination of the unsaturated fatty acid contents of the oils which lower plasma cholesterol, as listed in Deuel's comprehensive book,[11] usually contain linolenic acid, as well as the less unsaturated linoleate. Thus, soybean oil (3–11%) and corn oil (0.4%) are those most commonly used; the former is more effective in lowering cholesterol. Likewise, linseed (40–53%, the cake being used as a food in Eastern Europe and the U.S.S.R.), millet seed (6–8%), walnut (3.2%), beechnut (2.9%), mustard (2.7%), wheat, and rye are other sources of linolenate. Alcoholic extract of brain lowers plasma cholesterol[18]; it may contain at least one unsaturated fatty acid of the linolenate or arachidonate type. On the other hand, there is plenty of linoleic acid in one vegetable oil shown to raise plasma cholesterol—cottonseed oil (15%, equal to corn oil), as demonstrated by Prof. Ancel Keys. All of the cholesterol-raising fats listed by him are *deficient in linolenate*, although it is true that contents may vary according to the food intake (for animal fat) or the variety of plant, the climate, and the soil, which may account for discrepant results. Some of the oils used by Bronte Stewart contain linolenate, arachidonate, or longer chained more highly unsaturated fatty acids, with the possible exception of ground nut oil. For example, African sunflower seed oil probably contains linolenate, South American probably does not. Therefore, the common denominator of cholesterol lowering oils in man may actually be linolenate or a fatty acid of a higher degree of unsaturation, plus linoleate. Linolenate is a precursor of hexaenoate and linoleate of arachidonate.[19]

Bronte Stewart et al. obtained results with linolenic-deficient oils quite divergent from those obtained by others, especially in the case of olive oil, which usually raises plasma cholesterol. In fairness to their excellent and careful work, it is doubtful that a normocholesterolæmic Bantu would respond to an acute fat load in a manner identical with a hypercholesterolæmic Englishman or American. For the former obviously has a healthy cholesterol metabolism, while that of the latter is diseased to some degree or another, if we can believe the statistics. It is probable that the normal values of total plasma cholesterol are 100–160 mg. per 100 ml., higher values in Europeans and Americans representing disorder.

This attractive hypothesis, however, cannot account entirely for the atherosclerosis found so commonly in civilised persons all over the world, but often absent in the "uncivilised." The presence of extensive aortic calcification in some Egyptian mummies in the British Museum attests to its antiquity. In Japan, often cited as a sclerosis-free area, Kimura's careful study of 1007 necropsies showed gross coronary atherosclerosis of some degree in 80–100% of males of 35 years or older, although the incidence in 3600 less carefully studied cases was a little more than half that value in patients 65 and older. High-grade coronary disease, however, was present in less than 10%.[20] Similar incidences were found in Hawaiian orientals, although severe degrees were present in about half.[21] It is doubtful, therefore, whether we can attribute the presence or the absence of the disease to one factor—essential fatty acid deficiency—although this factor may be a strong influence in the severity and therefore the mortality rate through ischæmic and hæmorrhagic complications.

Not to confuse the point further, but merely to indicate other known influences of "civilisation" which may be accessory factors in abnormal cholesterol and fatty acid metabolism and in providing an intimal lesion in which cholesterol esters may deposit, we should not forget two. As Dr. Sinclair has well pointed out, vitamin B_6 or pyridoxal phosphate may be involved. This ubiquitous coenzyme not only acts as codecarboxylases and cotransaminases but promotes the conversion of linoleate to arachidonate and linolenate to hexaenoate in rats,[22] thereby increasing the unsaturation of partly unsaturated fatty acids. Furthermore, deficient states in monkeys result in subintimal lesions microscopically identical with those of early atherosclerosis[23][24] (providing a *locus* where lipids are deposited?), and deficient monkeys fed cholesterol exhibit much higher blood levels than do controls.[25] This heat-labile, light-unstable coenzyme is low in many processed foods, and many dietaries may be marginal during winter seasons.[26] Does a partly deficient man handle linoleate or even oleate less readily than one with adequate amounts of this vitamin?

The second influence is, strange to say, in trace metals. Pyridoxal probably requires a trace metal for coenzyme activity[27]; on two decarboxylases that metal is possibly zinc. Curran has shown that chromium increases hepatic synthesis of cholesterol and fatty acids in rats by 150%, vanadium depressing synthesis markedly[28] and even reducing aortic lipids by a half in cholesterol-fed rabbits.[29] Furthermore, a chelating agent which is not metabolised, ethylenediamine tetra-acetate, reduces plasma cholesterol markedly and rapidly when given intravenously and often reduces it to "Bantu levels" when given orally.[30] There are variable but often relatively large amounts of "abnormal" trace elements in American human tissues from all cities studied,[31] with fewer in American stillborn infants and traces to none in the tissues of "raw" African natives (I. H. Tipton, personal communication). Renal and hepatic cadmium, a decarboxylase inhibitor, chromium, tin, titanium, nickel, and lead are some of

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1956), may indicate the severe type of illness, and certainly its occurrence has not been established in simple hypercalcæmia, it was absent from all our cases Radiography does not provide an absolute distinction, for osteosclerosis, present in all cases of the severe form, has been observed, albeit of minor degree, in the simple form (Creery and Neill 1954), it was not detected radiologically in any of our cases but was found at necropsy in case 1 Finally, a cardiac murmur, absent in all our cases, has been heard in infants with the simple type (Lowe et al 1954, Creery and Neill 1954) and has been absent in some cases of the severe form (Schlesinger et al 1956)

The renal lesion of simple hypercalcæmia is not specific, for interstitial and subepithelial calcification has been observed in infantile renal acidosis (Butler et al 1936, Doxiadis 1952) and as an incidental finding at necropsy in various diseases of infancy (A M Macdonald, personal communication) Glomerular immaturity and small tubular mass have also been noted in chronic renal acidosis of infants without renal calcification (Hutchison and Macdonald 1951) These features, in our opinion, are not the cause of renal calcification and may simply be the consequences of failure to thrive None the less the possibility of direct glomerular damage cannot be excluded in view of the findings in the severe form of the disease, these, according to Schlesinger et al (1956), may range from minute foci of calcification throughout the cortex and medulla to gross cortical destruction Admittedly the severe cases have been characterised by prolonged and recurrent urinary infection, but the glomerular lesions have apparently not been regarded as infective, and Schlesinger et al suggest that hypercalcæmia may itself cause glomerular damage The greatest glomerular and cortical tubular destruction was found in the three severe cases of longest duration, whereas in the fourth case (Dawson et al 1954) glomerular changes were as slight as in our cases of simple hypercalcæmia, which proved fatal at a comparable age

Mental retardation has been present in all infants with the severe type of idiopathic hypercalcæmia who have survived to the age of 2 years (Schlesinger et al 1956) but not in infants who have recovered from the simple type The three infants we have described did not appear to be mentally retarded, but all died within the first year of life Neuronal damage in one of the two brains examined at necropsy (case 3) was probably caused by terminal anoxia and not directly by the hypercalcæmic state Nevertheless the calcification of a cerebral artery in case 1 shows that there is a risk of cerebrovascular damage even in the simple form of idiopathic hypercalcæmia

Hypervitaminosis D presents striking resemblances clinical and biochemical, to idiopathic hypercalcæmia, Radiologically there are insufficient data in the published reports of vitamin D intoxication to allow an adequate comparison, nevertheless osteosclerosis comparable with that seen in hypercalcæmia of the severe type has been recorded (Hess and Lewis 1928, Ross 1952) The cause of osteosclerosis in the two diseases has not been established, but its appearance and regression in idiopathic hypercalcæmia seem to be related to episodes of impaired renal function (Harris 1954, Schlesinger et al 1956)

The diagnosis of hypervitaminosis D in fatal cases of renal calcification, such as those of Thatcher (1931, 1936) has been criticised by Wolf (1943), who considered that the dosage of vitamin in these cases was too small to cause metastatic calcification except in the presence of some underlying disorder—e g, severe renal disease By his own experiments, however, Wolf confirmed that vitamin D in large doses can cause nephrocalcinosis in "healthy" infants The role of vitamin D in Thatcher's cases cannot now be assessed, but review of the histological changes in the kidney has shown them to be essentially the same as in our cases of simple hypercalcæmia (A R Macgregor, personal communication), in which the daily intake of vitamin D was at least 2000 I U at the time of admission to hospital

The cause of death of our three infants was clearly not renal failure, despite the involvement of so many renal tubules by the deposits of calcium We believe that the death of the second infant was precipitated by acute bronchopneumonia and widespread pulmonary thrombosis, and, theoretically, the formation of thrombus—conceivably initiated by emboli from veins in the leg—might have been favoured by cortisone (Cosgriff 1951) as well as by the hypercalcæmic state No adequate explanation for the deaths of the first and third infants was found One factor common to all three was persistent vomiting which proved very difficult to control Even so, the plasma electrolyte levels did not indicate a biochemical disturbance serious enough to cause death Unexplained deaths have previously been recorded in idiopathic hypercalcæmia (Harris 1954, Dawson et al 1954), and equally mysterious deaths in hypervitaminosis D, with renal calcification as the only gross lesion, have been attributed to a direct toxic action of the vitamin (Bauer and Freyberg 1946)

However close the resemblance between the two conditions—and the facts are surely suggestive—the evidence implicating vitamin-D intoxication in idiopathic hypercalcæmia is at best circumstantial Nevertheless so many factors may enhance the toxicity of vitamin D (Wolf 1943) that, until the cause of idiopathic hypercalcæmia is found, the amount given to infants should be kept under constant review

Summary

The clinical and pathological features of three fatal cases of the simple form of idiopathic hypercalcæmia are described and compared with those of the severe form and of hypervitaminosis D

The deaths of these three infants have not been satisfactorily explained, but a fatal outcome may possibly have been precipitated by persistent vomiting

Renal calcification was the salient pathological feature in all three Most of the deposits of calcium were in the outer medulla, the cortex being only slightly affected Some of the medullary deposits appeared to be closely related to the loops of Henle and contained amorphous calcium, such deposits were *associated* with focal degeneration of both interstitial tissue and tubules and with granulomatous inflammation The rest of the medullary calcium, and the few small cortical deposits, consisted of concretions in the interstitial tissue, and these produced tubular compression and distortion

The renal lesions are not specific, similar changes having been found in cases ascribed to hypervitaminosis D and in infantile renal acidosis, as well as in association with various other diseases of infancy

Metastatic calcification of a cerebral artery and osteosclerosis were present in one of the cases

We are grateful to Prof J L Henderson and Prof A C Lendrum for their advice and criticism, and to Dr A R Macgregor and Dr A M Macdonald for their generous help and for allowing us to study their cases The histological sections and photomicrographs were prepared by Mr R S P Fawkes, A I M L T

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the "abnormal"-*metals found, of which several are* apparently the results of "civilisation," showing marked differences in these three groups Some of these are antimetabolic Cadmium is especially high and accumulates with age Can an abnormal trace metal affect a pyridoxal enzyme system so as to cause a conditioned local deficiency ? If so, lipid metabolism might be altered

Therefore, intermittent or chronic deficiency of essential fatty acids in man, a distinct possibility in many areas of the world where atherosclerosis is endemic and almost universal, may be only one, albeit a large, factor in furthering the development of this most important disease It is possible that a high intake of saturated fats may produce deficiency when either intake is marginal or metabolic pathways are disturbed by exogenous influences On the other hand, we must not neglect biochemically related factors, of which trace metals and vitamin B_6 are two examples, for this disease is probably not the result of any one single disorder in all nations and races

We cannot wait, however, until all of the metabolic pathways of fatty acid, cholesterol, and collagen metabolism are clearly understood before attempting therapy by lowering plasma-cholesterol in man Tools are now offered which will do this without hazard or excessive inconvenience During the present interesting interim between the state of knowledge now and the advent of specific therapy, it has been our practice to lower blood-cholesterol in our patients by (*a*) reducing the intake of saturated fat by about 50%, (*b*) providing about 0 5 g linolenate per day by the use of soybean oil in salad dressing, sauces, and cooking, (*c*) giving the calcium complex of E D T A in doses of 1 0 g per day orally, and (*d*) giving an adequate intake of pyridoxine, on purely theoretical grounds (5 to 10 mg per day) It may be a long step, however, between low plasma cholesterol levels and demonstration of reversal of the arterial lesions

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HENRY A SCHROEDER

CIRCULATORY FAILURE IN MARYLEBONE ?

SIR,—In some lowly invertebrates the blood vessels are traversed in both directions, though it must be conceded to the purists that this does not happen simultaneously Up the evolutionary scale arteries and *veins* are differentiated, the blood traffic, so to say, being one-way only

Your older readers will recall the happy, albeit primitive, days when the streets of Marylebone were coursed either North and South or East and West, and the traffic was contained With its rapid increase over the past years evolved a strange and hybrid vascular system of one way vessels, two-way vessels, and arteriovenous aneurysms No doubt some traffic-happy authority had hoped thereby to improve the circulation of this increasingly cyanosed area Instead there has been a further and polycythæmic increase in the number of (if I may be forgiven the term) carpuscles, anisocytotic and even crash crenated, trying to circulate along the narrowing vessels For, to complete the pathology, rows and double rows of parked cars line these vessels and are virtually becoming organised into plaques Spasmodic occlusion occurs frequently, and it can be only a matter of time before mass thrombosis ensues and the circulation fails completely

Traditionally Harley Street and its environs has long been a medical precinct, and, despite some invasion by office and flat, it remains predominantly medical But its streets are being used to saturation point as convenient all day parking places for the cars of business people and shoppers from the adjoining parts of the West End To the doctor trying to reach his *professional* rooms, and *the patient trying to meet him in consultation*, it becomes increasingly difficult and time consuming to penetrate its congested roads and to find a temporary resting-place for a vehicle

As the *New Statesman* was once described of Bloomsbury, so *The Lancet* might still be called the parish magazine of the Harley Street area This, Sir, is my reason for drawing your attention to the above troublesome and disorganising situation

London W 1

S CHARLES LEWSEN

Obituary

WILLIAM HENRY WYNN

M D Lond, M Sc Birm, F R C P

Professor Wynn's sixty years of work in the Birmingham medical school began when he entered it in 1895, at 17, having previously won a scholarship at Mason's College from King Edward's Grammar School, Aston His ability was at once evident he gained the gold medal in physiology in the London B SC , he won prizes both for an essay on altruism and for an investigation of the medullated sheath of nerve-fibres, and he founded the students' representative council In 1901, the year when he graduated M B Lond, his M SC (obtained by thesis) was conferred at Birmingham University's first graduation ceremony He became pathologist to the General Hospital in 1903, and in the following year joined its clinical staff as assistant physician, being only 26

This was a time when bacteriology was having a strong influence on medical practice, and with his experience in the laboratory Wynn was particularly interested in applications of the work of Almroth Wright and others As a consultant he was not among those who felt that their task was fulfilled when they had provided a diagnosis, and in his wish to offer effective treatment he especially studied vaccine therapy *Though much of what he attempted has since* been outmoded, it reflected his desire not only to attack disease at its source but also to do something for conditions then largely untreatable His house-physicians and many others will remember the injections of his P S I vaccine which he employed against acute pneu*monia*—then a formidable disease Chronic infections, particularly of the respiratory tract, were also treated with vaccines, and often with apparent success Wynn's acute mind was searching into the problems of infection and immunity His special interest in diseases of the chest was transmitted to many of those working for him and with him, and introduced them into a branch of medicine which has since burgeoned In 1910–12 he helped the late Sir John Robertson in setting up the *tuberculosis service of* Birmingham, and some of the credit belongs to him for the integration of dispensary and sanatorium, of the therapeutic and the preventive aspects of the attack He was appointed physician to the sanatorium in Yardley and adviser to the Derby County Council

In 1926 he succeeded J W Russell as professor of medicine at Birmingham, and his twenty years' tenure of the chair was parallel with the rise of clinical medicine in its present form, employing more and more ancillary methods He was active, for example, in the earliest use of X rays in Birmingham A tribute published last autumn in the university gazette says that Russell, during his few years as professor, had set a new standard in the discharge of academic duty and that Wynn followed his example despite the inevitable sacrifice and inconvenience it entailed

PARTIAL GASTRECTOMY FOR PEPTIC ULCERATION IN THE AGED

W W Davey
M D Belf, F R C S, F R C S I
CONSULTANT SURGEON

Barry O Donnell
M Ch N U I, F R C S, F R C S I
SURGICAL REGISTRAR

WHITTINGTON HOSPITAL, LONDON

"There is no one so old but thinks he can live a year"—Cicero

Safe elective surgery is making an increasing contribution to the care of the aged Advances in anæsthesia, antibiotics, nutrition, and techniques have made genito urinary, orthopædic, and cancer operations safe in the elderly The old are benefiting from surgery as well as the young To be freed from a handicap which conditions life, thinking, and relationships is a gift to the old and a joy for remaining years Gastric surgery has lagged behind other specialties in applying rational principles of treatment to the older patient

Peptic ulceration is no respecter of age or income group, and, though the usual onset is in the twenties, thirties, and forties the relapsing nature of the disease means that many old people suffer from it But in our experience many septuagenarians and octogenarians may show the disease for the first time often in a virulent form The old people frequently need surgical relief and should not be denied it solely on fullness of years Often they are good subjects They are almost all lean and have escaped the ravages of atheromatous accidents, which may have carried away their fatter and perhaps more sanguine brethren in their sixties

We wish to show that partial gastrectomy, the established and rational surgical treatment for chronic peptic ulcer, is feasible and safe in patients over the age of 70 In our experience these patients have been among our most grateful and gratifying

It is an accepted tenet in the treatment of malignant disease that a major operation, soon forgotten, is worth while even for a year of comfortable life Why not extend the principle to this undermining and debilitating complaint in which the sufferers may have several years of high quality life before them? As people grow older their interests often narrow, and life may even revolve around their gastric symptoms To do away with these symptoms raises their level of happiness, and their minds are free for more constructive purposes

We analyse here our experience in 30 consecutive cases of elective partial gastrectomy in patients over 70 and endeavour to answer some of the questions this thesis inevitably raises

Investigation

The history and clinical examination were the most important investigations Most patients had fifty minutes' history taking and ten minutes' physical examination In this way the disability caused by the ulcer was carefully assessed

All 30 patients had barium meals, and 29 had fractional test meals The barium meals showed evidence of ulceration in 29 cases, and in the 30th a shallow ulcer was seen at gastroscopy The test meals were not in any way conclusive but suggested what lesion was likely to be present The average top readings for gastric ulcer were 50/25 N/10 HCl, whereas the average top readings for duodenal ulcer were 75/45 The preoperative weight of all these patients average the low figure of 8 st, ranging from 5 st 9 lb to 12 st

INDICATIONS FOR SURGERY

Why operate on these patients? They have run their allotted span of three score and ten years The first and greatest indication is persistent symptoms Our operations were considered with the patients' symptoms in view A patient does not mind having a disease if he has no symptoms It follows that the greatest surgical symptom—pain—was our principal indication If there is constant and recurring pain and a history of a dramatic episode, such as bleeding or perforation, then the decision is easily made

The second factor is the insurance and prophylaxis that operation confers Mulsow (1941), reviewing peptic ulceration in the aged, found that 33% of the deaths due to peptic ulceration were in patients aged more than 60 Patients do not die from uncomplicated peptic ulcer, though it may contribute to other causes of death In gastric ulceration the spectre of carcinomatous change is always present, but the real threat to life comes from complications that require emergency surgery We have found that Cole's (1953) statement "The aged tolerate elective surgery well but emergency surgery poorly" is true The mortality of perforation and hæmorrhage in the aged is high, whether they are managed medically or surgically Hæmatemesis has a mortality of 15 9% in patients aged more than 70 (Fraenkel and Truelove 1955) Mortality mounts with recurrent incidents, and 4 of our patients had previous perforations or hæmorrhages Many patients survive emergency operations only to succumb to postoperative complications They will often stand an operation but fail to stand a complication

The third factor is physiological Old patients do badly with prolonged rest in bed, the traditional pillar of medical treatment There are many objections to this The dangers of mental deterioration, thrombosis, contractures, bedsores, anorexia, and constipation are now well recognised As well as this the repair destruction cycle has taken place so often that it is too much to expect that the mobile mucosa will ever be adequately restored Mechanically unsound duodenums and attenuated cicatrised lesser curvatures do not improve on rest in bed An exception to this is the giant gastric ulcer of late, possibly arteriosclerotic, origin, which often shrinks dramatically on medical treatment and may even be quite silent

Economics is another consideration A third of our patients had no other means of support than the old-age pension, and many more had little else These people could not afford to sustain indefinitely the long-tried gastric diet with its expensive egg-and milk basis We have learnt not to recommend chicken to old-age pensioners, they simply do not get it Cooperation for long-term medical treatment is not so readily obtained in later life when living habits have become fixed and more difficult to change

Most important is the patient's mental outlook The answer to such a simple and direct question as "How long do you want to live?" often brings an answer which helps in making a decision about surgical treatment In the earlier patients we found that the decision to operate was imposed on us, but increasing confidence based on success has enabled us to be more positive in our recommendations

PREOPERATIVE CARE

Vital capacity and hæmoglobin were estimated and improved on if possible Supervised breathing exercises-

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NEUROMUSCULAR DISORDERS

Infantile Spinal Muscular Atrophy

Of the 67 patients in this group 29 were male and 38 female. In seven families there was more than 1 case in a sibship, but no case in a previous generation had occurred within living memory; the genetic pattern was compatible with the accepted autosomal recessive mechanism of inheritance. In two sibships containing more than 1 case the disease began at birth or shortly afterwards in each patient.

In 33 (50%) of these cases the disease was present at birth or began in the neonatal period. In the remaining 34 cases it began at some time between the second month and the end of the first year of life, except for 1 case in which weakness appeared to begin early in the second year. The age of onset made little difference to the natural history of the illness, which was usually inexorably progressive; the downhill course was perhaps more rapid in the cases of early onset. Within the period of follow-up 55 of these patients had died, invariably of respiratory infection; the earliest age at death was 5 weeks, the latest 12 years, but most patients died between the third month and the end of the fourth year. The 12 surviving patients were aged 4, 5, 5, 7, 7, 9, 9, 9, 11, 11, 12, and 20 years on follow-up. All were severely disabled with severe muscular atrophy, contractures, and skeletal deformity, but in many of them the disease had been apparently stationary for several years.

Although the age of onset and the tempo of the disease varied considerably, the clinical picture was remarkably uniform. In infancy these patients had often been at first sight healthy, well nourished, and intelligent. It was only on closer examination that the severe symmetrical progressive paralysis of the trunk and limb muscles had become evident. They had tended to be virtually immobile, with the arms abducted at the shoulder and flexed at the elbow and lying on either side of the head, and the legs flexed and externally rotated at the hips, with the knees flexed. This position taken up by the limp and hypotonic baby is characteristic. Spontaneous movements had been few and small in range, and the baby could not lift his head or turn over. If lifted the baby would hang loosely or "slip through the hands." The striking hypotonia of the paralysed muscles could be demonstrated by the remarkable range of joint movement: the feet could be placed behind the head, or the fingers turned back to touch the forearm. The deep tendon reflexes were usually absent or greatly depressed. Many patients had fasciculation of the tongue, and some, at an advanced stage, had paralysis of the pharyngeal muscles, with dysphagia and pooling of secretions in the pharynx. Intercostal weakness was often profound and respiration became purely diaphragmatic, with the result that a striking recession of the lower ribs during inspiration (at the diaphragmatic attachment) was almost invariable. Those children who survived beyond the first year soon lost their "puppy-fat" and widespread muscular atrophy became clearly evident. Some muscles were thin and thread-like and, after several years, virtually gave place to rigid fibrous tissue; others retained a few contractile elements under voluntary control, and some of these fasciculated freely. Hypotonia persisted until the unequal atrophy and inevitable increase of fibrous tissue caused contractures, bringing in their wake severe deformities of the spinal column, pelvis, and limbs.

The affected muscles were tested electrically in 23 of these cases and usually revealed loss of the faradic response; intensity-duration curves in 5 cases revealed complete or incomplete denervation of the muscles tested. Of 10 cases subjected to electromyography 4 showed spontaneous fibrillation; the interference pattern of maximal voluntary effort was greatly reduced in all the cases, but the surviving motor units were either normal or above average in amplitude and duration.

Specimens of muscle were obtained by biopsy in 10 cases and at necropsy in 5 others. In all of these specimens the characteristic findings of denervation atrophy (grouped uniformly atrophic fibres) were noted. In all the necropsy cases the number of anterior horn cells was severely reduced.

Benign Congenital Hypotonia

This term is used as a descriptive title for the syndrome which was observed in a total of 17 cases; all patients in this group showed an initially similar clinical picture, but 8 of them recovered completely while 9 showed some improvement but remain moderately disabled. Hence the natural history of these cases somewhat resembles Oppenheim's original description of *amyotonia congenita*, but the new title of benign hypotonia is preferred in view of the unfortunate connotations acquired by "amyotonia" since it was originally introduced.

Cases with complete recovery.—All 8 patients in the group were limp, floppy babies and all have recovered completely. At the time of follow-up the 3 males were aged 7, 8, and 11 years, and the 5 females 11, 12, 16, 16, and 18 years.

In each case amyotonia congenita had been diagnosed in infancy or early childhood because of failure to sit up, walk, or pass other physical milestones at the normal age; on examination at the time of the original diagnosis these babies had all been limp and floppy. There had been usually striking hypotonia of the muscles of the limbs and trunk, with pronounced hypermobility of joints. Although the severity of the abnormality varied from case to case, the over-all clinical picture and the natural history of the disorder in these cases were again relatively uniform. In contrast to the cases of spinal muscular atrophy, these babies had not been paralysed but had made spontaneous movements of the limbs and trunk, even though these movements seemed comparatively ineffectual compared with those of a normal child. None of them experienced any significant impairment of respiratory movement. Each of these children began to walk between the ages of 20 months and 5 years and thereafter made slow but steady progress, though for several years they were clumsy, tended to fall frequently, and could not climb stairs easily or keep up with other children of the same age. Eventually, however, all of them were normally active and on examination showed no neuromuscular abnormality or hypermobility of joints.

Electrical stimulation of the muscles in 5 of these children gave normal results, but in 2 cases electromyography in infancy had shown excess of polyphasic potentials on volition. Specimens of muscle obtained by biopsy in 2 of these cases and stained with hæmalum and eosin showed no abnormality.

The condition which afflicted these children corresponds closely to the recorded descriptions of essential hypotonia (Sobel 1926, Lidge 1954); the fact that they recovered excludes that form of joint hypermobility (Finkelstein 1916, Key 1927, Sutro 1947) which is unaccompanied by delay in development or muscular weakness, is often familial (as is evident in certain families of contortionists), and persists throughout life. The present cases are reported in detail elsewhere (Walton 1956a). My observations have led me to believe that laxity of joint ligaments was not an important factor in these cases; rather, their condition appears to have been due to a widespread congenital muscular hypotonia of undetermined ætiology which eventually recovered completely.

Cases with incomplete recovery.—Of the 9 surviving patients in this group 4 were male and 5 female, and at the time of follow-up they were aged 6, 6, 7, 11, 11, 15, 17, 30, and 53 years. Amyotonia congenita had been were taught to each patient, and careful inquiry was made into the possibility of the presence of a "cold" and, if such were found, operation was postponed for at least ten days after the acute infection Trial doses of any drugs likely to be used, such as pethidine and promethazine, were given

Most of our patients with recent symptoms of ulcer activity were given two or three weeks' rest in bed during these investigations, for we have learnt that there is a world of difference in the safety with which one can close the necrotic as opposed to the fibrotic duodenum, and the extra rest in bed *often converts the necrotic to the fibrotic* We have also the greatest respect for the giant posterior lesser curve gastric ulcer penetrating the pancreas—we prefer to remove it when healed

"KEEP DEATH OFF THE TABLE"

Half the cases were operated on under local anæsthesia Almost half the remainder underwent balanced anæsthesia of "local" infiltration with light general anæsthesia We used an anterior field and splanchnic block with 1 in 2000 amethocaine hydrochloride We have given up using adrenaline in the solution because of its occasional tendency to initiate auricular fibrillation, we have seen no toxic effects as a result of this Premedication that is accurate in timing and dosage is essential for success, and pethidine and promethazine as adjuvants are most useful drugs

The use of local anæsthesia presupposes an accurate established diagnosis and a planned operation Trauma, fumbling, and purposeless movements must be avoided More patients are suitable for local anæsthesia than are surgeons To have a conscious patient with one in the theatre is to be *constantly reminded of the fragile nature* of the person entrusted to one's care This is so easily forgotten under general anæsthesia, especially when one is confronted with some unusual technical problem

Paul, of Liverpool, said "Gentleness comes from the heart rather than from the hand" Under local anæsthesia gentleness is essential, and one quickly learns which are the *traumatising parts of the operation* Unnecessarily moving heavy retractors upsets the patient as much as does ligature of the left gastric pedicle

For the firm surface of the average operating table was substituted an inflatable 'Lilo,' which is much more comfortable for the patient and reduces the possibility of phlebothrombosis Comfort is important because nearly all these operations took longer than two hours When possible the patient was transferred from the operating table direct to bed

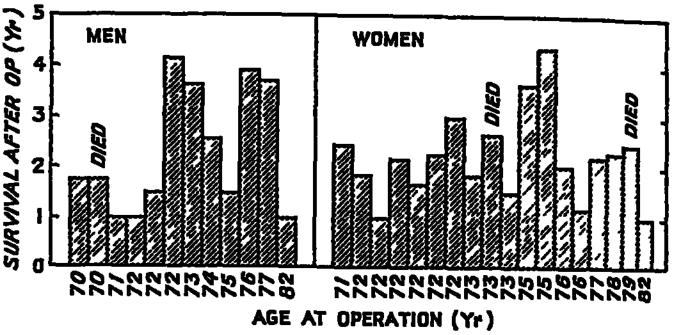
From our experience of emergency surgery for gastrointestinal hæmorrhage in the aged we have learnt that, in some cases where the tissues look poor, it is well to reinforce our two layer catgut anastomosis with a third layer of interrupted linen, thus forestalling the serious risk of delayed healing Before we close the abdomen, the splenic area is checked for the presence of blood, because a few ounces left to pool here may help to start an atelectasis at the left base

AFTERCARE

'In the aged more than half the postoperative deaths are due to bronchopneumonia" (Carp 1948), and we are constantly mindful of this Intramuscular penicillin 250,000 units six-hourly is given routinely for five days

So far as possible we try to have the same nurses caring for the patient, and the position of the bed in the ward is not altered This helps to prevent a confusional state

Most of the patients did not have an intravenous infusion, which tends to immobilise them, where it was essential, an effort was made to have a temporary rather than a continuous drip Rectal fluids are absorbed well by the prepared colon, and this was the method most often used during the first seventy two hours



Survival after operation

A close watch is kept for phlebothrombosis, and early mobilisation is tempered with discretion and mercy, *older tissues take longer to repair* Diarrhœa is a most serious complication in old people, and a "wait and see" attitude to it may be dangerous

Our patients left hospital after twenty-one days, and many had a further two weeks' convalescence

THE PATIENTS AND THEIR LESIONS

30 patients aged more than 70 had partial gastrectomies in four and a half years from February, 1950, to August, 1954 18 were women and 12 men In 10 the only means of support was the old-age pension

17 had gastric ulcers, 8 had duodenal ulcers, and 5 had signs of both Of the 17 gastric lesions 12 were in women, and of the 8 duodenal lesions 6 were in men Of the 5 patients with combined lesions 4 were women, 2 had their operations for duodenal ulceration, 1 for gastric ulceration, and the remaining 2 because of the combination 10 of the patients had duodenal ulcers alone or combined with an element of stenosis

An interesting subgroup were 4 patients who had hour-glass stomachs Their histories were from fifteen to thirty-five years, the average being almost twenty five

12 of the gastrectomies were of the Billroth I pattern, and the remainder were Polyas with a Finsterer Lake valve

The survival of the patients is charted in the accompanying figure

IMMEDIATE COMPLICATIONS

Death is the most important complication of operation There were no deaths immediately or remotely connected with the operations There were 2 severe chest infections 1 paralytic ileus was overcome by aspiration and intravenous fluid We had 1 burst abdomen

FOLLOW UP

All our patients were followed up as outpatients or visited in their homes by one of us 3 now have incisional hernias

From one to five years after operation the average of 27 hæmoglobins was 91%, and only 2 were below 80% In 13 patients the weight was unchanged—i e, within 7 lb of their preoperative weight 8 *gained* weight, the average gain being 14 lb, with a maximum of 23 lb 6 lost weight, the average being 12 lb and the maximum 19 lb There were no jejunal ulcers, actual or presumed, at the end of the period

Most of the patients were delighted with their operation, and on the whole we considered that their capacity was normal and that they were less liable to have post gastrectomy symptoms than are younger folk *Perhaps* this is because the gastric remnant is more lax and distensible in *older* people "Wonderful," "Never diagnosed at the age of 10 years in the patient aged 30 at follow-up, and at the age of 28 in the female patient aged 53 at follow-up.

Each of these patients had been a limp hypotonic baby, with an initial history strikingly similar to that of the cases, reviewed above, which recovered. Although they showed this picture of the "rag-doll" baby, spontaneous movements of the limbs were fairly good, and the striking flaccid weakness of infants with spinal muscular atrophy was not observed. Furthermore, the deep tendon reflexes were generally present, though depressed. All of these children were late in reaching their physical milestones and did not walk until aged from 18 months to 5 years. Even then they were clumsy and fell frequently, and all their muscles seemed small and weak. They all showed some improvement after first beginning to walk, but this improvement was arrested, and although they were able to carry out most everyday activities they remain moderately disabled. The 2 oldest patients said that their muscles had always been "generally weak" but there had been no change in their condition for many years.

On examination at follow up a uniform pattern of abnormality common to all the cases could be discerned. In all of them the skeletal muscles generally were abnormally small and slender and considerably weaker than normal; the upper facial muscles were involved in 3 cases, and the sternomastoids were usually particularly thin, more so than the posterior cervical muscles. In 2 cases the intercostal muscles seemed to be weak. The muscular abnormality was otherwise similar in the limbs in all the patients, except that in 2 of them the distal muscles were more powerful than the proximal. There was some evidence of persisting muscular hypotonia and of hypermobility of joints in all the cases, although this was slight in the 2 oldest patients. In 3 of the children, however, it was still striking at the ages of 6, 7, and 11 years. The tendon-reflexes were usually present, though sometimes depressed; in the patient aged 53 they were remarkably brisk. In 1 case there were slight contractures of the tendo Achillis, but serious deformities were uncommon; there was a moderate dorsal kyphoscoliosis in 3 patients.

Electrical testing of the muscles revealed no significant abnormality in 4 cases, but a pattern suggesting myopathy (numerous polyphasic and short duration potentials on volition) in 3 cases. Despite this finding muscle biopsy in 4 cases (including 2 of those with the "myopathic" electromyograms) showed no abnormality.

The resemblance of these cases to the benign congenital myopathy of Turner (1940, 1949) is striking. They correspond even more closely to Krabbe's (1946) description of congenital universal muscular hypoplasia. As Ford (1952) has pointed out, the only difference between the descriptions of Krabbe and Turner was that in 1 of Turner's cases muscle biopsy gave findings compatible with a myopathic disorder, whereas in Krabbe's case the muscle was histologically normal. In Turner's case, however, there was a complicating disease (bacterial endocarditis) which could conceivably have been responsible, at least in part, for some of the pathological changes in the muscles. The resemblance of these cases to the 8 described above which recovered completely is even more close and the only difference seems to be one of severity.

These observations suggest that the syndrome of "benign congenital hypotonia" is due to a congenital abnormality or pathological process which gives rise to profound muscular hypotonia, without paralysis, at, or soon after, birth. In some cases the patient recovers completely with the passage of time, while in others recovery is incomplete and the patient survives with small, weak, hypotonic muscles throughout life. It seems probable that the syndrome which Turner called "benign congenital myopathy" and that entitled by Krabbe "congenital universal muscular hypoplasia" should be included in this group. I do not believe that these children are suffering from a true myopathy or muscular dystrophy. This argument is developed, and cases are reported in detail, elsewhere (Walton 1956a).

Congenital "Myopathy" with Myasthenic Features

This case was in a patient who corresponded in many respects to Turner's description of "benign congenital myopathy" but also showed pathological fatigability, a persistent improvement in strength on treatment with ephedrine, and a temporary response to neostigmine (Walton et al. 1956). In this patient, too, the histological changes found on muscle biopsy were minimal, and it is doubtful whether she could be considered to have a myopathy in the accepted sense of the term.

Adams et al. (1953) suggest that some cases of recovery from amyotonia congenita may have been examples of infantile polyneuritis. No such case was recognised in this series.

Progressive Muscular Dystrophy

These 3 patients (all male) had apparently been normal at birth, but during the first year their limb movements had seemed to become weaker and the muscles flabby. In 2 of the cases there had been severe muscular hypotonia and some hypermobility at the joints; this finding, combined with the flabbiness, had led to the diagnosis of amyotonia congenita. All 3 infants had begun to walk late (at about the age of 2 years) and had then been clumsy, had waddled, and had fallen frequently. Subsequently their walking had deteriorated, and on follow up examination late in the first or early in the second decade they showed the characteristic features of the Duchenne type of muscular dystrophy, which begins in the first year of life in a significant proportion of cases; but hypotonia is an uncommon manifestation (Walton and Nattrass 1954).

Polymyositis

1 female patient had been noted to have weak limp muscles soon after birth, but without skin changes or pyrexia; she had not begun to walk until the age of 2 years and even then had been clumsy and had fallen frequently. She had become progressively weaker and developed contractures at the knees, elbows, and ankles; at the age of 8 years she became unable to walk because of increasing weakness and deformity of the limbs. Muscle biopsy revealed areas of degeneration and necrosis of muscle-fibres and inflammatory-cell infiltrates, with a striking increase in fibrous tissue—the picture of so called chronic myositis fibrosa, which I believe to be simply a chronic form of polymyositis (Walton 1956b).

Bovet (1936) described a case of acute polymyositis in an infant with the clinical picture of amyotonia congenita, but this experience seems to be uncommon.

CEREBRAL DISORDERS

"Cerebral Palsy"

Of the 6 patients 3 were male and 3 female; 4 had been born after a difficult assisted labour and had been cyanosed at birth. Subsequently, all 6 had been slow to develop and to pass their physical milestones. Amyotonia congenita had been diagnosed because of paucity of spontaneous movements, or lack of purposive activity, combined with general hypotonia of the limbs; there had been some hypermobility at proximal joints in 3 cases. In all the cases, however, the deep tendon-reflexes had been present and often active at the time of diagnosis. No case of this type showed the symmetrical immobility and respiratory difficulty seen in cases of spinal muscular atrophy.

On examination at the ages of 5, 8, 9, 11, 12, and 17 years 3 of these children were mentally backward, whereas the others were of normal intelligence. 2 showed better in my life," "New lease of life," "Not so well for years," "Christmas dinner with all the trimmings"—these are fair sample comments Our one poor result was in a woman whose ulcer did not show on barium meal but was discovered on gastroscopy Postoperative gastric biopsies show that she has a concomitant gastritis, and this rather than the ulcer is probably the cause of her symptoms

3 patients have since died Their deaths have been unconnected with surgery Cerebral thrombosis claimed one, a carcinoma of the splenic flexure with hepatic secondaries claimed another at the end of two and a half years, and the 3rd died of coronary thrombosis associated with chronic myeloid leukæmia after twenty one months

Partial Gastrectomy as Operation of Choice

Almost two-thirds of our patients had gastric ulcers Here the choice was simple it was either gastrectomy or nothing

The most contentious part of this paper is the selection of partial gastrectomy as the surgical procedure of choice for duodenal ulceration

Partial gastrectomy is the long established rational treatment, whereas gastro enterostomy is largely discredited at present But gastro enterostomy is often recommended for the aged, it is said to be quicker, safer, and equally effective Yet speed is not an important factor in a gastric operation, and shock is no longer a complication of gastrectomy Gastro enterostomy is not safe, because it is not equally effective After operation the patient may get relief of symptoms but is subject to the same lethal complications of peptic ulceration as before He is subject to the same complication that has led to the abandonment of gastro enterostomy in younger people—the hazard of marginal ulceration We could trace no evidence that older people are less liable to marginal ulceration The issue with which it has been confused is that there is a decrease in gastric acidity coincident with the advance of age, especially in men (Vanzant et al. 1932) But peptic ulceration in general is as common in the aged as it is in other age groups

> "10% cases of peptic ulceration occur in persons over sixty The age distribution of the general white population of the United States is just 10 8% over the age of sixty" (Mulsow 1941)

Our opinion is that, although the gastric acidity is decreased, the mucosal resistance is also decreased, and the end result is peptic ulceration

The proof that jejunal ulceration develops after gastro-enterostomy is from fact and inference

> Kiefer and McKell (1947) found 4 jejunal ulcers following gastrojejunostomy in patients aged more than 65 2 of these ulcers occurred in patients whose initial symptoms of peptic ulceration began at the age of more than 70
>
> One of us did a low Polya gastrectomy as an emergency for bleeding from a duodenal ulcer in a man aged 71, a year later he had a further operation for closure of a perforated anastomotic ulcer
>
> Charles Wells (personal communication) writes "Even the development of pyloric stenosis is an indication of continued activity The element of fibrosis is by no means an indication of diminished virulence The incidence of marginal ulceration after gastro-enterostomy is no less in old people than it is in the young"
>
> Ivor Lewis (personal communication) says that, if the duodenum is opened as the first step of the operation in cases of pyloric stenosis, one will nearly always find an actual ulcer still present This proves the dangers of stomal ulceration, which he found 'fairly frequently'

Decreased acidity is often caused by the gastritis which is secondary to pyloric hold-up When this is overcome by gastro enterostomy without attention to its precipitating factor, peptic ulceration, the gastritis resolves and the acidity increases again

Conclusions

Given adequate indications and careful preparation, surgical treatment for peptic ulceration in old people is safe

Partial gastrectomy has given promising results in our hands

Summary

Peptic ulceration, recurrent or new, is common in the aged, they stand its complications poorly

When elective surgery is indicated, we believe that partial gastrectomy is the operation of choice

30 consecutive elective partial gastrectomies in patients aged more than 70 are reviewed There were no deaths due to operation All of these patients have been followed up

We wish to thank Professor Wells and Mr Ivor Lewis for their personal communications

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SPORADIC NON-ENDEMIC GOITROUS CRETINISM

HEREDITARY TRANSMISSION

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Endemic cretinism results from a severe lack of iodine over several generations and is almost invariably associated with goitre The common type of sporadic non-endemic cretinism, on the other hand, is not associated with goitre, indeed it is usually considered to be due to an embryonic defect in the development of the thyroid gland (Dorff 1934), which is often assumed to be absent Nevertheless radioactive iodine (^{131}I) studies of cretins who, on clinical examination, seem to have no thyroid tissue at all have sometimes revealed enough ^{131}I in the neck to suggest that some thyroid tissue is present (Quimby and McCune 1947, Silverman and Wilkins 1953), which may be either ectopic or undescended (McGirr and Hutchison 1955), confirming an early anatomical observation in cretinism (MacCallum and Fabyan 1907)

The underlying cause of sporadic cretinism remains unknown Childs and Gardner (1954), who, seeking evidence of a hereditary tendency, investigated the families of 90 cretins, found that, though there seemed to be such a tendency, a familial prevalence was distinctly uncommon Consanguineous matings among the parents of the cretins was not strikingly commoner than in a control series of normal children

In contrast to this type of sporadic cretinism is what has been described as "sporadic cretinism associated with goitre" In this type of case familial prevalence and consanguinity of the parents are common (Osler 1897, Lerman et al 1946, Hurxthal 1948, Stanbury and Hedge 1950, Hubble 1953, McGirr and Hutchison 1953, Wilkins et al. 1954, Hutchison and McGirr 1954, Sexton and Mack 1954, Stanbury et al 1955a, 1955b), but isolated the signs of flaccid diplegia, and 1 of mild spastic diplegia; 1 had spastic diplegia with athetosis and cerebellar ataxia; and 2 had double athetosis.

Mental Defect

In 8 cases (5 in males and 3 in females) amyotonia congenita had been diagnosed because of failure to pass the physical milestones at the normal age, combined with moderate generalised muscular hypotonia. Hypermobility of joints had not been striking in these cases, and the deep tendon-reflexes had been present in all, but they had been limp flabby babies and had made fewer spontaneous movements than does the normal child.

On examination at the ages of 2, 7, 8, 9, 10, 12, 14, and 14 years 2 of these children were imbeciles, and moderate hypotonia of the musculature persisted, although there were no other neurological signs. 4 patients were feeble-minded and their skeletal musculature remained somewhat flabby; another was a hyperkinetic backward child with subaortic stenosis; and another showed moderate mental defect, congenital nystagmus, and severe myopia, but no neuromuscular abnormality.

NUTRITIONAL AND METABOLIC DISORDER

Scurvy

The 2 children with scurvy were twin sisters who showed severe muscular flabbiness and lack of spontaneous movement during the first 8 months of life. They improved rapidly on treatment with ascorbic acid after radiographs had revealed probable scorbutic changes in the limb bones, and the diagnosis had been confirmed by the blood-ascorbic acid levels. On examination at the age of 8 years they were healthy normal children.

No other examples of severe muscular hypotonia due to nutritional or metabolic disturbances in infancy were noted in this series; but I have subsequently observed manifestations of this type in a case of glycogen storage disease—an event previously described by Clement and Godman (1950) and by Krivit et al. (1953).

SKELETAL AND OTHER CONGENITAL DISORDERS

Arachnodactyly

The child with arachnodactyly had had loose hypotonic hypermobile limbs in infancy, but spontaneous movements had been good and vigorous, and she had begun to walk at the normal age, though she had tended to be clumsy. On examination at the age of 15 she was healthy and active, without any neuromuscular abnormality; but she had long spidery fingers and toes, hypermobility of her joints, and a high arched palate. Her father was similarly affected.

Multiple Congenital Defects

The girl with multiple congenital defects had also been limp and flabby as a baby and had begun to walk late. On examination at the age of 8 years there was no evidence of neuromuscular disease; there was a mid-dorsal scoliosis, and radiography revealed that T4 was a hemivertebra and the left 4th rib was absent; she also had dextrocardia. Hypotonia in congenital heart disease, such as Fallot's tetrad, has been described by Davison and Weiss (1929).

Congenital Dislocation of Hip

The diagnosis of amyotonia congenita in the patient with a congenital dislocation of hip was clearly a diagnostic error; lack of mobility and some hypotonia of the lower limbs, particularly the left, were later found to be due to dislocation of the left hip, and the patient made good progress once this was treated.

OTHER DISORDER

Spinal Ganglioneuroma

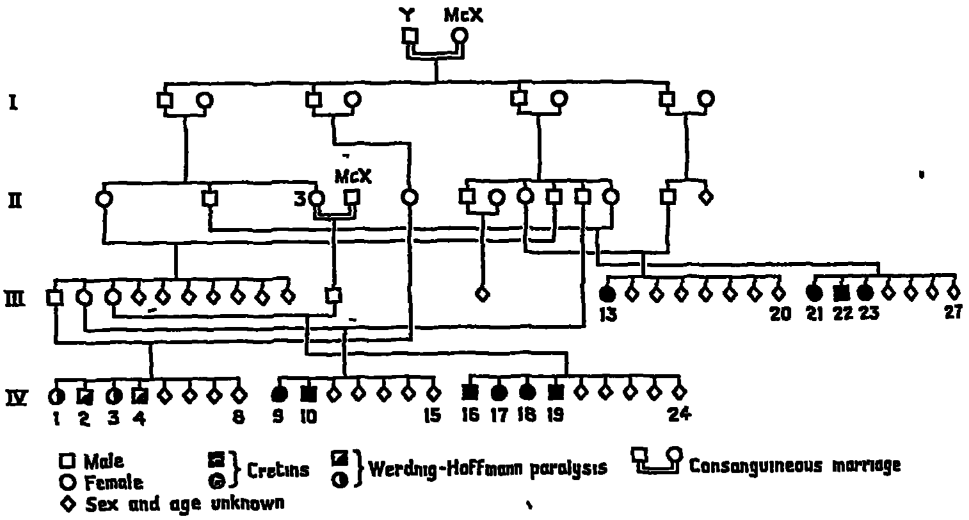
Progressive flaccid paralysis of the lower limbs in a male baby aged 6 months was later found to be due to a spinal ganglioneuroma.

Discussion

Brandt's (1950) conclusion—that the syndrome of amyotonia congenita, when taken to include all cases of generalised muscular hypotonia observed at, or soon after, birth, is due to many underlying disorders and not to a single disease—is confirmed by the findings in the present cases. It is evident that many babies presenting with this syndrome have spinal muscular atrophy and show the same inevitable deterioration as do those in whom the muscular weakness develops late in the first year. Although a few such babies survive for many years, and the disease appears to become arrested in some, yet without exception the children are left severely disabled and incapable of useful activity. In the infant afflicted with this disease muscular hypotonia and hypermobility of joints are profound; there are progressive impairment of spontaneous movement of the limbs and difficulty in respiration owing to intercostal weakness; the tongue may be seen to fasciculate; the tendon reflexes are absent; and bulbar paralysis may ensue. In an advanced stage the flaccid immobile baby, with shallow yet laboured respiration and "rattling" of secretions in the pharynx, presents a picture so characteristic that it cannot be confused with any other disorder.

In an earlier stage of the illness, however, diagnosis may be much more difficult because many other conditions may give a similar picture of muscular hypotonia. In benign congenital hypotonia this manifestation may be striking and the baby may be almost as limp and floppy as one with spinal muscular atrophy. On the other hand, these infants are not paralysed; though weak and late in developing they generally show a good range of spontaneous movements of the limbs. Respiratory difficulty is uncommon; even when present it is never so severe as in cases of spinal atrophy. Furthermore these patients show neither fasciculation of the tongue nor bulbar paralysis, and the tendon reflexes are usually retained, though they may be depressed. Clearly it is important to distinguish cases of this type from those with spinal muscular atrophy at the earliest possible moment, for their outlook is much more favourable. Negative findings on muscle biopsy may be of the greatest value in this context; in my experience biopsy in a case of spinal muscular atrophy never fails to show the characteristic appearances of denervation atrophy. I can offer no suggestion as to how to distinguish between the cases of benign congenital hypotonia which recover completely and those which improve but remain moderately disabled, except by follow-up studies. I have the impression that it is the less severely affected cases which recover completely, but at the moment this is no more than an impression. The nature of the neuromuscular abnormality in these cases is unsolved. Coers and Pelc (1954) have found that in 1 case of "amyotonia congenita" (which may have been of this type) the motor nerve endings, stained intravitally with methylene-blue, were "immature." Much work remains to be done before the significance of this finding can be appreciated, but it seems possible that this syndrome of benign hypotonia may result from varying degrees of abnormality in development of the neuromuscular apparatus. It appears that the term "benign congenital myopathy" (Turner) is a misnomer for cases of this type if "myopathy" is taken to mean, in its usual sense, "muscular dystrophy."

There remain to be considered the various cerebral, nutritional and skeletal disorders which in some of the present cases gave rise to generalised muscular hypotonia in infancy. It is evident that, although these children were limp and flabby and tended to "slip through the hands," the hypotonia and joint hypermobility were never so striking as in the cases of spinal atrophy. Nor, on the whole, were they so noticeable as in the benign



Pedigree of itinerant tinkers, showing appearance of goitrous cretinism and Werdnig Hoffmann paralysis

cases without any apparent familial prevalence have also been reported (Osler 1897, Hamilton et al 1943, Stanbury 1951, McGirr and Hutchison 1953, Wilkins et al 1954, Hutchison and McGirr 1954)

None of these cases of sporadic non endemic goitrous cretinism has been due to deficiency of iodine or to the ingestion of goitrogens Obviously in all of them the hypothyroid state was due, not to a simple lack of thyroid tissue (as it is in the common sporadic non-goitrous cretin), but to an inability on the part of the thyroid gland to meet the body's requirements, even after considerable enlargement of the gland, most probably as the result of stimulation by thyrotrophin produced by the pituitary gland in response to a hypothyroid state

Our understanding of the pathogenesis of goitrous cretinism has been greatly furthered by the use of radioactive iodine (^{131}I) Excessive avidity of the thyroid gland for iodine has been a constant feature of these cases, but evidence has also accumulated which suggests a block in the synthesis of the thyroid hormone Discrepancies between the findings of different workers indicate that the block is not always at the same stage in every case It seems likely that this block is due to enzyme deficiencies at different levels of synthesis in different cases

The high prevalence of goitrous cretinism in the families of our patients led us to postulate that the condition may be due to an inborn error of metabolism (Hutchison and McGirr 1954) A similar opinion has been expressed by Wilkins et al (1954) and Childs (1954)

We have since been able to add considerably to the family tree of our largest family group (cases 1–7 and 13 of Hutchison and McGirr 1954) and to correct some of the inaccuracies previously reported to us The fuller details of this remarkable family seem worthy of record

Y-McX Family Group

Such details of the family tree as have been discovered are shown in the accompanying figure The members of this family group are itinerant tinkers living in Kintyre, Argyll, and the Isle of Islay, Scotland From time to time they travel in other parts of Scotland, and very probably other members of the family group are scattered throughout the country, although we have not found it possible to trace any with certainty These people are always on the move and this fact, combined with the distance from Glasgow of their usual haunts, explains our difficulty in collecting accurate data Even now we have reasons (see below) to believe that the family tree given here by no means exhausts the ramifications of the Y McX genes throughout Scotland

The original male Y came from Ireland to Scotland about 160 years ago and settled as a blacksmith at Southend Kintyre He married a McX, his full cousin A female Y (II 3) married another McX, who was her full cousin We have not been able to obtain a satisfactory pedigree of the main McX family, which is probably scattered widely throughout the West and North of Scotland So far as we know, none of the marriages in generation I of the Y family was consanguineous but in generations II and III the amount of intermarriage has been astonishing, and possibly largely brought about by the increasing demarcation and isolation of these people by the rapidly widening gulf between their mode of existence and that of the other inhabitants of the country

The family tree (see figure) shows that 10 known goitrous cretins (III 13, 21–23, and IV 9 and 10 and 16–19) have appeared among 31 persons in four lots of siblings (III 13–20, III 21–27, IV 9–15, and IV 16–24) 6 females and 4 males—an approximately equal sex distribution The results of radioactive iodine studies in 8 of these have already been published (cases 1–7 and 13 of Hutchison and McGirr 1954) The 9th cretin (III 21) is the elder sister of III 22 and III 23 (cases 7 and 6 of Hutchison and McGirr 1954) One of us has examined her clinically in Kintyre but she has not yet been submitted to detailed study The 10th (IV 10) is the younger brother of IV 9 (case 5 of Hutchison and McGirr 1954) and was first seen at the age of 4 weeks as a goitrous infant without signs of hypothyroidism Such signs have recently appeared at the age of 2 years The result of ^{131}I studies on this child suggests that the goitrous cretinism in this family is due to a deficiency of the enzyme dehalogenase (McGirr and Hutchison 1956)

There have also been 4 cases of Werdnig Hoffmann paralysis (IV 1–4) in another lot of siblings 3 patients died after hospital investigations in Glasgow and Edinburgh had established the diagnosis beyond reasonable doubt The 4th case (IV 4) has recently been diagnosed None of the parents of the cretins or of the patients with Werdnig-Hoffmann paralysis showed any evidence of disease We have personally seen all these parents We have not, however, examined all the supposedly healthy siblings of the cretins

Discussion

It is obvious from the high familial prevalence of sporadic goitrous cretinism noted by ourselves and others in the United Kingdom and in the United States that this form of hypothyroidism must be genetically determined In none of the present cases was there anything to suggest iodine deficiency or the ingestion of goitrogenic substances Endemic cretinism usually appears in the family of a mother who is goitrous from iodine deficiency, whereas in the present cases the parents were, without exception, healthy

It is therefore most unlikely that the appearance of goitrous cretinism in the Y McX family group is related directly to their common environment On the other hand, the pedigree (see figure) satisfies three of the unsuccessfully used extermination measures for fifty years at very great cost in value of herds of cattle and flocks of poultry, to get rid of swine fever, foot and mouth disease, and fowl pest, but it has learnt little or nothing of cure of these conditions though smallpox, cholera, typhoid, plague, and tuberculosis have largely been eradicated without the aid of unprofitable destruction of this type While the spectacle of numerous rabbits dying of the disease along every road horrified the public the spread of the disease was regarded as despicable and talks of punishment of the ill doers even mentioned, now we learn from the press notices that the Government seek the result at vast expense

Since it is admitted by all good farmers that "rabbits are a sign of bad husbandry, bad estate management, and bad government," and that there is land which cannot be profitably used in any better way than for rabbits, why use such infectious measures, the ultimate effect of which cannot be determined? Land will only yield a certain quantity of food for animals, and as long as farmers have not the means to use it profitably let us be thankful for the rabbit rather than seek a barren wilderness

Birmingham JAMES T BRAILSFORD

ABDUCTOR PARALYSIS AT THE SHOULDER

SIR,—May one offer a short congratulatory note to Mr Sharrard and Dr Knowelden on the clarity and usefulness of their paper last week It became apparent many years ago that to splint the shoulder in abduction was somewhat of a negation of common sense Paralysed or weak muscles need protection against the over action of opponent muscles and "over stretching" Neither of these deleterious factors apply to the shoulder abductors merely because the arm is kept in the natural position at the side of the trunk Therefore, to abduct is not required

I have not splinted the shoulder in abduction for simple paralysis for some fifteen years, and have never regretted it This paper, by the size of its sample—359 cases—and its method of control, provides the proof of my beliefs which my small series could not supply

Manchester W SAYLE CREER

ELECTRON-MICROSCOPY OF ATHEROMA

SIR—The statement by Dr Keech and Dr Reed (Dec 31) that the fibres I depicted (Dec 10) are reticulin is, I think, a little far fetched They claim to see an accentuation of every third component in the banding, But a careful scrutiny of figs 5 and 8 will show that such accentuations as are seen do not occur consistently at every third component, and can hardly therefore be regarded as significant They make the arbitrary statement that the aortic intima consists of, besides elastic tissue and amorphous material, fibres 300–900Å in width, but if they will look at my figures 5, 7 and 8 they will see fibres of no more than 100Å in width My so-called failure to mention elastic tissue was, of course, because I had carefully excluded from my preparations all but the superficial layers of the intima

My work was designed either to confirm or to refute Professor Duguid's prediction that much of the substance of an atheromatous plaque would show the characters of fibrin, and I think I succeeded in confirming it, but I carefully refrained in the main body of my paper from applying the term fibrin, and I think that Dr Keech and Dr Reed are bold in applying the term reticulin It would be interesting to know by what reasoning they relate the material I obtained from a mass of very dense fibrous tissue to reticular tissue Incidentally I would like to know how Dr van den Hooff (Dec 31) is able to identify as collagen, fibres which do not conform to the recognised electron-microscopic appearance of collagen

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C. I. LEVENE

DOMICILIARY CONSULTATION IN PSYCHIATRIC PRACTICE

SIR,—Dr Philip Hopkins's letter (Dec 31) contains informative statistics on psychiatric patients in general practice Do I understand correctly from the table that none of the five patients diagnosed as schizophrenic were admitted to hospital? If so, further information about the clinical features and course of their illnesses, and of the action taken to help them, would be of interest

Warneford Hospital,
Oxford

IAN SKOTTOWE

*** This letter has been shown to Dr Hopkins, whose reply follows—ED L

SIR,—Dr Skottowe understands correctly that none of the five patients shown in the table accompanying my letter as diagnosed schizophrenic were admitted to hospital at the time of referral They were all referred to a psychiatrist, with whom rested the final diagnosis and the decision whether or not to admit them to hospital

CASE 1—A 26 year-old man consulted me on June 25, 1951, stating "I was with a girl friend last night and I suddenly had a terrible desire to kill her" In addition to this there had been feelings of unreality over the previous few weeks I had known him previously as a rather quiet withdrawn man Referral to a psychiatrist resulted in the diagnosis of schizophrenia, but while arrangements were being made for his admission to hospital he was arrested on a charge of repeated thefts over the previous few months and ultimately he went to prison for three months The magistrate was not influenced by the psychiatric report

CASE 2—On Sept 26, 1951, a 30 year old single woman came to me with a request to be referred to a plastic surgeon She stated that her nose had been getting bigger for some years and was now interfering with her appearance so much that people were talking about her She had, she said, previously had plastic operations on her nose in Cairo but the surgeon had made a terrible mistake She was plainly suffering from delusions and had been unable to work for some time I suggested that a psychiatrist could perhaps help her, and she agreed to go provided that she did not have to go into "an asylum" The psychiatrist's diagnosis was schizophrenia and he suggested that she should be admitted to a hospital for nervous disorders Neither the psychiatrist nor I have seen her since

CASE 3—A 31-year old single woman came asking to be referred back to a clinic she had attended eleven years earlier At that time there had been delusions mainly associated with men in her bedroom at night, a previous doctor had referred her to a gynæcologist to re-assure her that she was still a virgin and was not pregnant—but despite the reassurance she still insisted she was pregnant Following individual psychotherapy she had been able to continue with her work as a teacher, but her symptoms were worse when she consulted me on March 16 1953 I referred her back to the clinic as she requested, but before she could resume treatment as suggested she took a job as a teacher abroad. I have recently been told by this patient's mother that she is still working, but lives "a very secluded life"

CASE 4—On July 13 1953 a single man, aged 30, asked for a "tonic"—but after a lengthy interview he agreed to go to a psychiatric clinic I had been seeing him from time to time for the previous twelve months for "supportive" therapy, as he was clearly a chronic schizophrenic he had been brought up in a foundlings' hospital, had never known his parents, and had no friends At $14^1/_2$ years of age, he had been placed in the Regular Army as a band boy, after nine years he took his discharge, since when he had wandered from job to job He had been afraid to mix with people as he thought they talked and laughed about him, he always felt inferior and had become completely withdrawn I referred him for psychiatric assessment, as a result of which it was agreed that I should continue to see him for "supportive" therapy He managed fairly well by this means for some months, but eventually he left London, and I saw him no more

CASE 5—On Dec 12, 1953, a 25 year-old single man consulted me with a number of symptoms, I had seen him many times during the previous three years on account of [illegible] symptoms, mostly associated with anxiety He lived with his parents, with whom he had never got on well [illegible] no friends and tended to be withdrawn He wanted to paint, but although talented he could not keep any job for long as he was unable to concentrate and could not get on well with his employers or those he worked with He had feelings of inferiority, lacked self confidence, and was unable to sleep I thought he was worse than usual and referred him for psychiatric assessment He was at first thought to be suffering from a severe anxiety neurosis and was put on the waiting list for psychotherapy It was some time before this was started, and after about four months in treatment (weekly sessions for individual therapy) his therapist concluded that the diagnosis was schizophrenia Admission to hospital for insulin therapy was arranged, and after five months he was discharged considerably improved A month later, however, I had to have him readmitted by the duly authorised officer when he had an acute schizophrenic breakdown in which he attacked his father and broke up the furniture and fittings in his parents' home He was discharged in November, 1955, and is now attending a day hospital, where he is reported as doing fairly well but the report on his behaviour for December, 1955, states "He is painting well and plans to teach art, but he still wanders aimlessly and is unable to concentrate"

Unlike the consultant, the general practitioner cannot say to his patient that he can do nothing for him, the patient has no one else to help him, and only too often it is left to the general practitioner to think up some way in which to help even the most difficult chronic patient—with untreatable psychosis or inoperable cancer

It is only the schizophrenic in an acute episode or the certifiable chronic who is admitted to mental hospital—for treatment or custody When the mental hospital specialist's enthusiasm has waned, or when the patient refuses to stay longer in hospital, he is sent home as untreatable Nevertheless, it is surprising how some of these chronic schizophrenic patients can be kept usefully employed with occasional interviews for supportive therapy Watts[1] has described well the types of patient that the general practitioner may be called on to look after, and he rightly points out that if it is possible to keep them at home it is often better for the patient, and more economical for the country, to do so This is the type of case where often the day hospital, as described by Bierer,[2] can be of value, for again it is cheaper to keep the patient in a day hospital than as an inpatient in a mental hospital

On the other hand, if Dr Shottowe has any alternative methods he can recommend for the care of these often very difficult and trying patients I will be extremely pleased to know them—for there is very little help to be gained from the standard textbooks on psychiatry

London, N W 3 PHILIP HOPKINS

CONSULTANTS IN DERMATOLOGY

SIR,—Dr Franklin's generalisation (Dec 31), based apparently on his experience of one venereal diseases clinic, that the care of venereal diseases clinics may be safely relegated to dermatologists does not in the least alter my view, based on knowledge of the work of all the V D clinics in this country, that, so far as this country is concerned, such relegation would be a retrograde step

Dr Franklin's remark that "the work of the V D clinic can be readily learnt by any competent consultant" reminds me of an incident in the 1914–18 war, when I was adviser in V D to the War Office

The D M S of a certain Command, without reference to others, suddenly posted the pathologist of an important V D section of a military general hospital for service oversea, leaving that section without anyone capable of doing the V D pathology there The result was a moan from the commanding officer of the general hospital, which produced a "raspberry" from the D M S for the C O not having had an understudy available to take the pathologist's place, and an order to "detail a medical officer to proceed to the Military Hospital, Rochester Row, for a few days to learn the Wassermann test" The original pathologist, by W O direction, was back in his laboratory within a week of his havin been sent oversea The O C the general hospital, about th same time, received an order from his D M S that in futur all communications with the O C, Military Hospital, Rochest Row, must be "sent through this office"

London, S W 1 L W HARRISON

EXPELLING TAPEWORMS WITH MEPACRINE

SIR,—The rewards from oral treatment of tapeworm infestation with mepacrine have been so constant tha courage is rising to leave out some of the ritual hangin on from the old régime with male fern When drivin out a worm lying in the jejunum, is it not enough t make sure that there is no fæcal block to its passage And can sodium bicarbonate, except possibly in th achlorhydric, do anything to mucus round the worm scolex ?

A boy, aged 4, had a diet of fluids only (with glucose) and 'Milk of Magnesia' ½ oz morning and evening on Dec On Dec 28 he swallowed 500 mg of mepacrine at 6 A M, washing down each tablet with a sip of water At 7 A M h took *milk of magnesia* ½ oz, and at 9 A M he was given a soap and water enema By 9 50 A M he had passed th scolex He did not vomit till 9 40 A M, after a drink of milky tea By 2 P M he could manage chicken and milk

Till a tastier drug arrives, it is worth while bearing the bitterness of mepacrine, but has not the time come to wonder what the starving and bicarbonate are for ?

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E LL LLOYD

SPORADIC CRETINISM WITH GOITRE

SIR,—Your annotation of Dec 24 prompts us to comment on two recent publications by Stanbury and hi colleagues,[1 2] and to present additional information about a child of the tinker family previously described by us[3 4]

The evidence suggests that there are at least *three* distinct biochemical defects in thyroid-hormone synthesis —not two, as you state

Firstly, there may occur an inability to incorporate inorganic iodide into an organic iodine containing compound[5 6]

Secondly, there may be an impaired ability to couple two molecules of di iodotyrosine to yield thyroxine[1] In the patient in whom this defect was found, Stanbury and his colleagues did not (as you state) identify mono and di iodo tyrosine in the peripheral blood, but they did find tri iodo thyronine and thyroxine In the thyroid gland, however, *mono and di iodotyrosine were present in very large amounts* but thyroxine was detected only with the greatest difficulty

Thirdly, there may be an inability to conserve the iodine of the iodotyrosyl groups owing to deficiency of the enzyme dehalogenase, which normally acts within the thyroid gland by de iodinating these groups and so prevents their loss from the gland It was in the serum of the patient in whom this defect was found that Stanbury et al[2] identified mono and di iodotyrosine as well as thyroxine and tri iodothyronine This was the first time that the spontaneous occurrence of di-iodotyrosine in the peripheral blood was conclusively proved It seems likely, as you say, that the patients studied earlier by Hubble[7] and ourselves[3 4] may belong to this third group

During the past two weeks we have been investigating with radioactive iodine an *additional member* of our large tinker family

He was first seen two *years ago, at the age of 4 weeks* when it was noted that he was goitrous but euthyroid He has now been admitted to hospital because signs of hypo-

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[1] Watts C A H *Lancet* 1954 ii 85

[2] Bierer J *The Day Hospital* London 1951

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1 Stanbury J B, Ohela, K, Pitt Rivers R *J clin Endocrin* 1955 15 54
2 Stanbury J B Kassenaar A A H, Meijer J W A, Terpstra J *Ibid* p 1216
3 McGirr E M Hutchison J H *Lancet* 1953 i, 1117
4 Hutchison J H McGirr E M *J clin Endocrin* 1951 14, 869
5 Stanbury J B, Hedge, A N *Ibid*, 1950 10, 1471
6 Stanbury J B *Ibid* 1951 11 740
7 Hubble D *Lancet*, 1953 i, 1112

criteria usually accepted as indicating simple recessive inheritance (Roberts 1940)

(1) The parents of the affected persons are normal to outward appearances
(2) There is a striking familial prevalence three of the four lots of siblings contain more than one affected child The ratio of normal to affected persons (21 10) shows the usual excess over the 3 1 ratio which is typical of recessive inheritance because we have adequate information only about sets of siblings in whom at least one person is affected A number of normals in unaffected sibships must be unknown to us
(3) All the affected persons are the children of consanguineous marriages

Other characteristic, but rarely encountered, criteria of autosomal recessive inheritance are as follows

(4) Affected persons who marry normals will have only normal offspring in most instances
(5) Affected persons who marry affected persons will have affected offspring only

These last two criteria have not been satisfied in the present pedigree, but in view of the predilection for consanguineous mating it is not inconceivable that the thyroid treatment instituted by us may alter this position in time

Though it may properly be claimed that simple recessive inheritance cannot be proved on the strength of a single pedigree, the occurrence of familial prevalence and consanguinity in the families of other similar cases which we have cited makes it extremely probable that the present cases were so determined The appearance within the same pedigree of Werdnig-Hoffmann paralysis—a disease known to be inherited as a mendelian recessive (Gates 1946)—is interesting Here also the first three criteria of recessive inheritance mentioned above are fulfilled

We have alluded to the possibility that the gene producing goitrous cretinism in the Y-McX family may be operating elsewhere in Scotland We have already recorded the appearance of 3 siblings with goitrous cretinism in another family (Hutchison and McGirr 1954) These also were tinkers They were referred to us by Prof J L Henderson, of Dundee Careful inquiry by Professor Henderson failed to produce any evidence that they were related to the Y McX cretins, but (like us) he met some resistance in taking a family history from these people We have recently had the opportunity of applying radio-iodine tests to 2 more cretinous siblings with goitre, who were referred to us by the Renfrewshire local authority from a home for deprived children They gave results which were identical with those found in our earlier cases The parents of these 2 children were also itinerant tinkers but could not now be traced In view of the unique and self demarcated mode of life of tinkers, who tend to intermarry and to live a life apart from the rest of the community, it seems at least probable that the various cretinous siblings whom we have studied owe their condition to the same recessive gene occurring in the homozygous state.

Summary

The pedigree of a group of itinerant tinkers is presented It is noteworthy for the remarkable frequency of consanguineous mating

Within this family group there were 10 cases of goitrous cretinism and 4 cases of Werdnig Hoffmann paralysis

Goitrous cretinism and Werdnig Hoffmann paralysis are each due to the effect of single but quite separate autosomal recessive genes

We wish to thank Dr Catherine A Brown, executive school medical officer, Argyll County Council, for her great help in tracing the various members of the family group, and Professor Henderson for his efforts to find the connecting link between his cretinous tinkers and ours

References at foot of next column

VASOPRESSIN TANNATE IN OIL AND THE URINE CONCENTRATION TEST

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THE maximal ability of the kidney to concentrate the urine is generally considered to be a good indication of renal function, but to approach this concentration, at least twenty-four hours' deprivation of fluid is necessary (Miles et al 1954) Deprivation of fluid, however, is seldom strictly controlled and depends on the variable amounts of water in the food and on the vigilance of the nurses For the patient the test is nearly always unpleasant and occasionally, if a severe negative fluid-balance develops, it may be hazardous The patient's emotional reaction to being deprived of fluid may also cause the results to be quite misleading (Miles and de Wardener 1953) Furthermore, because of its unpleasantness and potential danger, the concentration test is nearly always performed on only one occasion, although its value would be much increased if it were repeated This natural disinclination to repeat the test is probably its greatest disadvantage

To avoid these disadvantages Miles et al (1954) investigated the possibility of substituting an injection of vasopressin tannate in oil for a long period of fluid deprivation The concentration of the urine after deprivation of fluid was compared in the same subjects with that obtained after the intramuscular injection of 5 units of vasopressin tannate in oil In 10 subjects convalescing from non renal diseases the concentration of the urine after deprivation of fluid was usually greater than after the injection of vasopressin , the discrepancy in 3 of them being substantial , in 9 subjects with renal disease there did not appear to be any difference between the two methods It was considered from these few results that vasopressin tannate was unlikely to be a sufficiently reliable substitute for deprivation of fluid in testing the kidney's maximal ability to concentrate the urine Since these findings were reported, however, the same experiment has been extended to 43 more subjects, of whom 17 were normal (Jones and de Wardener 1956) and 26 were patients, of whom 18 had renal disease and 8 were convalescent from non renal disease The collected results from all these 62 subjects are given below , they confirm that the concentration of urine after deprivation of fluid is greater than after the injection of vasopressin, but they also show that the difference is such that for

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reasonable to draw attention to the similarity between the experimental findings in animals and the present case It appears desirable to exclude the possibility of early pregnancy before administering cortisone to women of child-bearing age

We wish to thank Mr Alan Brews and Prof R J Harrison for permission to publish, and Mr R Q Cox for the photograph

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RUPTURE OF INTRA-ABDOMINAL ANEURYSM SIMULATING RENAL COLIC

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The symptoms referable to aneurysm of the abdominal aorta were analysed by Osler (1905), who stated that the pain due to rupture may resemble the pain of renal colic, gall stones, or appendicitis He cited a case (Bryant 1903) which presented with pain similar to that of renal calculus, agonising in severity and radiating into the left groin and testis Since then the frequency of aneurysm of the abdominal aorta has increased (Zech and Merendino 1954), and the proportion of arteriosclerotic to syphilitic aneurysms has been reversed Osler (1905) gave a ratio of 1 10 whereas Maniglia and Gregory (1952) found the proportion to be 5 2

This relative and absolute increase in the frequency of arteriosclerotic aneurysms has an important bearing on the symptoms Syphilitic aneurysms commonly erode the vertebræ, whereas arteriosclerotic aneurysms rarely do so, as a result pain is an early symptom in the former but comes on much later and less often in the latter Blakemore (1947) has pointed out that arteriosclerotic patients may in fact go to the brink of disaster before experiencing symptoms, and that the first symptom is often pain due to leakage from, or rupture of, the aneurysm

Recent advances in anæsthetic and surgical techniques have made the treatment of abdominal aneurysms a practical proposition, arteriosclerotic aneurysms are particularly amenable to treatment as they often arise distal to the origin of the renal arteries Blakemore (1947) produced satisfactory results in 3 patients with arteriosclerotic aneurysms employing a process of electrothermic coagulation, and Kinmonth et al (1955) have successfully substituted a tube of 'Orlon' cloth for a large abdominal aneurysm The fact that a condition which may be rapidly fatal can now be successfully treated makes early diagnosis imperative

We report here 2 cases of fatal rupture of arteriosclerotic intra-abdominal aneurysms, both of which presented with severe abdominal pain indistinguishable from that of renal colic

Case-reports

Case 1—An engineer, aged 62, had been well until the day before admission to hospital While travelling on a train in Germany he suddenly experienced severe pain in the left loin It lasted only a few seconds but was accompanied by a feeling of faintness The journey to England was continued without further incident, but shortly after leaving Liverpool Street Station next day the pain recurred with such agonising intensity that he lost consciousness He was admitted to St Bartholomew's Hospital as an acute abdominal emergency There was no relevant past or family history

On examination he had recovered consciousness but was still shocked, with pulse rate 58, pulse regular, temperature 95°F, respirations 30 a minute, and blood pressure 90/35 mm Hg He was obese, his pupils reacted to light and accommodation, and the fundi showed narrowed arterioles with arteriovenous nipping There was tenderness in the left loin with guarding Bowel sounds were normal

Investigations—Examination of the blood showed Hb 68%, white cells 13,700 per c mm (polymorphs 90% lymphocytes 8%, monocytes 2%), erythrocyte sedimentation rate 12 mm in the first hour (Westergren) The urine contained a trace of protein but no blood, the blood urea level was 80 mg per 100 ml Plain radiography of the abdomen showed no gaseous distension, subdiaphragmatic air, or renal calculi Electrocardiography showed left ventricular hypertrophy with patchy myocardial ischæmia

Course—An hour after admission the patient felt better, his blood pressure had risen to 160/80 mm Hg and pulse rate to 100 Three quarters of an hour later he had an attack resembling typical renal colic, which consisted of severe pain in the left loin radiating into the left groin and penis His blood-presure fell, but he did not lose consciousness Atropine sulphate gr $^1/_{100}$ was given subcutaneously, and the pain subsided Three and a half hours later he again collapsed, his blood pressure falling to 95/40 mm Hg, but on this occasion there was no pain For the next twelve hours, throughout the night, he remained shocked but pain free Next morning a definite pulsatile mass was palpable in his left loin

Exploratory laparotomy was performed by Mr John Hosford, who found that a large aneurysm of the abdominal aorta had ruptured into the retroperitoneal tissues No treatment was possible, and the patient died thirty one hours after admission and sixty one hours after the onset of the first symptom

Necropsy revealed widespread atherosclerosis affecting especially the coronary vessels and the abdominal aorta There was marked left ventricular hypertrophy, the kidneys appeared normal, and there were no calculi in the urinary tract Immediately distal to the origin of the renal arteries the abdominal aorta had a large fusiform aneurysmal dilatation with additional sacculation to the right, the maximal circumference being 19 cm The left lateral wall of the abdominal aorta 3 cm above the bifurcation had an irregular tear 2 5 cm long The rupture communicated with a retroperitoneal hæmatoma which surrounded the left kidney and ureter and extended into the soft tissues of the pelvis on the left side Sections of the abdominal aorta showed extensive atheromatous lesions

Case 2—A cable operator, aged 55, had been a known hypertensive for five years with a blood pressure of 240/140 mm Hg, and two years before admission he had had an isolated episode of hæmaturia On the morning of the day of admission he developed, following defæcation, an aching right sided abdominal pain which radiated into the right testis The pain subsided after a few minutes but recurred momentarily with much greater intensity in the afternoon This second attack of pain was succeeded by a desire to defæcate again, but before he could do this he lost consciousness He was admitted to St Bartholomew's Hospital as an acute abdominal emergency half an hour later When first seen his complaint was of severe pain in the right testis and an aching pain in the right iliac fossa and groin There was no other relevant past or family history

On examination he was obese, shocked, and in severe pain, with temperature 95°F, pulse rate 114, pulse regular, respirations 22 a minute and blood pressure 65/50 mm Hg His pupils reacted to light and accommodation, and his fundi showed narrowed arterioles with arteriovenous nipping He had diffuse lower abdominal tenderness with guarding on the right side and severe tenderness in the right groin Bowel sounds were present, and the external genitalia were normal The right testis was not retracted but the right cremasteric reflex was absent The femoral pulses were palpable and equal clinical purposes, it seems justifiable to substitute vasopressin tannate in oil for a long period of deprivation of fluid.

Methods

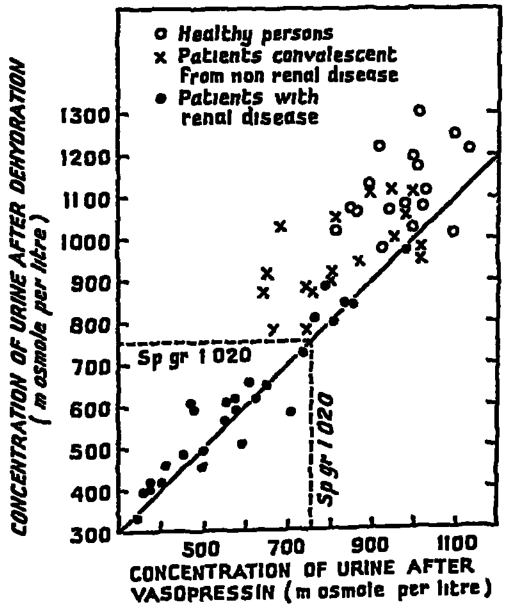
Deprivation of fluid was for thirty-six hours from 8 A.M., except the 17 healthy subjects, who were deprived of fluid for forty-eight hours from 8 P.M. During this time soups, ice cream, and fruit were also withheld. The urine tested was that passed during the last eight hours of the period of deprivation—i.e., from noon to 8 P.M.

The effect of injecting vasopressin was observed one to two weeks after the fluid-deprivation test. Vasopressin tannate 5 units in oil was administered subcutaneously at 7 A.M., and the urine tested was that passed between noon and 8 P.M. on the same day. During this day all the subjects tested were allowed to eat and drink what they wished, but in addition the 17 healthy subjects were given 1000 ml. of water an hour after the injection of vasopressin for reasons already published (Jones and de Wardener 1956).

The osmolar concentration of the urine was calculated from the depression of its freezing-point. A mercury thermometer was used in the 19 original cases (Miles et al. 1954) and a thermistor in the remainder (de Wardener and del Greco 1955). The standard deviation of a reading with the thermistor is ±0.0102°C, corresponding to ±5.5 milli-osmole per litre.

Results

The results are illustrated in the accompanying figure, which shows the osmolarity of the urine after deprivation of fluid plotted against the osmolarity after an injection of vasopressin tannate in oil in 62 subjects. The scale of the abscissa is the same as that of the ordinate so that the line drawn at 45° to the abscissa represents the line along which the points would lie if the concentration of the urine after deprivation of fluid were the same as that after the injection of vasopressin. It can be seen, however, that the results have a linear relationship which lies slightly above this line, indicating that the concentration of the urine following deprivation of fluid is greater than after the injection of vasopressin. It is also evident that this difference becomes less as the osmolarity of the urine approaches that of plasma (about 300 milli-osmole per litre).



Osmolarity of urine after 36–48 hours deprivation of fluid compared with that following injection of vasopressin tannate in oil in 62 persons. diagonal line shows where points would lie if deprivation of fluid and vasopressin tannate concentrated urine equally.

Discussion

The concentration of the urine is greater after fluid deprivation than following an injection of vasopressin tannate in oil, but this difference only amounts, in terms of specific gravity, to approximately 0.002 at a specific gravity of 1.022, and becomes less at lower urine concentrations. (The correlation between specific gravity and osmolarity of the urine has been obtained from the data of Miles et al. [1954].) It therefore seems justifiable, in testing the kidney's ability to concentrate the urine maximally, to substitute an injection of vasopressin tannate in oil for a long period of deprivation of fluid.

The reproducibility of this method is satisfactory. When vasopressin was given on three occasions to each of 9 healthy persons, the standard deviation of an estimate of the greatest concentration of the urine was 82 milli-osmole per litre (in urine 33 milli-osmole per litre is approximately equivalent to sp. gr. 0.001). Comparable figures for repeated deprivation of fluid were available in only 3 healthy persons each of whom was tested on two occasions, so that a proper comparison is impossible; it can only be stated that the greatest difference found in any one person was 46 milli-osmole per litre.

In the observations reported here the urine had to be collected at controlled intervals so that the comparison between the two techniques should not be confused by diurnal changes; but, since the effect of 5 units of vasopressin tannate in oil on the concentration of the urine continues for at least twenty-four hours, there is no need to do this for routine purposes. It is only necessary to measure the specific gravity of all samples of urine passed during the twenty-four hours following the injection of vasopressin tannate.

The one serious disadvantage of the use of vasopressin tannate in oil is that the vasopressin tannate is in suspension. When it has been standing the vasopressin collects as an insignificant brown discoloration at the bottom of the ampoule, and it is necessary to warm and shake the ampoule vigorously before use. It is also an advantage to use a large-bore needle to transfer the oil and vasopressin from the ampoule to the syringe.

There have been no complications following the administration of vasopressin tannate in oil except a feeling of torpor in the 17 healthy persons, who were also given 1000 ml. of water. This symptom did not develop in patients who drank only what and when they wished. Finally, freedom from side-effects and the greater convenience of the test when done with vasopressin allow the test to be repeated fairly frequently (weekly), thus greatly increasing its value.

Summary

The concentration of urine after deprivation of fluid has been compared with that following an injection of vasopressin tannate in oil in 17 healthy subjects, 18 patients convalescent from non-renal disease, and 27 patients with renal disease.

The concentration of the urine after deprivation of fluid was slightly greater than after the injection of vasopressin. This difference was least noticeable when the specific gravity of the urine was less than 1.020.

It is suggested that when an estimate of the kidney's maximal ability to concentrate urine is required for clinical purposes, an injection of vasopressin tannate in oil can be justifiably substituted for a long period of fluid deprivation.

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Investigations—The urine contained a trace of protein but no blood the blood urea level was 80 mg per 100 ml, serum amylase 6 Wohlgemuth units, and plain radiography of the abdomen revealed gall stones

Diagnosis—Torsion of the testis was excluded by the normal appearance of the testes Severe renal colic was thought to be the next most likely diagnosis, but acute pancreatitis, perforated peptic ulcer, and coronary thrombosis were considered in the differential diagnosis It was suggested by one of us that "dilatation of, or leakage from, the abdominal aorta or a peripheral (intra abdominal) artery, such as the renal artery, would explain the picture," but this opinion was not held sufficiently strongly to lead to laparotomy

Course—The severe pain subsided in thirty minutes, but a dull ache in the right loin and groin remained The blood-pressure rose to 120/80 mm Hg No new physical signs appeared, but over the course of the next three days there were transitory attacks of pain which radiated from the right loin to the groin The pain appeared to be relieved by subcutaneous atropine sulphate Despite an adequate fluid intake the output of urine decreased and the blood urea level rose to 180 mg per 100 ml On the third day the patient again collapsed with severe pain in the right loin and groin, and he died an hour later—ninety two hours after the appearance of his first symptom

Necropsy revealed gross left ventricular hypertrophy The gall bladder contained gall stones, but the kidneys were macroscopically normal, and there were no calculi in the urinary tract The aorta showed a little atheroma, mainly in the abdominal region, and there was a saccular aneurysm 2 5 cm in diameter in the lateral wall of the right common iliac artery 4 cm from its origin There was a linear rupture 1 cm long in the wall of the aneurysm The adventitia had been dissected from the media over an area extending 3 cm from the tear, the gap between the two layers containing blood clot In continuity with the tear there was a large retroperitoneal hæmatoma filling the right iliac fossa and right half of the pelvis and extending superiorly as far as the perirenal area Section of the kidneys showed benign hyper tensive disease, and the aorta showed moderate atheromatous changes in the intima, but the wall of the aneurysm showed no evidence of arteriosclerosis or syphilis

Discussion

Arteriosclerotic aneurysms develop almost exclusively after middle age Of 97 patients with such lesions reported by Estes (1950) all were aged more than 40, and about 70% were aged more than 60 Rupture of or leakage from such an aneurysm may never occur, the condition remaining undiscovered until necropsy, alternatively it may give rise to symptoms which lead to its being diagnosed before it ruptures

Of Blakemore's (1947) 26 patients 5 presented with a pulsatile abdominal mass 1 with pain resembling that of duodenal ulcer, and 1 with symptoms referable to duodenal ileus and obstruction

Only 4 of 15 patients described by Scott (1944) had symptoms—in each case aching pain in the lower abdomen and back

More rarely symptoms may result from pressure on other intra abdominal organs, but very much less frequently than is the case with syphilitic abdominal aneurysms An aneurysm may rupture silently, leading to rapid death, or into the gastro intestinal tract, most frequently the duodenum, producing hæmatemesis and/or melæna

Rupture is often preceded by a leak, in which case the patient may present with severe pain as an acute abdominal emergency

Of Blakemore's (1947) 26 patients 11 presented with severe pain heralding rupture

Of 61 cases reported by Zech and Merendino (1954) in 24 severe pain came on before rupture and in 7 laparotomy was undertaken for what were thought to be acute abdominal emergencies The preoperative diagnoses were perforated peptic ulcer (4), urinary retention (1), pancreatitis (1) and volvulus (1)

Of the patients reported by Hubeny and Pollack (1940) 2 presented with acute pain preceding rupture, and both were diagnosed as having a perforated peptic ulcer Whether these cases were syphilitic or arteriosclerotic is not stated

Of great importance is the time which may elapse between the onset of the first pain due to the initial leak and death from rupture In Estes's (1930) series were 6 patients who survived ten hours, five days, four weeks four weeks, six months, and four years respectively after the first leak In 8 of the cases reported by Zech and Merendino (1954) small leaks had sealed before the aneurysm ultimately ruptured In the 2 present cases the intervals between the first pain and death from rupture were sixty-one and ninety-two hours It is during this period that surgical treatment might be attempted

It is not clear why the pain resembled renal colic in the present cases It is unlikely that it was due to sudden dilatation of a blood vessel, but the dissection of the iliac artery in case 2 might explain the initial severe pain It is possible but improbable that the presence of blood clot surrounding the ureter on the affected side in each case caused ureteric spasm and pain It seems more likely that the pain was due to leaking blood dissecting the retroperitoneal fascial planes and muscles of the first and second lumbar segments, for Kellgren (1937) has shown how pain resembling that of renal colic may be produced by injecting saline solution into the interspinous ligaments and muscles of the first lumbar segment

There were two striking clinical features seen in both patients the extreme degree of shock, which was comparable to that seen in association with myocardial infarction, and the relative speed with which the severe pain disappeared The absence of firm evidence of other intra-abdominal conditions which could cause the symptoms might have led us to consider more seriously a vascular cause for the pain, particularly as both patients were aged more than 50 and had widespread signs of arteriosclerosis Case 2 had, however, had a previous episode of hæmaturia and also showed radio graphic evidence of gall stones, while the diagnosis of renal colic was supported in both cases by proteinuria and a raised blood urea level An interesting clinical point in case 2 was the absence of the right cremasteric reflex, probably resulting from pressure of blood clot on the right genitofemoral nerve

It would be unwise to generalise on the basis of these 2 cases, but the sudden occurrence, in an arteriosclerotic subject, of a relatively short lived but severe abdominal pain associated with severe shock should suggest the possibility of its being due to a leak from an intra abdominal aneurysm

Summary

The first symptom of an arteriosclerotic intra abdominal aneurysm may be severe abdominal pain of sudden onset, resulting from a leak and mimicking that of other acute abdominal emergencies

With the advent of new anæsthetic and surgical techniques treatment of such aneurysms is now practic able, and since an appreciable time may elapse between the onset of the first symptom due to a leak and death from rupture, early diagnosis is of paramount importance

An account is given of 2 fatal cases of ruptured intra abdominal aneurysm, both of which presented with severe pain resembling renal colic

We are grateful to Dr E R Cullinan and Mr John Hosford for permission to publish, and to Dr R Finlayson and Dr P J A Butcher for the necropsy reports

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BACTEROIDES IN INTRA-ABDOMINAL SEPSIS

THEIR SENSITIVITY TO ANTIBIOTICS

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MOST cases of localised and generalised peritonitis are caused by organisms from the intestine The organisms usually incriminated in surgical textbooks are *Escherichia coli* and other members of the coliform group and aerobic streptococci Anaerobic streptococci and clostridia are sometimes mentioned, but the anaerobic non sporing bacilli of the Bacteroides group are usually ignored

The pioneer work of identifying these organisms was done by Continental bacteriologists

Loeffler (1884) observed *Bacteroides funduliformis* (*Bacillus necrophorus*) in calf diphtheria

Veillon and Zuber (1898) found them in appendicitis, and Halle (1898) in diseases of the female genital tract

Vincent (1896) found a fusiform bacillus of the same group in ulcerative *lesions of the throat*

Similar organisms were subsequently demonstrated in normal mouths (Tunnicliff 1906, Slanetz and Rettger 1933) and in the healthy alimentary canal (Eggerth and Gagnon 1933, Weiss and Rettger 1937)

Bacteroides are the predominant organisms in the lower intestine, where they greatly outnumber *Esch coli*

For some time after the early work on Bacteroides their role in the causation of human infections was largely neglected for several reasons the comparatively slow growth and the delicacy of Bacteroides compared with the other bacteria which often accompany them in pus and may overgrow them in cultures, the frequent omission of anaerobic methods from routine bacteriology, and, perhaps, the failure to ensure an adequate carbon-dioxide tension in anaerobic apparatus A deficiency of carbon dioxide may inhibit the growth of some strains (Lewis et al 1940)

More recently the importance of Bacteroides infections in many parts of the body has come to be more widely recognised

Weinberg et al (1928) found anaerobic gram negative rods, accompanied by many other organisms, in acute appendicitis Schmitz (1930) also found them numerous in appendicitis

Harris and Brown (1927) found Bacteroides in 6 patients with postpartum infections

Thompson and Beaver (1932) reported 2 cases of fatal bacteræmia and noted 10 others in the literature

Cohen (1932) isolated several species of Bacteroides from 16 lung abscesses

Lemierre (1936) described cases of Bacteroides septicæmia in which the infections spread from lesions of the mouth and jaw, the endometrium, the appendix, and other sites

Dixon and Deuterman (1937) reported 6 postoperative abdominal infections

Beigelman and Rantz (1949) reviewed 47 infections in 34 of which the Bacteroides were associated with other organisms

McVay and Sprunt (1952) observed 35 cases in five years, the infections involved the respiratory system, the gastro-intestinal tract the female genital and urinary tracts, and the skin

Clark and Wiersma (1952) and Carter et al (1953) reported infections originating in the female genital tract in 47 and 153 patients respectively

Alston (1955) reviews this subject and describes 12 cases due to *Bacteroides necrophorus*

There have not been many reports of the sensitivity of Bacteroides to antibiotics

Foley (1947) and Beigelman and Rantz (1949) found that Bacteroides were often resistant to penicillin and streptomycin

McVay and Sprunt (1952) tested a few strains with penicillin, streptomycin, sulphadiazine, and aureomycin and found aureomycin to be much the most effective

Fisher and McKusick (1953) found that strains varied greatly in sensitivity to penicillin and streptomycin, but most were highly resistant, all six strains tested with chloramphenicol and all seven with aureomycin were sensitive

Garrod (1955) describes the results of a thorough investigation of the sensitivity of four species of Bacteroides (55 strains in all) to seven antibiotics He found that all four were relatively resistant to streptomycin and sensitive to chloramphenicol and oxytetracycline Three of the four species were sensitive to penicillin

We report here a study of the bacteriology of intra-abdominal sepsis Our objects were to find how often Bacteroides were present compared with other organisms, and to determine the sensitivity of Bacteroides to antibiotics and sulphonamide We regarded all gram-negative anaerobic non sporing bacilli as Bacteroides, although this definition covers a heterogeneous group of organisms

Material and Methods

Most of the organisms were isolated from pus from suppurative lesions in the abdomen, sent to the laboratory for routine examination in the year from Sept 30, 1954, to Sept 29, 1955 There were 34 specimens from either localised or generalised peritonitis caused by appendicitis, 18 specimens from peritonitis of other causes, and 46 swabs from discharging wounds of the abdominal wall These 46 were selected for anaerobic study from 156 abdominal-wound swabs because the clinical features of the cases or study of the direct smears indicated the probability of anaerobic infection In several of these wounds the pus was forming inside the abdomen and discharging through a drainage tube or a fistula but in a few the infection was in the abdominal wall In addition, 13 acutely inflamed appendices were obtained from the operating-theatre as soon as possible after operation and were studied in more detail than was possible with specimens sent to the laboratory for routine examination

Smears and cultures were made from pus and from the peritoneal surfaces and walls of the appendices, care being taken to avoid contamination from their lumina Careful microscopy of gram-stained smears was found to be important Bacteroides were often clearly distinguishable from coliform bacilli, being more slender and shorter or, less often, filamentous or fusiform Aerobic cultures were made on MacConkey agar and on 5% horse-blood infusion agar plates Anaerobic cultures were made on blood-agar and were incubated in an atmosphere of hydrogen containing 5% carbon dioxide in McIntosh and Fildes (1916) jars All the cultures were examined after one day's and two days incubation at 37°C, and many of the anaerobic plates were incubated longer Organisms which grew only on the anaerobic plates were retested for anaerobiosis by subculturing them on aerobic and anaerobic blood-agar One or more subcultures were often required to separate the Bacteroides from the anaerobic cocci and other organisms accompanying them Strains were preserved for future examination by freeze-drying with an Edwards' centrifugal freeze dryer suspensions made in horse serum

Sensitivity of Bacteroides to Antibiotics and Sulphonamide

Sensitivity tests were put up on anaerobic blood-agar plates with penicillin, streptomycin, chloramphenicol, oxytetracycline, chlortetracycline tetracycline, erythromycin, bacitracin, neomycin, and polymyxin B For most of the tests a disc method was used (Fairbrother and Martyn 1951, Fairbrother and Jennings 1955) The sensitivity of a smaller number of strains was measured more exactly by a quantitative method in which doubling dilutions of the drugs were incorporated in the plates, the lowest concentration which much reduced the growth of the organisms after forty-eight hours' incubation was taken as the lowest inhibiting concentration As a control the Oxford staphylococcus, grown anaerobically, was included in each batch of strains tested with all the drugs

Reviews of Books

Atlas Illustrating the Topographical Anatomy of the Head, Neck and Trunk

The late Johnson Symington, M D F R C S, F R S, professor of anatomy, The Queen's University, Belfast Edinburgh Oliver & Boyd 1956 £5 5s

THIS atlas first appeared in 1917, and the plates and copyright were bequeathed to the Anatomical Society of Great Britain and Ireland by Professor Symington's daughter in 1932 In response to many requests, the council of the society has now decided to republish the atlas, using the original blocks The plates are life-sized half-tone drawings of a series of cross-sections taken at regular intervals through two male adult bodies, one serving for the trunk and the other for the head and neck The accompanying reconstructions show the levels of the sections in relation to the skeletal features The plates are printed on thick glossy paper and are stored in a stout and convenient portfolio The reproduction is good, and the main features of each section are adequately labelled, the whole atlas forms a justly renowned contribution to cross-sectional anatomy Since the pictures are life-size, direct measurements may be made on them from the surface to any desired structure, and experience has already shown their very great value to surgeons and radiologists A new generation of anatomists will also welcome the reappearance of this old friend of their seniors, for there can be no doubt of the usefulness of cross-sections in making the student revise his topographical knowledge

Nursing Care of the Newly Born Infant

W S Craig, M D F R C P, professor of pædiatrics and child health, University of Leeds In collaboration with M F G Buchanan, M R C P E, R J Pugh, M R C P, M Pattullo, R G N, S C M, and M J W Taylor, R G N S C M M T D Edinburgh E & S Livingstone 1955 Pp 472 35s

THIS is an excellent work which every midwife should read, and which every obstetrician should insist is kept in his department

Not long ago the newborn infant was often looked on as a by product of the art of obstetrics and obstetricians bothered very little about this side of their business Pædiatricians were "new fangled upstarts who were forbidden entry, so that the care of the infant fell to the midwife who wielded far more power than either her training or knowledge justified Happily that phase is passing, and the midwife now shares with the pædiatrician the nursing care of the newborn This book will be of immense value in teaching her the reasons for what she does, and moreover it never suggests that she takes any therapeutic action beyond her ability Of equal importance is the stress laid on observing those minutiæ of behaviour whose early recognition may make all the difference between death and survival

The text is liberally illustrated but, with few exceptions, the colour photographs are noticeably less effective than those in black and white

Mistakes are remarkably rare, but one on p 168 on the use of full cream dried milk, may lead to some carbohydrate diarrhœa The section on mothercraft is a little less impressive than the rest of the book, it is often open to doubt whether doctors or midwives really know more about this subject than mothers themselves

A successful future is assured for Professor Craig's book

Cardiac Diagnosis

A Physiologic Approach Robert F Rushmer, M.D, associate professor of physiology and biophysics, University of Washington Medical School Philadelphia and London W B Saunders 1955 Pp 429 80s 6d

AT the start of his clinical work, the student is often told to study the principles of medicine in his textbook of physiology Unfortunately most books on applied physiology fail to make close contact with everyday medicine, and there is a big gap between the pure physiology book and most textbooks of medicine This gap is now filled in cardiology by Dr Rushmer's valuable book It will attract all those interested in understanding the principles of cardiology, from student to cardiologist

The book is well written and illustrated, each legend being self-explanatory The selection and arrangement of the material is excellent, and everything is based on general principles which would be difficult to find elsewhere in book form As Dr Rushmer points out at the beginning of the chapter on electrocardiographic interpretation, the approach to this subject may be empirical or theoretical Successful empirical interpretation involves long experience and lengthy description, making it impracticable for most cardiologists On the other hand, the theory of electrocardiography is now sufficiently accurate to give a good working knowledge of the subject, and its principles are clearly described in this book

The logical approach sometimes results in anomalies, such as the appearance of thyroid disorders under the heading of myocardial ischæmia When hypotheses are many and conflicting the author has lost a little of his enthusiastic simplification, and this is evident in the chapter on heart-failure This is not the book in which to look for clinical details, but it is a pity to find no mention of the waterhammer pulse in the section on patent ductus The systolic murmur of mitral incompetence is described as mid systolic, finishing before the second sound, which fits neither the facts nor the theory since the pressure difference between auricle and ventricle and hence regurgitation and murmur, must be great at the time of closure of the aortic valve

Multiple Neurofibromatosis

A Clinical, Pathological and Genetical Study Frank W Crowe, M D William J Schull, PH.D and James V Neel, M D, PH D Institute of Human Biology, University of Michigan Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1956 Pp 181 36s

THIS is in essence a statistical and genetical study of 223 cases of neurofibromatosis (the word multiple is surely redundant) in Michigan

Just under 28% of these people were attending hospital for conditions unrelated to the disease, while about 18% came for cosmetic reasons only 78% had six or more cafe au lait spots, whereas no normal person was seen with this number A consistent finding of much diagnostic value was the violaceous colour associated with the tiniest neurofibromas, which from the first were papular (demonstrable by oblique light) and tended to be invaginated Another was the frequency with which osseous lesions were noted

About half the patients had affected relatives and it was calculated that the rate with which the gene or genes responsible for the trait arose through mutation must be approximately 1×10^{-4} per gamete per generation this, it is claimed, is the highest yet encountered for a dominantly inherited trait No significant intrafamily similarities in tumour location were noted except for the tendency of palmar and plantar neurofibromas to be present in some families and not in others The cases, however, were hardly numerous enough for investigation of the inheritance of acoustic neuromas

The authors make interesting observations on the pathology of neurofibromas and especially the presence in them of mast cells They draw attention to the inadequacy of most case histories of optic-nerve gliomas and hint that this condition may, more often than we think, exist in association with neurofibromatosis Further study may show that the subnormal mentality so common in families of patients with neurofibromatosis often has a structural basis

Advances in Virus Research

Vol III Editors Kenneth M Smith, F.R S, virus research unit, Molteno Institute, Cambridge, Max A Lauffer, department of biophysics, University of Pittsburgh, Pennsylvania New York Academic Press London Academic Books 1955 Pp 338 £3 4s

THE reviews in *Advances in Virus Research*, which now occupies a very useful place in the reading of those who study viruses, are written by people with first-hand knowledge of their subject so that many of the articles reach a higher standard of critical analysis than is found in most reviews The editors also do well in avoiding catalogues of references except polymyxin B, for which the control organism was a laboratory strain of *Esch coli* Sensitivity to bacitracin, neomycin, tetracycline, and chlortetracycline was determined by the disc method only, and sensitivity to polymyxin B by the quantitative method only

To measure the inhibiting effect of strict anaerobiosis on the activity of streptomycin, the sensitivity of the Oxford staphylococcus was determined under aerobic and anaerobic conditions simultaneously The effect of added carbon dioxide on the streptomycin (by lowering the pH) was examined by determining simultaneously the sensitivity of four cultures of Bacteroides in pure hydrogen and in hydrogen+5% carbon dioxide For this comparison strains were selected which grew as well in hydrogen as in the mixture of hydrogen and carbon dioxide

Sensitivity to sulphadiazine was determined by the method of Harper and Cawston (1945), usually with 10 mg of sulphadiazine per 100 ml During the earlier part of the work tests were done with 50 mg of sulphadiazine per 100 ml, but several strains gave identical results when retested with 10 mg of sulphadiazine per 100 ml

TABLE I—FREQUENCY OF ISOLATION OF VARIOUS BACTERIA FROM ABDOMINAL SUPPURATIVE LESIONS

—	Acute appendicitis (special series)	Peritonitis and abscess caused by appendicitis	Other intra-peritoneal sepsis	Abdominal wound discharges*	Total
No of specimens	13	34	18	46	111
Coliform bacilli	12	25	8	21	66
Other aerobic gram negative bacilli	0	3	3	9	15
Aerobic streptococci	7	12	4	17	40
Staph aureus	0	0	2	8	10
Micrococci and *Staph albus*	1	4	2	3	10
Other aerobes	1	0	0	4	5
Bacteroides	11	16	9	31	67
Anaerobic streptococci	10	10	5	18	43
Clostridia	2	1	2	2	7

*Selected for anaerobic incubation (see text)

Results

The organisms most commonly identified in the 111 specimens examined were Bacteroides in 67 specimens, coliforms in 66, anaerobic streptococci in 43, and aerobic streptococci in 40 (table I) The cultures of exudates on the surfaces of inflamed appendices yielded relatively more anaerobic streptococci and Bacteroides than did the cultures of peritoneal pus This difference probably reflects the greater care with which cultures from the appendices were studied The cultures were nearly always mixed, but in many specimens Bacteroides were the predominating organisms and often they were numerous Pure growths of a coliform were obtained from 3 specimens of *Staphylococcus aureus* from 3, of *Staph albus* from 1, and of Bacteroides from 1 specimen only Clostridia were usually scanty compared with the other organisms present, they were noted in moderate or large numbers in only 7 specimens, but probably were sometimes overlooked when greatly outnumbered by other bacteria

The Bacteroides strains usually grew quite easily and after forty eight hours' incubation gave colonies 0 5–1 0 mm in diameter or sometimes larger The colonies were smooth easily emulsifiable, usually greyish and semi-translucent, and with a low convex surface and an entire edge and produced no obvious hæmolysis Many closely resembled the colonies of the anaerobic streptococci which often accompanied them The growth of many Bacteroides was encouraged by carbon dioxide in the anaerobic atmosphere Eight strains were cultured simultaneously on blood agar in hydrogen and in hydrogen+5% carbon dioxide All grew well in the mixture, whereas in the hydrogen 3 grew feebly, 3 grew moderately well, and 2 gave colonies as large as those grown in hydrogen+carbon dioxide

TABLE II—SENSITIVITY OF BACTEROIDES TO ANTIBIOTICS AND SULPHADIAZINE TESTED BY THE DISC AND HARPER CAWSTON METHODS RESPECTIVELY

Antibiotic	No of strains tested	Sensitive	Moderately sensitive or doubtful	Resistant
Penicillin	57	2	3	52
Streptomycin	57	1	2	54
Chloramphenicol	57	54	3	0
Oxytetracycline	57	54	3	0
Chlortetracycline	23	22	1	0
Tetracycline	17	16	1	0
Erythromycin	54	30	17	7
Bacitracin	17	0	2	15
Neomycin*	11	0	0	11
Sulphadiazine	38	32	0	6

*Each neomycin disc contained 30 µg

Bacteroides probably were present even more often than appears from our results On several occasions we failed to isolate them although we suspected their presence from microscopy of the pus This may have happened when they were present in relatively small numbers and were therefore easily overgrown in mixed cultures, or when we were dealing with the more delicate and slowly growing varieties, or with strains which may have been destroyed by overlong exposure to the air during examination of the plates (Hine and Berry 1937) Even small numbers of *Esch coli* are readily detected in culture, but Bacteroides—even those of comparatively easy growth—must be fairly numerous if they are to be detected in the complicated mixed cultures usually obtained from abdominal pus

The results of the sensitivity tests are given in tables II and III The two methods agreed well All the strains tested were sensitive to the tetracyclines and chloramphenicol Most of them were sensitive to sulphadiazine, and more than half were fully or moderately sensitive to erythromycin Most were resistant to penicillin and to streptomycin Their resistance to *strepto*

TABLE III—QUANTITATIVE SENSITIVITY TESTS LOWEST INHIBITING CONCENTRATION OF ANTIBIOTICS FOR BACTEROIDES AND CONTROL ORGANISMS GROWING ON ANAEROBIC BLOOD AGAR

Antibiotic	Bacteroides	Control organism
Penicillin	1 strain 0 075 unit per ml 1 „ 0 15 „ 1 „ 0 6 „ 1 „ 5 0 units „ 7 strains 10 0 „ 2 „ 20 0 „	Oxford staphylococcus 0 03 unit per ml
Streptomycin	2 strains 31 2 µg per ml 1 strain 62 5 3 strains 125 10 „ 250 „ 5 „ 500 and over	Oxford staphylococcus 31 2 µg per ml (Oxford staphylococcus aerobic 1 9 µg per ml)
Chloramphenicol	1 strain 1 5 µg per ml 9 strains 3 1 „	Oxford staphylococcus 3 1 µg per ml
Oxytetracycline	2 strains 0 15 µg per ml 13 „ 0 3 „ 1 strain 1 2 „	Oxford staphylococcus 0 15 µg per ml
Erythromycin	2 strains 0 06 µg per ml 1 strain 0 12 „ 2 strains 0 25 „ 3 „ 0 5 „ 1 strain 1 0 „ 1 „ 1 0 „	Oxford staphylococcus 0 06 µg per ml
Polymyxin B	3 strains 250 units per ml 20 „ 500 „ and over	*Esch coli* 1 unit per ml

Three articles in the new volume reflect the present interest in virus nucleic acids There is a fascinating and shrewd survey by Seymour S Cohen of comparative biochemistry and virology a thorough account of the chemotherapy of viruses, with the accent on compounds which interfere with nucleic acid metabolism, by R E F Matthews and J D Smith, and a very interesting description of bacterial transformations by Harriet Ephrussi Taylor An article by J W Beard, D G Sharp, and E A Eckert on tumour viruses is concerned mainly with the Shope papilloma and avian erythromyeloblastic leucosis viruses *This is the only article* which deals specifically with animal viruses, and the views it gives will command respect if not universal agreement K M Smith discusses the development of insect viruses as *studied by morphological methods* *K Maramorosch describes* the evidence which establishes conclusively the multiplication of plant viruses in their insect vectors, a finding which is full of striking implications concerned with the origin and nature of viruses Finally, L O Kunkel writes on the phenomenon of cross protection between strains of Yellows type viruses

Das Phasenkontrastverfahren in der Hämatologie

H G HANSEN, DR MED, oberarzt, University Children's Clinic, Kiel, and ALEXANDER ROMINGER Hamburg Stormarn Verlag 1955 Pp 169 DM 16

THIS book shows very well the results obtainable with phase-contrast microscopy applied to blood and bone-marrow studies There are some 250 excellently reproduced photomicrographs, and the range of illustrations is remarkably complete Technical detail about the photographs is given, and it must be pleasant to work with such well-suited apparatus If anyone wishes to study the possibilities, and the limitations, of this technique, he cannot do better than consult this volume

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Practical Hæmatology (2nd ed London J & A Churchill 1956 Pp 229 20s)—The second edition of Dr J V Dacie's valuable handbook is half as long again as the first Previous *sections have been expanded and new ones* added, such as those on the L E cell and abnormal hæmoglobins The book still concentrates on the quantitative tests of hæmatology and omits any descriptive morphology, for which other books are available to the student The new edition has been rewritten to such an extent that it is almost a new book The section on blood coagulation is entirely revised and now gives details of tests such as the thromboplastin generation test and the assay of antihæmophilic globulin Tests for platelet antibodies are given, but Dr Dacie finds none of them entirely satisfactory This assessment of the value of new methods is a feature we are glad to see, and it is clear that no method has been included just because it is new There is an adequate section on blood groups The detail about recommended methods is notably complete and ensures that this edition will be as welcome and as constantly used as its predecessor

Some of the Answers (Ilfracombe Stockwell 1956 Pp 160 10*s* 6*d*)—In his 25 short chapters of advice Dr G C Milner ranges over subjects great and small—from piles, colds and chilblains to religion and economics On all he has definite views Much of his advice is such as might be expected from a thoughtful and experienced family doctor and he has helpful things to say about worry and anxiety, matrimony, pregnancy, childbirth, and the elements of economics On some other subjects he is less happy Tinct quin ammon, saline douching and frequent nose blowing for the early cold, lying prone for epistaxis and scrubbing with boiled nail brush and covering with plain elastic adhesive bandage for grazes will seem doubtful expedients to many, and it is hard to believe that ' there are many occasions when a baby of six months is the better for being slapped hard across the buttocks

Histamine (London J & A Churchill 1956 Pp 472 50s)—Last year the Physiological Society and the British Pharmacological Society joined forces with the Ciba Foundation to hold a series of meetings on this subject in honour of Sir Henry Dale O M The proceedings of these symposia have now been published under the editorship of Dr G E W Wolstenholme and Miss Cecilia O Connor

New Inventions

AN ELECTRONIC STETHOSCOPE

WE have designed a stethoscope including a miniature battery-operated amplifier, contact microphone, and conventional ear-pieces Experience of existing electronic stethoscopes showed a number of undesirable features they impart a "mechanical" quality to the sounds heard in the ear-pieces and harshness in the upper register, there is a background hum, and extraneous noises are simultaneously picked up and amplified, and the stethoscopes are very costly and often cumbersome These faults have been successfully eliminated *in our* stethoscope

The microphone was designed to convey sounds arising from the source with which it is in contact and is *insensitive to all outside noises* The only extraneous *noises heard are those which resonate in the chest* or in that part of the body on which the microphone is placed

The amplifier, being compact ($1^3/_4$ in × $3^1/_4$ in × $1^3/_8$ in) *and light (18 oz)*, is easily carried suspended from the neck, and the instrument can be used wherever a stethoscope is used There are two outlets so that two people can use ear-pieces and hear identical sounds One *of the outlets can also be used for a tape-recorder* or a loudspeaker, which is excellent for teaching There are two input sockets so that two microphones may be used simultaneously

It has been found possible to attach it to a portable electrocardiograph and so obtain tracings of heart sounds, which is a most inexpensive method of phonocardiography The instrument has only three controls, of which one regulates volume and the other two restrict the upper and lower frequency ranges The latter make it possible to hear the heart sounds (which are of very low frequency) to the exclusion of breath sounds and other noises in the higher frequency range Thus outside noises in the ward or those of a passing train are completely excluded

The clinical applications of this instrument are endless, and it is ideal for teaching It enables foetal heart sounds to be picked up with ease, and murmurs related to arteriosclerotic narrowing of the great vessels are readily amplified

The apparatus is being produced by Ursonic Ltd, 11, Old Queen Street, London, S W 1

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mycin was usually much greater than that of the Oxford staphylococcus, although streptomycin was less effective against this organism under anaerobic than under aerobic conditions (table III) The use of pure hydrogen in the anaerobic jar made no appreciable difference to the streptomycin sensitivity of the strains whose growth was not affected by the omission of carbon dioxide

All the strains tested with bacitracin, neomycin, and polymyxin B were resistant to these substances

Penicillin and streptomycin are often given simultaneously in the treatment of peritonitis We tried to determine whether these drugs could enhance one another's action to a degree which would make them clinically effective in Bacteroides infections Ten strains of Bacteroides were plated on blood-agar containing various concentrations of penicillin and streptomycin The presence of a subinhibitory concentration of either drug did not increase the sensitivity to the other more than twofold

During the investigation organisms apparently similar to the intra-abdominal Bacteroides strains were isolated from other sites on 41 occasions Twenty-three strains were isolated from postpartum high vaginal swabs Other sources included 1 salpingitis, 1 empyema, 1 Bartholin abscess, and 1 abscess of scrotum Most of the vaginal strains appeared to be behaving as commensals

It is not easy to determine the clinical effect of an antibiotic on Bacteroides strains in patients with intra-abdominal sepsis, because other organisms are usually present and successive samples of pus are often difficult to obtain The following case did provide evidence of the effectiveness of oxytetracycline

A man, aged 56 was operated on for pelvic appendicitis in August, 1955 An abscess was found lying against the lateral pelvic wall The remains of a partially destroyed appendix were removed with considerable difficulty In view of the extensive induration and of the possibility of an escaped stercolith having been left behind, it was felt that a residual abscess might form The patient was readmitted to hospital in October with a purulent discharge from the wound and complaining of severe low back pain, thought to be probably due to a residual abscess He was treated with penicillin and streptomycin and left hospital after five weeks He was readmitted on Nov 21, 1955, with severe low back pain and a temperature of 101°F A large abscess pointing in the right loin just above the iliac crest was opened next day and found to be tracking up from the pelvis A drainage tube was inserted, through which there was a copious discharge of pus each day until antibiotic treatment was started On Nov 24 and 26 the pus was examined , smears showed many slender gram negative bacilli and a very few streptococci, and cultures yielded a few aerobic micrococci and profuse growths of Bacteroides resistant to penicillin and streptomycin and sensitive to oxytetracycline chloramphenicol, and erythromycin The patient was given oxytetracycline 2 g by mouth on Nov 26 followed by 1 g daily On Nov 28 the discharge had diminished , a smear showed very few gram negative bacilli, and culture yielded a scanty growth of Bacteroides The same result was obtained each day until Dec 3, when oxytetracycline 3 g was given, followed by 2 g daily There after the Bacteroides disappeared from the smears, and daily cultures were sterile The amount of discharge decreased each day and ceased on Dec 7, when the patient left hospital He continued to take oxytetracycline until Dec 11, and has kept well since

Discussion

Mixed infections are the rule in intra-abdominal sepsis, and it is difficult to assess the virulence of the different organisms This difficulty applies as much to *Esch coli* (which is commonly regarded as a pathogen) as to other organisms In the absence of better criteria of virulence it must be assumed that varieties of bacteria which are commonly numerous are of pathogenic importance On this basis the most important bacteria are *Esch coli*, aerobic and anaerobic streptococci, and Bacteroides The Bacteroides are probably the most numerous of all

The treatment of intra-abdominal sepsis is, of course primarily surgical and antibiotics are by no means always required When they are, they usually must be given promptly, and the initial choice of drug must often be based on a knowledge of the bacteria usually present in similar infections

It would be wrong to dogmatise about the antibiotic treatment of a condition whose bacterial causation is as complex and variable as peritonitis Penicillin and streptomycin are often given simultaneously to control infection by gram-positive organisms and by coliform bacilli, and many surgeons believe that they are beneficial Several workers have found the tetracyclines to be effective adjuncts to the surgical treatment of peritonitis and some (Wright et al 1949, 1951, Wright and Prigot 1951 Prigot and Maynard 1955) consider that they are better than the older drugs Cantrell and Stafford (1955) found that subphrenic and other intra-abdominal abscesses followed appendicitis less often since the introduction of broad-spectrum antibiotics Our sensitivity tests showed the tetracyclines to be highly active against Bacteroides , they are also active against most coliform bacilli strepto cocci, and clostridia The tetracyclines are therefore probably superior to penicillin and streptomycin, which are unlikely to influence abdominal infections in which Bacteroides are the main agents This conclusion is strengthened by the published reports of Bacteroides infections of various organs cured with tetracyclines (Rantz 1951, Marson and Meynell 1953) Garrod (1955) also suggests that a tetracycline should be used for infections originating in the lower bowel The tetracyclines, like other antibiotics, cannot be used without some risks therefore they should not be used in conditions in which antibiotics are not clearly needed—e g uncomplicated appendicitis

Those who prefer to use penicillin and streptomycin in peritonitis should be prepared to substitute a tetracycline if these drugs prove ineffective In particularly severe infections it may be advisable to give streptomycin with the tetracycline, to ensure a more rapid bactericidal action on coliform bacilli Stern and Elek (1955) found that a mixture of streptomycin and a tetracycline had a bactericidal action on coliform bacilli and suppressed resistant variants

It should be remembered that our sensitivity tests were done with strains of intestinal origin Garrod (1955) shows that other strains may be different, especially in their sensitivity to penicillin

Summary

In 111 specimens of pus from the abdomen organisms of the Bacteroides group were often present in large numbers Other organisms which were often numerous were *Esch coli*, aerobic streptococci and anaerobic streptococci

Most of the Bacteroides strains were resistant to penicillin, streptomycin, bacitracin, neomycin, and polymyxin B All were sensitive to tetracyclines and to chloramphenicol Most were sensitive to sulphonamide and moderately or fully sensitive to erythromycin

We wish to thank Mr R V Cooke for permission to publish the case-report, and Mr L J Waller for valuable technical assistance

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References continued overleaf

THE LANCET

LONDON SATURDAY, JUNE, 30, 1956

21st-Century Man

FOR many years the public of the Western countries has been warned about next century Science, the prophets have said, will destroy man He will be annihilated by atomic bombs (the products of unregenerate science), or be herded in ant-like societies whose rulers (thanks to science) can spy on him by television, influence him by waves or steal his brain and replace it with their own—projects all curiously familiar to a medical listener More respectably, man will simply starve through overpopulation caused by our folly in extending medical care to our poor relations, or become half-witted through failure to propagate an intellectual aristocracy While there is time, let him turn back, let him abandon science and revert to common sense, the tribal deities, and the past

Our generation, certainly, is qualified to recognise danger It has seen what can be done by a HITLER, and it still lives in the knowledge that a handful of psychopaths could bring human history to an end But in recognising danger we need not lose our sense of proportion, and we should know by this time that the forces most likely to translate such threats into reality are first, paranoid fear, and secondly a conviction that the future holds nothing for us Warnings we may need, but the prediction of doom through science should be seen as mostly nonsense, and its goblins as part of a psychoneurotic if not psychotic, fauna The dangers to humanity are, as always, grave, but at no time has man been better placed to deal with them The true defence is not to turn back to anything but to turn forward—not less knowledge and freedom but more This is a task which medicine and science cannot afford to neglect The faster the change in our societies, the greater the need to foresee and prepare

In a ' speculative projection of 21st-century man lately published by the California Institute of Technology,[1] it is impressive to find the writers unanimous in repudiating the starvationist ' theory of future history The world s population is increasing and will continue to do so but if the newcomers are not fed the reason will not lie in the inability of technology to feed them According to the California workers irrigation and reclaiming of marginal land, and the control of insect pests would in themselves suffice to raise food output by nearly half Beyond that lie the possibilities of new crops the substitution of synthetics and of microörganisms for animal foods, and the harvesting f the sea, where nine-tenths of the world's photonthesis takes place ' what we need said one rticipant ' is to breed a sea-going pig Work on ch lines is already in progress (some will have seen " mechanical cow built by N W PIRIE and his workers at Rothamsted), and though the appeal food research to governments is less than that of tructive undertakings, it goes on, and may go er For the California scientists the limiting factor his expansion is the availability of skilled men in the initial stages of technological revolution the number of man-hours per calorie or per kilowatt hour may fall, but it is now climbing back to, and even beyond its old level with the difference that the new kind of labour requires aptitudes and training of a very high order in a very large number of people Here the problems are medical as well as technical for psychological stress among scientists research men and skilled technicians is already clinically evident, and there would be further strains in a society which had no place for the stupid But shortage of skilled cadres—important though it may be—is not the limiting factor that we should ourselves put first If the world is not fed when technology could feed it, or healed when medicine could heal it, the reasons are most likely we should say, to lie in the form of human societies and the prejudices and interests they harbour In other words they are political

It is easy at this point to turn away, remarking that " science has no place in politics But the fact remains that the two major political issues of the world today are both of them largely issues of science—the first being the extension of high living standards to all nations, while the second is the tendency for social organisation to become a vehicle for national and personal aggression If these issues are to be dealt with by scientific causal analysis—instead of by the combination of dogma and vested interest which has hitherto been customary—the medical scientist cannot opt out of them Whether the approach of social psychology is less vitiated by personal and cultural prejudice and bias than that of ' politics as we understand it only time can show admittedly the discipline of science does not always succeed in controlling the scientist's judgments against the pull of his prejudices But it is clear that ways and means better than those of the present can and must be found

One part of the political future of man is already being influenced by science in a sense opposite to that prophesied by the pessimists In the past, societies which drew their dynamic from rigid ideologies and conformities were not seriously hampered by them in imposing themselves on the world and their neighbours In some respects these ' armoured cultures ' were at an advantage they lost their art, their literature and their capacity for enjoyment but not their competitive efficiency But once scientific technology comes to be the chief qualification which enables a society to compete this situation is likely to change In such a world ideologies have immediate and evident consequences relativity may be a philosophical concept, but if it is an erroneous one we must alter the design of our electronic equipment Thus a society may have to choose between ' bourgeois ' genetics and no beef, or between ' communistic economics and no production Moreover, the continued competitive efficiency of a neotechnic culture will depend on the attitudes of the men it produces—their receptivity, spontaneity, capacity for social action, and lack of biases—and these will be continuously exposed to practical tests When the most biased dictator of the future sets his most fanatical henchmen to build up a supersonic air force they will still be unable to train pilots without at the same time training and employing psychologists whose studies of human behaviour will call the dictator s mental state in

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[1] See *New York Times* May 27, 1956

A NEW POSTOPERATIVE DENTAL DRESSING

DEQUADIN CHLORIDE IN GELATIN SPONGE

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To obtain and encourage uneventful healing following oral surgery, including dental extractions, is the aim of every practitioner. Owing to the remarkable power of recovery of the oral tissues, unpleasant sequelæ are rare, and of these, septic sockets and hæmorrhage are the chief offenders. They are sufficiently inconvenient, nevertheless, to call for preventive measures to reduce or eliminate their occurrence, and for special treatment should they arise. Septic sockets embarrass both the patient and the operator. The pain and debilitation suffered by the patient with a dry socket is profound indeed, and nobody can appreciate this unless they have had one themselves.

Hæmorrhage after a dental operation may be (*a*) immediate or primary (at the time of the operation), (*b*) secondary (usually within twenty-four hours), or (*c*) recurrent (several days after the operation). There are various ways of treating these hæmorrhages, and one successful method has been in the insertion of gelatin-sponge preparations incorporating an antibiotic and thrombin. Suturing the wound and other methods may be combined with this treatment.

Thoma (1945) believes that three factors are necessary for straightforward postoperative healing:

(1) A bactericidal and bacteriostatic agent is needed because absolute asepsis is difficult to achieve and maintain during the operation.

(2) A local hæmostatic agent is desirable, because secondary hæmorrhage, although generally slight, is common during the first twenty-four hours and sometimes occurs after the hæmostatic effect of the local anæsthesia has subsided.

(3) To prevent the breakdown of too large a blood clot, thus furnishing an excellent medium for bacterial growth, a way to eliminate space must be found.

Sutton (1948) states that an agent, or combination of agents, used for this purpose should have the following properties:

(1) *Absorption*.—For immediate closure of a wound, it is essential that anything placed in it is completely absorbed.

(2) *Hæmostasis*.—To prevent oozing or slight bleeding, the material itself must be hæmostatic or allow incorporation of a suitable hæmostatic agent.

(3) *Bacteriostasis*.—The material should either have bacteriostatic properties itself or be a suitable vehicle for a variety of antibiotics.

(4) *Non-antigenicity*.—The material must not induce sensitivity or carry the risk of an anaphylactic reaction.

(5) *Clot support*.—The material must help to maintain the structure of the blood clot and at the same time it must not interfere with normal repair.

(6) *Non-irritability*.—It must not cause mechanical or chemical irritation.

(7) *Sterilisability*.—The material when used must be sterile and ease of sterilisation is important.

(8) *Ease of use*.—It must be simple to handle and insert.

(9) *Availability*.—The supply must be assured at a reasonable cost.

Materials Previously Tried

Several such materials have been developed and investigated in recent years, including alginates, oxidised cellulose, fibrin foam, and gelatin sponge. Gelatin sponge seems to conform most closely to the ideal substance. In the past, gelatin sponge has been used almost entirely in the prevention and control of postoperative hæmorrhage and for eliminating the "dead space" in large closed oral wounds. It has also been used for socket implantation after extractions. In the closed wounds, the gelatin sponge seemed effective and was absorbed without putrefaction. In open wounds it often became foul and healing was impaired—probably because it acted as a culture medium. Unpleasant sequelæ have also been reported by Jenkins (1946), Taylor and Kaplan (1950), and Moore et al. (1954).

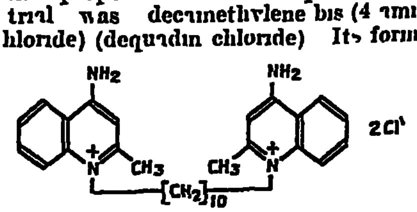
Sponge soaked in penicillin reduced the sequelæ to some extent, but views differ about how much penicillin to use (Fleming and Fish 1947, Silverman 1949) and there is always the danger of sensitisation and the production of resistant organisms. Other disadvantages were that some bacteria were already penicillin resistant, penicillin is inactivated by serum, and the technique is time consuming. Whether the penicillin remains active in the tooth socket for long enough to achieve any worthwhile bacteriostasis is also debatable; the findings of Holland and Tain (1954) suggest that it does not.

It seemed that a more effective bacteriostatic or bactericidal agent must be found and incorporated; for Silverman (1949), using the sponge alone, noted that there was no variation in incidence of postoperative pain, compared with untreated sockets. Results in the extraction clinic (local anæsthesia) at King's College Hospital agree with this finding.

A New Combination

After unsatisfactory trials, using various materials, had been carried out in the dental department of this hospital, a new combination was evolved. This consisted of gelatin sponge impregnated with 0·1% 'Dequadin chloride'.

During the development of laudexium ('Laudolissin'), *a synthetic muscle relaxant of the true curarising type*, it was observed that solutions of the drug had considerable antibacterial activity. Many simpler related compounds were therefore synthesised and tested for antibacterial properties. The compound selected for clinical trial was decamethylene bis (4-aminoquinaldinium chloride) (dequadin chloride). Its formula is:



Its antibacterial properties and pharmacology have been investigated by Babbs et al. (1956). Its salts inhibited the growth of all microbial species used in

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question, and engineers who, if their machines are to leave the ground, will be unable to accept the dogma that 2=3 However much we allow, as we must, for the human power of double-think, which affects scientists as much as (some would say more than) their fellows, the continued growth of analytical and purposive study of Nature must give rise to more analytical and purposive study of ourselves, of society, and of the pretensions of would-be leaders or rulers

21st-century man will have his own troubles He may look back at ours as an age of inequality and ideology, in which societies still delegated authority to essentially aggressive or prohibitive people, as the age in which it became possible first to control disease and hunger and then (by applying the same methods of thought) to control the antisocial, irrational, and incoordinate sides of human conduct which obstructed the application of knowledge, and possibly as the golden age of science in general Since the exponential progress of knowledge can hardly go on indefinitely without some pause, our grandsons may spend the 21st century in drawing breath, and in allowing civilisation to catch up with the practical and intellectual progress made in the time of strife and excitement which preceded it But if they read our literature, they will have less respect for the Jeremiahs and the Jonahs who foretold judgment than for the Ezras who urged their contemporaries to rebuild the Temple

British B.C G

THE rather tentative official support for B C G in this country in the past few years has been fortified by a statistically unassailable experiment[1], and, although the vaccine cannot yet be freely used, there are signs that control is being relaxed So far all the B C G vaccine routinely used in this country has been imported But the first report of a British B C G, a freeze dried vaccine, has now appeared[2] Freeze dried vaccine, if it is as consistently potent as the liquid products, has obvious advantages It can be kept for many months at room-temperature without serious loss of potency, so that each batch can be fully tested before it is released Instead of having to be ordered in advance and used without a delay, the freeze dried product can be kept in store and is promptly available—an obvious advantage to those who use it infrequently and in small quantities Freeze-dried vaccines have been manufactured and tested in many countries, notably in France,[3] the United States,[4] Russia,[5] and Japan[6 7] The extensive Japanese experience of its manufacture has recently been reviewed by OBAYASHI in a W H O monograph[8]

The new British vaccine was produced in the Glaxo laboratories and after detailed bacteriological and animal tests, two batches were put to clinical trial LORBER and his colleagues[2] vaccinated 276 newborn infants After six weeks 88% of those vaccinated with one batch and 77% of those vaccinated with the other gave a positive tuberculin skin reaction But twelve weeks after vaccination the proportions of "converters" had risen to 96% and 92% This delay in the appearance of the sensitivity produced by freeze-dried vaccine was also noted by EBINA et al The vaccination lesions were small and in only 8 infants were there palpably enlarged axillary lymph nodes None had any detectable general disturbance of health The vaccine was kept at room-temperature during the fourteen weeks of the trial There was no important change in the vaccine during this period and counts of viable cells were of the same order as at the start of the investigation LORBER et al believe that this particular British freeze dried vaccine would not be suitable for vaccination of contacts, for it may be desirable in contacts to induce tuberculin skin sensitivity as quickly as possible with the least risk of failure This is, however, not a serious deficiency, for most of the vaccine required in this country will probably be needed for routine vaccination of those not especially exposed to infection

Hypercalcæmia in Infancy

SINCE the benign[1] and severe[2] types of idiopathic hypercalcæmia in infancy were first described, many cases have been recorded,[3–16] and we have from time to time discussed these developments[17 18] The clinical pattern is well defined anorexia, vomiting, constipation, and failure to thrive, with raised serum calcium and blood-urea levels The outlook in the simple group is generally good, although there have been occasional deaths, but in the severe type, with physical and mental retardation, patchy osteosclerosis, renal failure, and hypertension, recovery is often incomplete and death is not rare In a recent issue Dr MORGAN and his colleagues[19] described 15 cases seen in Dundee during a period of two years and they gave a detailed account of metabolic studies in 2 hypercalcæmic infants Their conclusions confirm previous reports of high calcium retention,[8 11 15 20] and the beneficial effects of low-calcium diet and of cortisone,[9 21] which, they found, increased the fæcal calcium Dr MORGAN and his associates do not favour the use of calcium-chelating agents, such as disodium ethylenediamine-tetracetic acid (E D T A) because of the gastro-intestinal irritation they produce Like most of those who have studied this syndrome, they feel that the most likely cause is an over action of vitamin D Dr LIGHTWOOD and his colleagues in the pædiatric unit at St Mary's Hospital, London, laboratory investigations, including gram-positive, gram-negative, and acid-fast bacteria, and fungi including *Candida albicans* Unlike many other quaternary ammonium salts it was not inactivated by serum

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Gelatin sponge impregnated with dequadin chloride was used in two ways. (*a*) when the dental surgeon judged that postoperative sequelæ were likely it was used prophylactically and (*b*) when postoperative complications were present, it was used as treatment

It was used prophylactically in over 900 cases in which extractions were performed under local anæsthesia In many of these more than one tooth socket was so treated Pieces of gelatin sponge were inserted into the wound immediately after extraction, before a covering pack was placed over the wound (a normal routine procedure) The sponge was lightly inserted care being taken not to consolidate it before putting it in or to pack it tightly into the socket If the sponge was consolidated. the results were less satisfactory The wound was sutured when necessary in these cases it was easier to place the sponge in the wound after inserting the sutures but before tying them because the sponge tended to be squeezed out of the wound during suturing

In approximately 97% of the cases healing proceeded normally. and in many of these hæmorrhage or dry sockets would, judging from the history and the conditions at operation, have almost certainly ensued without the prophylactic use of the dequadin chloride sponge There was no postoperative hæmorrhage in any of the prophylactically treated cases Although a few septic sockets developed despite prophylactic treatment, most of these involved either lower impacted or buried third molars or sockets where excessive extraction manipulation had previously occurred

When a dry socket resulted it was treated with the dequadin sponge, upon which was deposited a few drops of a sedative such as 'Dentalone' The patient was told to report back if pain and lack of healing persisted In almost all of the cases treated a further visit was unnecessary If they did return the dequadin sponge plus dentalone dressing was repeated when there was pain present, the dequadin sponge alone was used if the pain had subsided

Many varied treatments for dry sockets have been tried in this department, but this technique has been the most satisfactory so far

Patients who had had difficulties after previous dental extractions reported good healing with the prophylactic therapy

Hæmorrhage from sockets not treated prophylactically was treated with dequadin impregnated sponge sutures were sometimes used No septic socket followed this treatment, as has happened previously when ordinary gelatin sponge or oxidised cellulose gauze had been used, and no swelling supervened though this was a common event with sockets treated with cellulose gauze

Conclusion

Dequadin chloride, a potent non-toxic, and non-irritant antiseptic appeared to supplement the gelatin-sponge therapy by preventing and counteracting infection in the wound. by preventing putrefaction of the sponge, and by encouraging healing Compared with the results of previous investigations of postoperative complications there seemed to be a reduction in the incidence of such sequelæ when the dequadin chloride sponge was used No definite conclusion can be drawn because of the unknown variables, but our observations suggest that it is a valuable treatment The incorporation of dequadin chloride into gelatin sponge may have a wider application in general surgery and medical practice

My thanks are due to Dr R Cocker director of dental studies for permitting this investigation to my assistants Mr P Belsham, Mr G Hawkes Mr L. Shinn Mr T Farrell, and Mr W Johnson, and to the medical and research departments of Messrs Allen & Hanburys for their coöperation in producing and supplying the experimental dequadin-chloride sponge

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DIFFUSE INFILTRATION OF THE LUNGS ASSOCIATED WITH CRYPTOCOCCUS LUTEOLUS

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5TH DEPARTMENT OF PÆDIATRICS CENTRAL HOSPITAL FOR INFECTIOUS DISEASES, BUDAPEST

The number of published reports of cryptococcosis is relatively large Collins et al (1951) reviewed 241 cases and Cohen and Kaufmann (1952) 220 In each of the published cases *Cryptococcus neoformans* was the pathogenic agent On invading the body this yeast usually attacks the brain and meninges, causing subacute or chronic, but almost invariably fatal, disease. The lungs have been suggested as the most likely portal of entry but Hirsch and Coleman (1929) assumed that, when the meninges were affected, the yeast invaded them via the nasopharynx The central nervous system has been estimated to be involved in a third of the cases of pulmonary cryptococcosis by Langeron and Vanbreuseghem (1952) and in 42% by Swartz (1949)

Primary pulmonary cryptococcosis that remains localised to the lungs is rare Linden and Steffen (1954) knew only 9 cases including 1 of their own Since then single cases have been reported from Belgium (Van Goidsenhoven et al 1954), Canada (Eisen et al 1955) and Hungary (Vitez et al 1955) Only 4 of the cases so far published were of the disseminated nodular type

Cox and Tolhurst (1946) are of the opinion that primary pulmonary cryptococcosis is more common than one would expect on the basis of reported incidence These workers believe that cryptococcosis often escapes detection owing to spontaneous recovery and to lack of spread and of signs and symptoms Beck et al (1955) agree with this view

In the case reported here the infecting yeast was *C luteolus* which is closely related to *C neoformans*

Case-report

A girl aged 4½ years was admitted to this hospital with the diagnosis of recent measles present whooping cough, and suspected submiliary tuberculosis of the lungs She had begun to cough sixteen days earlier and had had an exanthem suggesting measles eight days before admission. Four days before admission she had pyrexia (102.2°F) and was given four injections of penicillin for supposed pneumonia Case notes which accompanied her from another hospital said that auscultation had revealed diffuse crepitations areas of bronchial breathing, and râles in the lungs The liver had been enlarged, its lower margin being palpable 4 cm below the right costal arch No other physical changes had been detected lately described[22] the management of a single case of hypercalcæmia with a virtually calcium-free milk The calcium balance was strongly positive during the active stage, it became negative on a low-calcium diet, and more strongly so when a low-calcium cereal was given in addition This change may be due to the high content of phytate and inorganic phosphorus in the low-calcium cereal the consequent binding of intestinal calcium would increase the fæcal loss Cortisone had a quicker initial action, but there may be undesirable side-effects, such as the risk of intercurrent infection A diet low in calcium is difficult to prepare and manage, but it seems to give adequate results without the hazards of cortisone A point of great interest in the St Mary's patient was the disappearance of hypertension and cardiac murmur during treatment these are signs usually found only in children severely affected It seems likely that the clear-cut distinction between the simple and severe cases[23] is to some extent artificial, since examples of an intermediate type occasionally appear

Last week Dr **Forfar** and his colleagues discussed 5 cases of infantile hypercalcæmia, and a possible 6th They are not satisfied that the syndrome can be fully explained on the basis of intolerance to vitamin D As points against the vitamin-D hypothesis, they showed that some at least of these infants were not particularly sensitive to large doses of calciferol, and that calciferol does not increase the urinary output of calcium, as would be expected in hypervitaminosis D They also showed that, in 1 child, citrate metabolism was more in keeping with rickets than with hypercalcæmia In 4 out of 5 cases they found an increase in plasma-cholesterol levels—a finding previously reported[8–10 16 20] without comment Their conclusion, with statistical support is that there is a significant positive correlation between serum-calcium and plasma-cholesterol levels, which would not have been expected had the cause of the condition been vitamin-D intoxication Idiopathic hypercalcæmia of infancy may result, they believe, from a disturbance of cholesterol metabolism leading to the formation of a toxic calcium-raising substance of sterol type allied to vitamin D, which itself may be an aggravating factor The cholesterol disturbance may be due to infection This is an attractive if rather speculative explanation The points against vitamin D will require confirmation, and future research might include an effort to link this disorder of cholesterol metabolism with the abnormality of plasma vitamin-A levels reported by **Fyfe**[24] He found in 8 cases that the fasting and post-absorption levels of vitamin A were higher than in controls Even if no direct relation were to be found between these two findings, further work might reveal other and more fundamental disturbances of fat metabolism It should not be overlooked that both cholesterol[16] and vitamin-A derangement[25] could be secondary to a renal lesion as has been found in the nephrotic syndrome One point which is hard to explain on the cholesterol hypothesis is why the condition so common in Great Britain and Northern Ireland should be virtually unknown in North America, where the diet and infections of infancy are little different from those of this country

Another contribution to this subject appears on an earlier page of this issue, where Dr **Rhaney** and Dr **Mitchell** extend the pathological picture in a report of three children who died of hypercalcæmia The most striking lesion was renal calcification, mainly medullary These changes are non-specific and have been found in hypervitaminosis D, renal acidosis, and in other diseases of infancy

From the evidence which has accumulated in recent years, we may conclude that infantile hypercalcæmia is a relatively common condition in Britain, that it is the cause of much ill health and interference with growth, and that it is sometimes responsible for mental defect and even death As Dr **Rhaney** and Dr **Mitchell** point out, the evidence implicating vitamin-D intoxication in idiopathic hypercalcæmia is, at the best, circumstantial Much obviously remains to be done to define the ultimate causes, and in the meantime we should acknowledge that the recognition and better understanding of this peculiar syndrome have led us to realise that many babies in these islands are now receiving more vitamin D than they require[26] If a general reduction in the intake of vitamin D to physiological levels (say, 400 to 800 international units per day) were to be followed by a decline in the incidence of hypercalcæmia throughout the country, the case against vitamin D would be the stronger Until the problem is solved, babies should be given doses of the vitamin within the physiological range which we know to be adequate in protecting nearly all of them against rickets

Annotations

THE ROYAL NORTHERN HOSPITAL'S CENTENARY

At the age of 30 Sherard Freeman Statham was a promising assistant surgeon at University College Hospital when, on May 14, 1856, he playfully slapped the exposed buttocks of a man on the operating table, thereby raising a laugh from the class John Erickson, the professor of surgery, who was about to operate, later reported this boisterous episode to the dean of the faculty He complained, too, that his spirited colleague had, on the same day used improper adjectives and expletives to a patient who was reluctant to inhale the chloroform before " a very dangerous capital operation " The council of University College deplored such conduct and after interviewing Statham and hearing the views of the medical and lay committees, they directed that he should cease to be assistant surgeon The disconsolate surgeon returned to his rooms at 42, Mortimer Street, and what passed through his mind we do not know But he was not one to remain idle for long and his restless energies were soon directed, it seems, to the mounting needs of the poor of North London, for whom medical and surgical care barely existed He thereupon secured the lease of modest premises in York Road (now York Way), King's Cross, and, with the support of his dentist brother, and of Dr G F Whidborne and Dr C P Croft, he founded the Great Northern Hospital with some 16 beds The doors were opened one hundred years ago, on June 30, 1856

The story of this great hospital's achievements from its beginnings to the present day has been recorded by Dr E C O Jewesbury in a fine history[27] prepared

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[22] Stapleton T Macdonald W B Lightwood R *Lancet* June 16 1956 p 932

[23] Lightwood R C Stapleton T *Ibid* 1953 ii 255

[24] Fyfe W M *Ibid* May 5 1956 p 610

[25] Kagan B M Thomas, E M Jordan D A, Abt A F *J clin Invest* 1950 29 141

[26] Creery R D G Neill D W *Lancet* 1955 ii 372

[27] The Royal Northern Hospital 1856–1956 By E C O Jewesbury M D M R C P London H K Lewis 1956 Pp 157 17s 6d

There was said to be an increased amount of urobilinogen in her urine, and a blood count had shown red cells 5,160,000 per c mm , Hb 80%, and white cells 31,000 per c mm (polymorphs 31% lymphocytes 61%) Radiography of the chest had revealed in both lungs numerous disseminated soft nodular shadows and distension of hilar shadows with bundle formation suggesting tuberculosis A Pirquet test and a Mantoux test in a dilution of 1 1000 had been negative Lumbar puncture had produced clear cerebrospinal fluid (C S F) under increased pressure and containing no cells Pandy and Waltner tests had been negative

On admission to our hospital the patient was moderately developed and thin, weighing 12 6 kg She had cyanosed lips and nails On her skin a few pigmented spots were visible like those of measles No abnormality was found on percussion of the chest, but on auscultation extensive diffuse metallic moist râles were heard over the lungs The pulse rate was 120, with the pulse rhythmic, equal, and easily suppressible The cough was typical of whooping cough No symptoms or signs suggesting involvement of the central nervous system were detectable

Investigations —A considerable amount of urobilinogen was present in the urine A blood count showed red cells 4,420,000 per c mm and white cells 20,000 per c mm (polymorphs 39%, lymphocytes 59%, plasma cells 2%) The erythrocyte sedimentation rate (E S R) was 16 mm in the first hour (Westergren) A Mantoux test in a dilution of 1 1000 was negative

Treatment and Course —The child was given 'Tiocomycin ' 4 g in four days and penicillin 8,400,000 units and streptomycin 5 6 g in fourteen days Pyrexia disappeared in four days, but later her temperature rose again slightly Coughing subsided, and she began to gain weight Sixteen days after admission she again had pyrexia (104°F), and physical examination revealed insignificant changes in the lungs The E S R was 75 mm in the first hour (Westergren) A blood count showed red cells 4,360,000 per c mm and white cells 16,800 per c mm (metamyelocytes 4%, polymorphs 68%, eosinophils 2%, monocytes 3%, lymphocytes 23%) The urine was practically normal Blood culture remained sterile Lumbar puncture produced clear C S F under normal pressure and containing 10 cells per c mm , protein 0 28 mg per 100 ml , and sugar 63 mg per 100 ml A Pandy test showed slight opalescence Nothing abnormal was found in the central nervous system Radiography of the chest (fig 1) revealed ill defined round opacities of different sizes in both lungs, decreasing in number hilifugally , they had no definite outlines and were found mainly in the upper lobes They were somewhat fewer at the apices and considerably fewer in the inferior lobes and near the diaphragm The hilar shadows were of normal density and showed no extension Both halves of the diaphragm had sharp outlines and moved freely The heart was normal in shape, with a slight bulging of the pulmonary arc The mediastinum was free Since this radiographic pattern did not fit the picture of any known disease, especially submiliary pulmonary tuberculosis, it was suggested that the changes might be due to mycosis To exclude tuberculosis Mantoux tests were made on Nov 2 and Dec 28, 1954 and on Jan 7, 1955 The results were all negative, although the dilution used was 1 in 100 Bronchial swabs obtained on laryngoscopy were sent to the mycological laboratory of the State Institute for Public Health on Oct 12, Oct 23, and Dec 22, 1954 They were taken via a rubber tube introduced into a bronchus through a laryngoscope

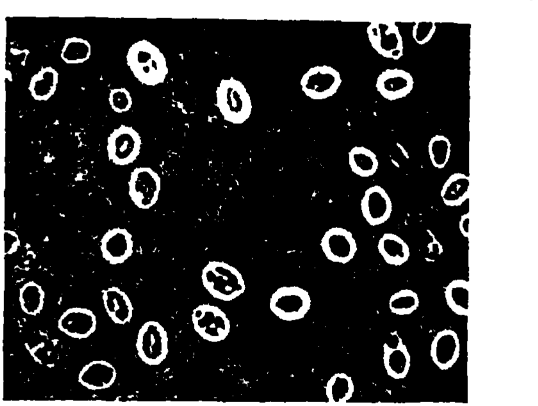

Fig 2—Microscopical appearances of a pure culture of *Cryptococcus luteolus* in china ink

Mycological Studies —Three samples of bronchial secretion taken in this way grew a yeast on media commonly used for this purpose (Sabouraud agar, malt agar, blood agar, and malt extract) and typing was according to Lodder and Kreger Van Rij (1952) All three samples were centrifuged, and the sediment was mixed with china ink and examined microscopically, yielding one ovoid or elongated, sometimes budding and encapsulated, organism to every two or three fields From each sample a pure culture of a blastomyces was recovered All three cultures were identical, and the yeast had the following main properties On growth at 26°C for three days in malt extract elongated or oval, sometimes budding cells, about 4 μ × 6 μ, were detectable Pseudomycelia and hyphæ were absent A thin film was present on the surface of the fluid medium The cells grown in malt extract at 26°C for thirty days were enclosed in a thick mucous capsule Growth in Sabouraud agar at room temperature or at 37°C for thirty days produced a highly lucent, yellowish brown, definitely mucous colony at the bottom of the test tube After thirty days' growth in Gorodkowa and Adams agar at 26°C or at 37°C asci were not detectable by spore staining In corn meal agar no chlamidospores were formed The organs assimilated glucose, galactose, maltose, and saccharose, but not lactose or potassium nitrate, and did not ferment carbohydrates These characters identify the organism as *C luteolus* (fig 2)

Animal Inoculation —10 mice were inoculated intracerebrally with a heavy suspension of the yeast in physiological saline solution The mice had no signs during sixty days' observation Then another 6 mice were inoculated in the same way and these too were free from signs when killed sixteen days later We failed to grow the yeast from the brains of these mice and attempts to detect it by direct examination failed Histological examination yielded negative results The intracerebral route of inoculation had been chosen in view of the fact that this method proved to be the most efficient for demonstrating the pathogenicity of the closely related *C neoformans* Experimental evidence was obtained that *C luteolus* did not affect the central nervous system of the mouse Since our patient had no nervous symptoms either, it has been suggested that this yeast may act specifically on the lung only To elucidate this point, experiments on animals are being made in which the yeast is introduced directly into the lungs by intrathoracic injection and by aspiration

Course of Patient's Illness—Until the final results of the mycological studies were available the patient was given an additional 19,000,000 units of penicillin, 18 g of streptomycin

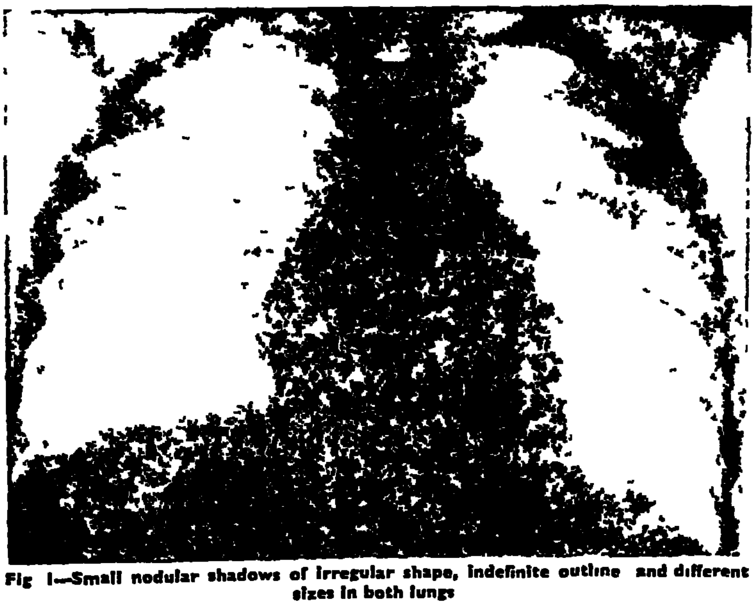

Fig 1—Small nodular shadows of irregular shape, indefinite outline and different sizes in both lungs

for the centenary. The early days were spent in the densely populated neighbourhood of the New Cattle Market and the Great Northern Railway Station with its growing maze of goods yards. Within twelve years the lively embryo of a hospital had outgrown its premises so that the next stage had to be spent in Caledonian Road. Here artisans and labourers in need of attention flocked to the well managed outpatient department, where finely dressed people were refused admission. Three quarts of cod-liver oil and an ounce of quinine were dispensed each day, and a donation of half a crown was guaranteed to secure immediate attention. As we said at the time, it was a *model outpatient department*. In 1888, however, a newly built and fully grown hospital, the pride of Islington and the adjoining districts, first graced the Holloway Road, and there it has remained. Poor Statham, whose initial contribution of £1430, so generously given, appears to have been followed of necessity by other donations, died at 32 of phthisis. He was a bachelor and left only £500. The "Founder of the Great Northern Hospital, London" is buried at Stone, near Aylesbury, in the church where he was baptised. The scarlet tunic with epaulettes, and the trousers, which he wore in the Schleswig Holstein campaigns, together with his watch and medals, are preserved as a memento of an erstwhile gallant soldier who had early interests in war surgery and army hygiene. Perhaps it was indifferent health which deterred him from going to the Crimean War as he had asked to do, and perhaps the subsequent frustration accounted for those indiscretions which led to his dismissal from University College Hospital—and to the foundation of another charity.

The Royal Northern Hospital, it may be justly said, has had a meteoric career. From the start it attracted fine consultants, zealous administrators, and boards composed of far sighted laymen. It has also been fortunate in securing, throughout most of its life, the patronage and continued interest of the Royal Family. Successfully it overcame the threat of insolvency, and in doing so it was the first to introduce such things as pay-beds which at the time (1894) were opposed on principle by the general practitioners of North London and by *The Lancet* and *British Medical Journal*. But when, in 1888, a heavy legacy duty deprived the hospital of much-wanted money, we spoke sharply in support of the Royal Northern. "In other countries the State maintains the hospitals. In ours this duty is not only thrown on private individuals, but even their charity is taxed."

Quite apart from its merits as a story Dr Jewesbury's book will give encouragement to those who believe that the tradition of voluntary service need not lapse because funds for the hospitals are now provided publicly.

THE BLIND IN OUR MIDST

In the next twenty years the blind in England are likely to increase in number from the present 94,000 or so to 140,000 or more, and by 1958–59 schools for the blind will have to cater for some 2200 children, instead of some 1400 as in recent years. These forecasts, amply supported by figures, are contained in the latest of Prof. Arnold Sorsby's valuable periodic reviews.[1] Professor Sorsby finds that registrations of blindness increased by over 7000 between March, 1952, and the end of 1954. This increase is accounted for mainly by blindness in those aged 70 or over; in 1954, 69% of those newly registered as blind were in this age group. Accordingly there has been a steady increase in the proportionate incidence of blindness due to senile macular degeneration. There has also been some increase in those aged 1–4 and 5–15. Retrolental fibroplasia is the cause of blindness in more than half of those aged less than 1 and rather more than 25% at ages 1–4. (The geographic distribution of retrolental fibroplasia is uneven. "It would almost seem as if there is a central island area in the country with a low incidence.")

As regards prevention, cataract is the one *important* cause where fuller exploitation of existing measures should help to reduce the incidence of blindness. Among the new registrations in 1951–54, 84% of those with cataract had had no treatment. At registration many of these patients are old and frail, but they could probably have undergone operation comfortably and safely some years earlier. Of clinical developments, Professor Sorsby writes:

> "If the congenital and hereditary affections are included amongst the general medical disorders, some 80 per cent or more of the blind under 50 present fairly well defined problems in general medicine. Hope in these affections lies not in an expansion of the surgical facilities available, but in the creation of clinical units which can draw on the potentialities of both ophthalmology and general medicine, even if this involves some departure from the traditions of ophthalmology as an essentially surgical speciality."

DORMEZ-VOUS ?

Is Frère Jacques restless? And does Cheselden stir a little in his grave? The era of lithotomy may be giving way to an age in which stones are dissolved by a method founded on logical chemical precepts. Since we reviewed[1] this subject Lagergren[2] has described his biophysical investigations of urinary calculi. His findings from the examination of 600 calculi by X-ray diffraction confirm those of earlier workers—namely, stones are not the simple affairs our clinical nomenclature implies. The stones he studied were composed of a complex mixture of eleven distinct crystalline substances, and in one stone a substance defying identification was observed; whewellite, weddellite, apatite, and struvite were common, but uric acid was relatively uncommon. *Microradiography showed the distribution of the various substances within a stone*: a stone might have a core of one substance surrounded by another, and in a laminated stone made up of different substances each lamella consisted of one component only—as though the chemical, and, therefore metabolic, factors contributing to its growth changed during its existence. Such studies, together with an understanding of the architecture of a stone, as revealed by microradiographs, provide the proper foundation for treatment, since exploration of the biochemical processes involved in the formation of stone cannot possibly begin until it is known what stones are.

Even with our knowledge as it stands today we use chemical methods in an attempt to prevent the recurrence of stone formation—by decreasing the crystalloids in the urine, by preventing with hyaluronidase their aggregation or increasing their solubility by acidification or alkalinisation, as the case may be, or by preventing the absorption of phosphorus from the alimentary tract. Treatment on these lines is, however, a severe imposition on the patient, who has either to maintain permanently an unpalatable diet or continue to swallow unpleasant aluminium gels. Furthermore, each remedy is specific for what is thought to be the substance of the stone, within the crude and erroneous categories of oxalate, urate, and phosphate. And what practising urologist today has sufficient technical assistance to discover the nature of the core of a patient's stone? The substance at the core is of primary aetiological importance since it may differ and 7 6 g of isoniazid The pyrexia subsided by lysis, and the patient remained apyrexial for the rest of her stay in hospital except for a slight rise of temperature for a few days She developed mild hepatitis on Oct 9, but recovered from it uneventfully Vitamins and tonics were given, and the patient was entirely free from symptoms The changes in the lungs detected by radiography remained stationary for a long time and were not influenced by administration of 'Paraben' 3 g given over three days Later the radiographic appearances slowly changed beginning in the less affected inferior lobes and spreading gradually to the upper lobes

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[1] Ministry of Health. Blindness in England 1951–54. Report by Arnold Sorsby. H.M. Stationery Office. Pp. 53. 3s. See also *Lancet*, 1953, ii, 981.

[1] *Lancet*, 1955, ii, 1177.

[2] Biophysical Investigation of Urinary Calculi. By CURT LAGERGREN. Stockholm, 1956. Sw. Kr. 25. *Acta radiol., Stockh.* suppl. no. 133.

Discharge and Follow up—The child was discharged on Jan 26, 1955 when she was completely free from symptoms, had no complaints whatever, and weighed 15 7 kg She has since been examined at intervals of three to four weeks, and her E S R and blood counts are persistently normal Radiography of her chest on June 28, 1955 showed practically no nodular shadows In both hilar areas, around the upper pole, there were numerous thick bundles with a few small pale nodular shadows, with indefinite outlines, on the right side only The lower pole of the hilar areas showed a few soft trabecular shadows running towards the diaphragm

Discussion

Of the 9 cases of primary pulmonary cryptococcosis reviewed by Linden and Steffen (1954) 5 were diffuse pulmonary affections (2 the small nodular type) and 4 torulomas The present case was a toruloma Similar pulmonary changes have been described by Van Goidsenhoven et al (1954) and Eisen et al (1955) The present case resembles that published by Eisen et al also in that the radiographic changes did not fit the pattern of any of the diseases that should be considered in the differential diagnosis This fact pointed to mycosis, and the suspicion was borne out by cultural examinations in all 3 cases

In assessing the radiographic changes in our patient's lung, residual changes due to preceding measles and whooping cough had to be considered too In the published cases mentioned and in our case there were, however, certain radiographic signs which were somewhat typical though not pathognomonic hilar involvement was either absent or very slight, disseminated nodular lesions were present at the apices and near the diaphragm in very small numbers only or not at all, and the single nodular shadows varied in size and shape, and their outlines were less definite than those of tuberculous lesions This agrees well with the histological findings of Hirsch and Coleman (1929) who found, in their patient with secondary pulmonary cryptococcosis associated with meningeal involvement, nodular pulmonary lesions whose outlines were irregular and less definite than those of the lesions of miliary tuberculosis The nodular lesions in the present case were present in the upper lobes, which is also in accordance with what Hirsch and Coleman found

It is the mycological evidence, however, that gives particular significance to the present case In all the cases published so far the pathogenic agent was *C neoformans*, but in the present case the yeast recovered from all three specimens of bronchial secretion obtained by direct suction was *C luteolus*

C leuteolus was first isolated from air by Saito in 1922, in Tokyo, by the method of Lodder and Kreger-Van Rij This yeast is extremely rare, and this is the first time that it has been found in Hungary It is closely related to *C neoformans*, the well-known pathogen causing cryptococcosis The two species differ but slightly in morphology, inasmuch as on growth under identical conditions the *neoformans* cells are spherical and the *luteolus* cells ovoid or elongated In view of the close relationship between these two species, Lodder and Kreger-Van Rij (1952) direct attention to a potential pathogenicity of *luteolus* and emphasise the importance of experiments on animals

Although so far we have not been able to prove experimentally that this yeast can act as a pathogen, we can assume that it can do so in man, because in the present case no other pathogenic agent was detected by radiographic clinical, or microbiological methods

Summary

A case of diffuse pulmonary infiltration, associated with *C luteolus*, in a girl aged $4^1/_2$ years is described

C luteolus was recovered on three occasions from bronchial secretion obtained on laryngoscopy

We have been unable to find any published report that *C luteolus* is pathogenic to man Its pathogenicity to animals also still awaits final corroboration

C luteolus is closely related to the well-known pathogen *C neoformans*

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CORTISONE THERAPY IN EARLY PREGNANCY RELATION TO CLEFT PALATE

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WE report here the occurrence of a cleft palate in a baby whose mother received cortisone therapy in early pregnancy, and review the experimental evidence that cortisone treatment of laboratory animals in early pregnancy may lead to congenital cleft palate in the offspring

Case-report

A woman, aged 30, with four years' history of idiopathic steatorrhœa was treated with a gluten free diet, oral iron, and vitamins, but her condition remained unsatisfactory, and persistent diarrhœa and anæmia led to her third admission to hospital for trial cortisone therapy

On admission on Nov 9, 1954, she was pale and thin, and weighed only 6 st 8 lb Chvostek's sign positive Œdema of legs Abdominal and pelvic examination normal Hæmoglobin 71% (Haldane) (10 5 g per 100 ml) Serum calcium level 6 5 mg per 100 ml Plasma protein level 5 2 g per 100 ml (albumin 2 9 g per 100 ml, globulin 2 3 g per 100 ml) Fat balance 80% absorption over 4 days

Gynæcological and Obstetrical History—Menarche at the age of 13 Normal menstrual loss lasting 5 days Cycle predominantly 28 days, but periods of amenorrhœa lasting 2–3 months had occurred, notably after the previous admissions to hospital Last menstrual period (Oct 8–12) began 32 days before her admission First pregnancy at the age of 24, threatened abortion in first trimester but otherwise uneventful, terminating in the spontaneous delivery of a full term normal baby At the age of 26 vaginal bleeding after 10 weeks' amenorrhœa, the cause of which was unknown, but pregnancy could not be excluded

Family History—No known congenital defects on either side of family

Progress—Treatment with oral cortisone 100 mg t d s and normal diet was begun on Nov 29 In view of the menstrual history and the negative findings on examination no significance was attached to the 8 weeks' amenorrhœa The patient's general condition improved, and the dose of cortisone was reduced (see fig 1) On Jan 3 1955, she was discharged home on a maintenance dose of cortisone 12 5 from the cortex and thus provide the clue to the initial metabolic disturbance The method of attack advocated by Prien and Walker[3] has much to recommend it Apatite (basic calcium phosphate) is the commonest substance in urinary stones, moreover, half those stones which are predominantly calcium oxalate are found to have formed around a small nucleus of calcium phosphate In its detoxicating function, glucuronic acid is excreted as a glucuronide in conjunction with the substance to be eliminated, by giving salicylate the glucuronide content of the urine is increased, and glucuronides increase the solubility of calcium phosphate, in proportion to their concentration Prien and Walker have given both acetylsalicylic acid and salicylamide with good results to 19 patients subject to recurrent stone, with effective suppression of stone formation in 17, with the encrustation of indwelling catheters was also prevented thereby

Here, then, is a biochemical approach to treatment which commits the patient only to a familiar pill It is not inconceivable that solution of stones already formed may eventually be achieved along these lines So Dr Whytt[4] and Joanna Stephens may yet have the last laugh over the lithotomists Their principle was correct, though the effective solvent is unlikely to be lime water and soap or a concoction of calcined snails, the seeds of wild carrot and burdock, hips and haws, all burnt to a blackness and mixed with soap and honey[5]

A FURTHER OUTBREAK

The return (announced in the *Times* of June 21) of the infection which appeared about the same time last year, and led to the closure of the Royal Free Hospital for several months, raises questions which were left unanswered by the group of articles which we published on May 26, dealing with what seems to be the same disease The full report of last year's outbreak—which affected all grades of the Royal Free staff (residential and non-residential, medical and non medical) but left the patients virtually unscathed—is eagerly awaited for any light it may throw on ætiology and length of incubation period From the available evidence the incubation period seems to be not longer than a week, but we do not yet know whether a patient who has a relapse (as many have done) regains infectivity in the process

The resemblance to encephalitis lethargica in a mild form is too striking to be ignored after an initial period characterised by malaise, nausea or vomiting, somnolence, and slight fever, accompanied in most cases by ocular manifestations such as diplopia and nystagmus and occasionally by otitic symptoms such as tinnitus, neurological features appear in a varying proportion—some transient, others lasting months or even years Emotional lability with hysterical symptoms is a conspicuous feature of severe cases, making the diagnosis difficult in the absence of specific diagnostic tests At present electromyography serves to distinguish the condition from hysteria on the one hand and paralytic poliomyelitis on the other It would be interesting to know whether cases diagnosed as poliomyelitis with spasm are not in reality examples of it

The fact that 11 cases came to light at one fever hospital last year during the period when poliomyelitis was prevalent suggests that the infection may have been widely scattered in the community Other London hospitals are also known to have had cases among their nurses, though none had an outbreak with the same "explosive" character as the Royal Free From last year's experience, and the presumption that many of the staff have acquired immunity, one might expect that the present outbreak there will be promptly checked Acquaintance with this disease, however, confirms its elusiveness, and probably most of the nurses and many of the domestic and clerical staffs have changed in the interval In the modern hospital, doctors seem to be the most stable section of the population

TREATMENT OF VOLKMANN'S CONTRACTURE

The stigma which was so long attached to Volkmann's contracture still sticks, though it is now sixteen years since Griffiths[1] made it clear that the condition is in fact due to traumatic arterial spasm and that the application of overtight plasters and splints is seldom more than a minor contributory cause Rarely does the surgeon have the opportunity of exposing the damaged artery and attempting to relieve the spasm before irreparable damage is done to muscles and possibly nerves, more often he is faced with the resulting paralysis and contracture The attack on this problem has recently been intensified and more radical methods of treatment have yielded gratifying results

For many years treatment was directed solely towards correcting the flexion deformity of the wrist and digits In its simplest form this consisted in applying some form of splint to stretch the contracted muscles slowly but forcibly Except in the milder cases, the deformity rapidly recurred after the splint was removed Various operations, such as the muscle slide operation of Max Page or some form of bone shortening, such as carpalectomy, were rather more successful But the contracture and the deformity it produces are merely signs of massive ischæmic necrosis of the affected muscles, and these methods of treatment could not be expected to restore their contractility At best the patient was enabled to take advantage of the trick action in which active dorsiflexion of the wrist naturally produces some degree of flexion of the digits

Recognising this defect of all previous operations, Parkes[2] took advantage of this trick action and restored a really useful range of flexion by transplanting one of the active extensors of the wrist into the tendons of flexor digitorum profundus, all the useless contracted tendons having previously been divided at a higher level to overcome the deformity A great advantage of this transplant is that the patient needs no re education, the transplanted unit naturally contracts with the remaining dorsiflexors of the wrist, and the summation of the effects of the trick action and the action of the transplant gives a good range of flexion of the fingers

Seddon[3] has recently described an even more radical method in which the aim is to excise the whole of the infarct before restoring flexion by transplanting an active tendon This enables him to assess the degree of ischæmic damage to the median nerve, and when spontaneous recovery seems unlikely he excises the whole of the ischæmic portion Continuity is then restored either by a free graft, using that portion of the median nerve at the elbow which originally innervated the long flexor muscles of the forearm, or, in cases where both median and ulnar nerves have suffered extensive ischæmic damage, by an ulnar-to median pedicle graft, as described by St Clair Strange[4]

There has undoubtedly been a considerable advance in the treatment of this crippling deformity Naturally each patient requires careful assessment before operation, the timing of which is also important In the less severe cases where the deep forearm muscles bear the brunt of the ischæmia, the remaining function in the flexor sublimis can be transferred to the tendons of flexor profundus after division of the profundus at a higher level When all the flexors are involved but the median nerve is functioning, Parkes's method gives an excellent result so long as the

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[3] Prien E L Walker B S *J Amer med Ass* 1956 160 355
[4] Works of R Whytt Edinburgh 1768 p 337
[5] Clark Kennedy A E Stephen Hales London, 1929 p 127

[1] Griffiths D L *Brit J Surg* 1940 28 239
[2] Parkes A *J Bone Jt Surg* 1951 33B, 359
[3] Seddon H J *Ibid* 1956 38B 152
[4] Strange F G St C *Brit J Surg* 1947, 34 423

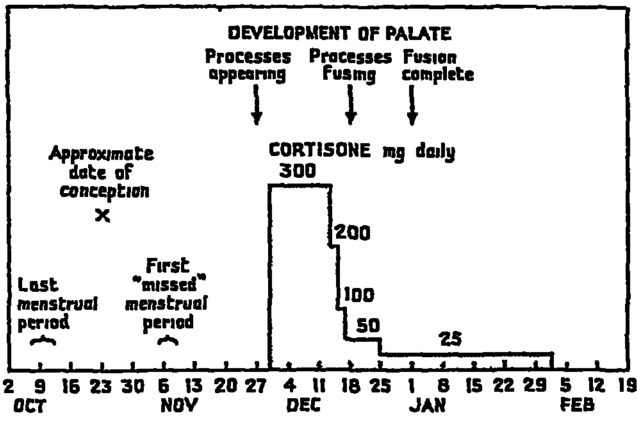

Fig 1—Relation of cortisone treatment to pregnancy

mg b d, the continuing amenorrhœa being attributed to cortisone therapy

Follow up—When she attended as an outpatient on Feb 2, her uterus was enlarged to a size equivalent to that of an 18 week pregnancy Cortisone was discontinued, the total dose received being 6 05 g The patient remained in good health, with a normal blood pressure throughout the remainder of her pregnancy, the steatorrhœa improving both clinically and biochemically On July 30, 2 weeks past the expected date of delivery, she was readmitted for medical induction of labour This was unsuccessful, and since some doubt existed about the maturity of the fœtus she was discharged On Aug 11 she was readmitted in labour and delivered spontaneously of a fresh stillborn male baby The placenta was relatively small and weighed 8 oz—i e, a thirteenth of the weight of the baby

The baby appeared to be full term on macroscopical and radiological examination Weight 6 lb 8 oz No external abnormalities The palate (fig 2) had a large postalveolar cleft The lungs were collapsed, and the trachea and main bronchi contained thick meconium stained mucus Several small hæmorrhages were present beneath the visceral pleura and epicardium No further abnormalities were found, and the appearances suggested that death resulted from intra uterine anoxia

Experimental Evidence

Congenital malformations have received increasing attention during the past twenty years This has led to the concept that the process of normal development is influenced by both genetic and environmental factors, but, since the effects of the latter may simulate those of the former, it is often impossible to distinguish between them General reviews relating to this have been presented by Gruenwald (1947), Warkany (1947), Boyd and Hamilton (1950), and Giroud (1954)

Experimental evidence of the teratogenic effect of cortisone was first reported by Baxter and Fraser (1950) Using the house mouse, an animal in which "spontaneous" cleft palate (without hare lip) is rare, they administered cortisone to pregnant females and produced cleft palates in 44% of the offspring The prevalence of cleft palate in the offspring of treated mothers varied between 4% and 100% in different *strains of mice, the result* depended partly on the genotype of the mother and partly on that of the fœtus (Fraser and Fainstat 1951, Fraser et al 1954)

Fainstat (1954) treated pregnant rabbits with intramuscular cortisone and reported 17 cleft palates among 35 embryos from the 7 treated does In the rabbit also, the spontaneous occurrence of cleft palate without hare lip is apparently rare

It is apparent from these papers that the outcome of pregnancy in the treated animals is related to the dosage of cortisone, the period of gestation during which it is administered, and the genotypes of the mother and the fœtus The highest prevalence of cleft palate in the offspring was obtained when treatment with cortisone was begun a few days before the time of normal closure of the palatal processes, thereby suggesting that it interferes with the development of the palate

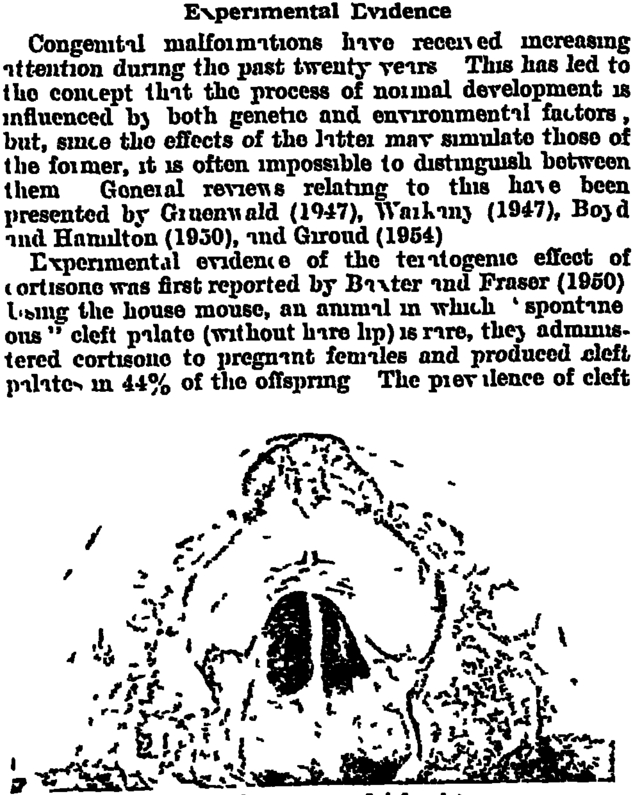

Fig 2—Inferior aspect of cleft palate

Discussion

Three aspects of this problem require careful consideration (1) was the cleft palate reported here merely a chance finding?, (2) are the conclusions of the experiments on laboratory animals applicable to man?, and (3) in view of the increasing use of cortisone, why have congenital defects in human babies not been reported before?

A study of the series of clefts of the lip and palate reported from Denmark by Fogh Anderson (1946) and from Britain by Oldfield (1950) and Holdsworth (1954) reveals a prevalence varying from 1 600 to 1 1000 live births Of these 25–36% are isolated clefts of the palate, which were noted to be more common in female babies in two of the three reported series In Denmark hereditary factors were present in 30–40% of the total group, but in British cases they were only present in 11% and 18% Fogh Andersen (1946) stated that isolated clefts of the palate seldom appeared to have a hereditary basis These observations are inconclusive in determining the ætiology of the cleft palate in the present case

If the results of the experiments on laboratory animals are applicable to man, to get a cleft palate it would be necessary to administer an effective dose of cortisone immediately before the time of closure of the palatal processes In man these processes appear about the 45th day, and closure is normally complete by the 12th week In the present case it appears reasonable to assume that fertilisation took place on or about Oct 22, hence cortisone therapy began on the 38th day of pregnancy and continued throughout the time during which the palatal processes would normally have been fusing Though it is accepted that there are objections to a comparison of the dosage used in animals with that used in man, on the basis of a milligramme of cortisone per kilogramme of body weight, it has been suggested (Greenhill 1952) that an equivalent dose for a human being would be 4–8 g of cortisone Our patient received a total of 6 g, of which 4 g was given between the presumed 38th and 52nd days of pregnancy

There are many reports of the use of cortisone in human pregnancy, but in almost every instance it was administered after the 8th week and in a dosage considerably smaller than that used in the present case These doses may not have been large enough to produce congenital abnormalities Wells (1953) treated 29 cases of nausea and vomiting in early pregnancy with cortisone Of the 27 women followed up 24 gave birth to normal babies, and the remaining 3 to babies with congenital malformations other than cleft palate, none of which were attributed to the treatment

Conclusion

Though there is no justification for attributing the cleft palate reported here to the administration of cortisone to the mother in early pregnancy, it appears extensors of the wrist have full function and the tendon transplant can be kept well away from the area of severe ischæmia. In the worst cases with necrosis of the median nerve, Seddon's more radical methods offer the best hope of restoring recovery.

There remains the problem of the paralysis of the intrinsic muscles of the hand which may result from ischæmia of the ulnar nerve. Parkes is at present working on a method in which the inert tendons of flexor sublimis are used to act as check ligaments to minimise clawing of the fingers, and this may well prove to be a further useful contribution to the reconstructive surgery of established Volkmann's contracture.

ADRENOCORTICAL FUNCTION IN PHYSIOLOGICAL STRESS

PATHOLOGISTS have long known that changes in certain organs are common to a great many different diseases. Conspicuous examples are the atrophy of the thymus and the loss of adrenal lipids in children dying of septic and toxic diseases. The first to formulate a definite non-specific syndrome common to many diseases was probably Widal,[1] who described the "hæmoclastic crises" characterised by a postprandial leucopenia in diseases of the liver; he compared it with the "shock-like" drop in circulating leucocytes after injection of foreign protein and with similar phenomena in paroxysmal hæmoglobinuria and allergic and infectious diseases. A more detailed description of unspecific hæmatological changes came from the work of Arneth[2] and particularly of Schilling,[3] who established the biological leucocyte curve common to many infectious diseases. He distinguished three phases: (1) the neutrophil battle phase with neutrophil shift to the left and eosinopenia; (2) the monocytic phase of resistance; and (3) the lymphocytic eosinophilic phase of recovery. About the same time, a series of investigations originated in the observation that various acute febrile illnesses had a beneficial effect on entirely unrelated pathological processes. Two familiar examples are the regression of Hodgkin's disease and nephrosis during measles. Weichardt[4] studied the effects of parenteral administration of proteins and he referred to a general activation of the protoplasm including its enzymes.[5] Wagner Jauregg reported remissions in general paralysis of the insane after injections of tuberculin, and this observation led to malaria therapy.

There followed Selye's work[6,7] on the alarm reaction, the general adaptation syndrome, and diseases of adaptation resulting from the derailment of a physiological defence mechanism. He claimed that a great many very different stresses produced in laboratory animals an involution of the thymico-lymphatic apparatus and an enlargement of the adrenal cortex, with an increased discharge of cortical hormones in addition to liberation of adrenaline. Since cortical extracts, cortisone, or corticotrophin (A.C.T.H.) also produce atrophy of the thymus and lymphatic tissues, and since hypophysectomised animals show neither enlargement of adrenals nor thymico-lymphatic atrophy when exposed to stress, these observations suggested that the pituitary received the primary stimulus and that the adrenal was the central organ of the *general adaptation syndrome*. Much time was devoted to histological and histochemical changes in the adrenals in unspecific stress and attempts were made to assess the functional state of the adrenal cortex in such conditions. Selye's ideas stimulated thorough and often critical investigations, particularly of the histological and histochemical aspects.[8–13] Much work has been done on the distribution and identification of cortical lipids, phosphatases, and dehydrogenases. But the attempts to identify ketosteroids were sternly criticised by Boscott and Mandl.[14] Depletion of the adrenal cortex of lipids was made the basis for conclusions no less dogmatic than the opposite assumption of old pathologists that adrenals with abundant lipids were hyperactive and those with depleted lipids were exhausted. Depletion of lipids may be due to rapid discharge, to exhaustion of enzymes necessary for their synthesis, or even to irreparable degeneration. There are hopes that simultaneous estimation of lipids and of enzymes of the Krebs cycle, such as succinic dehydrogenase, may lead to more conclusive results.[15]

In clinical investigations, too much significance has been attached to the Thorn test, on the assumption that lymphopenia and eosinopenia is clear evidence of increased cortical function. It has been shown, however, that adrenaline produces eosinopenia in adrenalectomised animals sustained by cortisone.[16] Moreover, a stressor which evokes discharge of adrenaline will influence the white cell picture by vasoconstriction and by direct action on the target organs—two effects which do not run parallel.[17] Similarly, increased urinary output of 17-ketosteroids need not indicate adrenal hyperfunction, since, in the adult male at least, their main source is the testis. *Investigations are therefore welcome in which the* effects of stress have been carefully compared with those of corticotrophin. Such investigations have been carried out for several years in Boston by a large team of workers, including clinicians, endocrinologists, pathologists, psychiatrists, and statisticians.[18–20] Members of a college boat racing crew were studied during a four-mile race, during the intensive preparation and test trials, and on control days. The subjects examined also included coxswains, a crew manager, students presenting a clinical case for the first time, candidates for a PH.D. degree, and a mixed professional group during the showing of a documentary film of primitive tribal rites. The inquiry also included an untrained man who took part in a three-hour 17-mile run, 4 patients with Addison's disease during exercise, and a patient with bilateral adrenal cortical hyperplasia. Eosinophil counts and estimations of 17-ketosteroid, 17-hydroxycorticoid, and uropepsin excretion[21] were carried out. Psychological tests included the Rorschach test and thematic tests in which the imaginative response to pictures is evaluated. In most cases the physical and psychological stress resulted in a drop in the eosinophil count, and an increase in the urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and uropepsin; but in several cases there was a discrepancy between the drop in the eosinophil count and the rise in urinary 17-hydroxycorticoids. Loss in the sweat was suspected but excluded. Sometimes the drop in eosinophils was the only positive test. The excretion of 17-hydroxycorticoids was increased during the race, but not on practice days which involved an equal amount of muscular activity. It seems that, in trained persons at least, psychological factors are more important in cortical stimulation than muscular work.

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thyroidism have appeared. The high, poorly-sustained gland uptake of I^{131} and the high protein-bound-I^{131} values are similar to those which we have previously reported in this family group. The findings in this child suggest even more strongly than in our previous cases that a considerable proportion of the plasma iodine (26·8%) is di-iodotyrosine. Chemical examination suggests that 60·8% of the iodine in the urine is di-iodotyrosine. Paper chromatography of a butanol extract of the urine confirms that di-iodotyrosine is being excreted in substantial amounts. These findings support the view that the members of our tinker family have the same enzymatic defect as that described by Stanbury et al.[3] in their most recent publication.

We agree with you that sporadic cretinism with goitre is genetically determined.[4] Study of the family tree of our patients, fuller details of which we hope shortly to publish, convinces us that the pedigree satisfies the criteria of the simple recessive inheritance of a single gene.

Glasgow

E. M. McGirr.
J. H. Hutchison.

ETHYL BISCOUMACETATE AS INHIBITOR OF SICKLING

Sir,—Last year Griffiths[8] reported inhibition of the sickling phenomenon, in a patient with the sickle-cell trait, after administration of ethyl biscoumacetate ('Tromexan'). Since then we have had the opportunity of treating four such patients with ethyl biscoumacetate. Sickling of the red blood-cells was not altered in any way during or up to three days after cessation of the ethyl biscoumacetate therapy. We feel that it is unlikely that the phenomenon noted by Griffiths was related to administration of this drug.

University College of the West Indies,
Jamaica, B.W.I.

J. A. Tulloch.
K. L. Stuart.

UNFAIR TO SURGERY

Sir,—I hope you will allow us to comment briefly upon your annotation on Regional Ileitis (Dec. 17). In the course of this you say: "Resection cannot therefore be regarded as a cure", and again: "It therefore seems that surgery has no place in cure. . ." Doubtless with the dictum so ably enunciated by the Bellman[9] in mind ("I have said it thrice: what I tell you three times is true") you add yet once more: "but while surgery can offer no cure . . ." In spite of Dr. Cooke's beautifully presented lecture,[10] and realising that two cases are of little significance, we nevertheless feel that these are worth a short mention.

Case 1.—In 1932, at the age of 20, a medical student began to have attacks of epigastric pain and vomiting accompanied by loss of weight and some malaise. This was the same year in which Crohn[11] and others first described regional ileitis. Four years later Mr. Harold Wilson operated upon this young man and found that the terminal three feet or so of his ileum was involved by a condition which he thought to be tuberculous but which was later correctly identified by Dr. A. H. T. Robb-Smith as regional ileitis. The affected ileum and part of the ascending colon were resected. Nineteen years later this patient is as fit as a fiddle.

Case 2.—In 1941, at the age of 28, another medical student noticed lassitude, much loss of weight, and generalised abdominal pain. Two years later symptoms of subacute intestinal obstruction were apparent. This patient was by now house-surgeon to Mr. Wilson who, with the help of his surgical chief assistant (case 1), removed some two feet of almost completely obstructed ileum and a severely diseased cæcum. Thirteen years later this patient is as fit as another fiddle.

Your annotation dwells in detail on the steatorrhœa and electrolytic imbalance which accompanies ileitis, but neither of these patients suffers now from disordered bowel function or abnormal stools. Furthermore they can claim, like the Oysters[12] that "some of us are out of breath and all of us are fat." Both are satisfied that their disease is cured and both believe that surgery cured it.

But then, of course, we were the patients.

London, W.1
Bourne End.

Michael Harmer.
Joe Bailey.

RUPTURED UMBILICAL HERNIA

Sir,—Until I read Dr. de Glanville's interesting article (Dec. 24) on a case of ruptured umbilical hernia I had no idea that the condition was so rare. So many umbilical herniæ in elderly people have little more than skin and integument covering them that such a disaster has always seemed to me to be more than a possibility. Dr. de Glanville found only five reported cases; to his case therefore I would like to add a seventh.

In 1951 an elderly Italian, in the course of a bout of coughing, felt that "something had gone wrong" with the umbilical hernia which had not so far troubled him through the three decades of its existence. On examining himself he was astonished, but apparently not very alarmed, to find his intestines lying freely exposed under his shirt. He called a taxi and was taken to the Italian Hospital. He was not shocked and seemed a little surprised at the necessity for operation.

After a careful cleansing of the extruded bowel (which included many feet of small intestine and the sigmoid colon) I darned the umbilical hernial orifice with floss silk. The reduction of the sigmoid colon proved a little difficult as it was greatly distended and appeared to be the site of a chronic volvulus; this may well have been a factor in the final rupture. The repair was scarcely more satisfactory than the condition of the tissues on which it had to be done, but nevertheless the old man made a good recovery.

By an odd coincidence this man was readmitted to hospital last week with intestinal obstruction in his recurrent umbilical hernia. At operation the bowel was found to be gangrenous and perforated with peritonitis involving the general peritoneal cavity as well as an incarcerated sac. The perforation in the bowel was converted into a colostomy, and the general peritoneal cavity drained. The patient's general condition was poor, but a second and equally unsatisfactory repair was attempted. He has survived operation but his ultimate recovery this time is problematical.

London, W.1

Geoffrey E. Parker.

"MUNCHAUSEN'S SYNDROME"

Sir,—If a tallish man, aged 26, with a right facial palsy, a recent right endaural incision, perhaps with thread sutures still in position, old right postauricular scars and a "crew" hair-cut should seek medical assistance there may be a doctor chancing to read this who will be glad of the following information.

Such a patient was admitted under my care on Dec. 4, 1955, complaining of right parietal headache, a right facial palsy of two weeks' standing, and right aural discharge. He said that he had had three mastoid operations on the right ear within the past eighteen months. In the ward he was found to have a temperature swinging between 99 and 101°F, and as he was extremely intolerant to the suggestion of having a lumbar puncture, having had 11 previously with much pain, I persuaded him to have an anæsthetic to carry out this essential investigation. The cerebrospinal fluid was found to contain 11 white blood-cells per c.mm. and 110 mg. of protein per 100 ml. In view of this and the persistence of the temperature and the temporal headache, and in the absence of sufficient signs to indicate a brain abscess, I explored the right mastoid in the expectation of finding pus in a dead labyrinth, cochlea function having been shown to be absent.

At operation it was found that a most thorough radical mastoidectomy had been already performed. There was no pus in relation to the widely exposed dura mater of posterior and middle cranial fossæ, nor on lifting the dura towards the apex of the petrous bone was any evidence of infection discovered. Partial removal of the promontory of the inner ear revealed only fibrous tissue. The endaural incision was, therefore, closed with thread sutures.

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[12] Carroll, L. Through the Looking-Glass, 1871; Chapter 4.

From a chance remark our suspicions were raised about the validity of the pyrexia, and inquiries revealed that during the past eighteen months a patient answering his description had been in numerous hospitals (in London, Plymouth, and Dublin), and as late as Nov 24 he had had a craniotomy at a hospital in London on account of a suspected lesion of the cerebellum or right temporal lobe None had been found

On Dec 14, the day after the mastoid operation described, the patient took his own discharge in hasty preference to investigation by a psychiatrist

I shall be very glad indeed to help any colleague confronted with this unusual case

King's College Hospital,
London, S E 5

S R MAWSON

AN UNWANTED EFFECT OF B C G VACCINATION

SIR,—I have recently started my second year of B C G vaccinating in Swansea Like many other local health authorities we are vaccinating school children in the 13–14-year age group who are Mantoux-negative and have a clear chest radiograph, and whose parents have consented

A slight alteration in administrative arrangements has given an opportunity of repeating the Mantoux test in a sample of children who were vaccinated in 1954 The reversion-rate seems likely to be very small I have, however, seen one or two further examples of an unusual, if trivial, consequence of the vaccination procedure which I first observed in 1954 A few children who received B C G vaccination then have a small, red, persisting papule at the site of the post-vaccination Mantoux test

The only explanation I can find is the use for a few sessions of P P D solution with a phosphate buffer which caused considerable local pain on injection This particular P P D aroused complaints from other parts of the country and was replaced by a solution buffered with borax and boric acid, which gives rise to no pain Possibly the former P P D solution, as well as causing pain, produced the papule

The papule is not a notable blemish on even the fairest skin, but I should be interested to read of other vaccinators who have encountered this phenomenon or of an alternative explanation of it

ANTONY ESSEX CATER
Swansea
Deputy medical officer of health

CERVICAL VERTIGO

SIR,—I was pleased to see that cervical joint lesions have been recognised as a cause of vertigo Following a report by Mr Terence Cawthorne,[1] I pointed out[2] that 15% of his patients gave a history of injury He believed that the injury damaged the labyrinth, but I was of the opinion that the head injury jarred the cervical joints, and said that there was no doubt at all that manipulation of the cervical joints could relieve vertigo in suitable cases

In each of the cases described by Dr Ryan and Dr Cope (Dec 31) there had been some form of trauma, and in each there was a latent period after injury before the vertigo developed I suggest that during this latent period adhesions form round the apophyseal joints, and that it is stretching of these adhesions with the setting up of abnormal afferent impulses there that disturbs the neck reflexes and causes vertigo Accurate analysis of the intervertebral-joint movements in these cases would probably have revealed the exact site of the joint lesion

In my experience manipulation of the neck has been most effective in relieving vertigo, and I have noticed that local joint fixations have been released by manipulation I suggest that the traction which appeared to cause vertigo in the cases mentioned would stretch the adhesions but not break them, and thereby merely irritate the joint lesion

While a collar may be helpful in some cases, particularly in the early acute phase, it is my experience that manipulation accurately applied to the faulty joint will achieve much quicker results

London, W 1

ALAN STODDARD

THALASSÆMIA IN A SCOTTISH FAMILY

SIR,—There are Scottish families whose members have served with distinction in the Navy for generations They may be said to have "thalassæmia" in that they have the sea in their blood But no educated man would suspect that thalassæmia is now supposed to mean anæmia characterised by jaundice, splenomegaly, reticulocytosis, decreased erythrocytic fragility, and a mongoloid appearance[1]

Let us drop this illiterate monstrosity before it defiles medical literature What is wrong with "Cooley's anæmia"?

London, W 1

HENEAGE OGILVIE

DANGER—CLINICIANS AT WORK

SIR,—On reading the first issue of your esteemed journal in this Leap Year, I am somewhat disturbed by the conclusions in three of the main papers

On p 5, Dr Doll and his colleagues assure us that, in spite of the century old custom, dieting with bland foods does not increase the rate of healing of peptic ulcers

On p 9, Mr Sharrard and Dr Knowelden discuss the ineffectiveness of splinting in the treatment of abductor paralysis at the shoulder—an accepted treatment for many years In fact, we are told it may even be harmful

Even worse, on p 19 Dr Brodie and his colleagues state that the general carrier rate of *staphylococci* is *doubled* as a result of admission to hospital, and thus hospital infection is due to resistant strains This may partly explain that dangerous condition—pseudomembranous enterocolitis

When I was a student I faithfully believed my teachers that we had entered a scientific age and that the days of cupping, bleeding, and purging were over, and Semmelweis might rest peacefully in his grave as his task was done

I am not suggesting that we abolish clinicians They are a necessary evil, but I would suggest, as a New Year resolution, that all who are interested in preventive medicine (I do not refer exclusively to those in the public health service) should do all in their power to make it unnecessary for clinicians to practise their therapeutic arts

Public Health Offices,
Ilford

I GORDON
Medical Officer of Health

WERTHEIM'S HYSTERECTOMY

SIR,—It will soon be five years since Mr John Howkins described in your columns his conception of a synchronous combined abdominovaginal hysterectomy,[2] and it is interesting to speculate upon the comparative unpopularity of this procedure today Probably many gynæcologists have no colleague of adequate experience who would be available to share the operative responsibility at a time convenient to both Possibly a theatre staff trained in conventional gynæcological procedures might find difficulty in making the abdominal and vaginal fields simultaneously equally accessible It is certain that many surgeons whose operations are preceded by radiotherapy consider total vaginectomy quite unnecessary

In the last few months a modified technique of extended vagino abdominal hysterectomy has been elaborated

With the patient in lithotomy position a circular incision is made as far up the vagina as seems desirable in each individual case, at least half the canal being removed The dissection then proceeds as described by Mr Howkins until bladder and rectum are freed from the cervix and the paramctrium is

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[1] *Brit med J* 1952 ii, 931
[2] *Ibid* p 1043

[1] Israëls L G Suderman H J, Hoogstraten J *Lancet* 1955 ii, 1318
[2] *Lancet* 1951, i 872

Public Health

AN OUTBREAK OF TYPHOID FEVER ASSOCIATED WITH CANNED OX-TONGUE

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In December, 1954, an outbreak of typhoid fever, in which the vehicle of infection was apparently a can of ox-tongue occurred in a market town with a population of 4150 in the North Riding of Yorkshire. Because of the presence of influenza virus B infection in the area and because of the treatment of the patients with chloramphenicol in the belief that they had influenza in the earliest cases typhoid fever was not diagnosed until more than five weeks after the onset of symptoms.

The Cases

33 persons, 21 females and 12 males aged 14–76, were affected. 30 had symptoms of typhoid fever, 2 were symptomless excreters, and 1, who had no illness and from whom *Salmonella typhi* was not isolated had agglutinins suggesting recent typhoid infection. Of the 30 clinical cases 10 were confirmed by the isolation of the epidemic strain—*Salm. typhi* Vi phage type E1—16 were confirmed serologically, 2 had a clinical illness like typhoid fever but were not investigated in the laboratory, and 2 had an illness similar to that of many of the other patients and lived in houses where there were confirmed cases of typhoid fever, but their serological findings were not typical, and *Salm. typhi* was not isolated from their urine or fæces.

23 cases were primary and 4 secondary. 3 cases may have been infected primarily or secondarily.

The presence of typhoid-H agglutinins in persons with no history of inoculation with T.A.B. vaccine was considered to indicate infection with *Salm. typhi*. All those included had typhoid-H titres of 1/160 or higher, though the first serological examinations were in most instances made about nine weeks after the onset of symptoms. Typhoid-H titrations are not usually considered to be of diagnostic value in persons who have been inoculated with T.A.B. vaccine (Felix 1924) because of the possibility of anamnestic rises in H titres during non-specific fevers. The typhoid-O response, however, is regarded as specific though it is impossible to distinguish typhoid from paratyphoid-B fever by this titration, because of the somatic factor 12 which is common to the two organisms and produces agglutinins in both diseases. For the sake of completeness typhoid-H as well as typhoid O titres are given in the following details of 5 persons who had had T.A.B. inoculation:

	Typhoid H titre	*Typhoid O titre*
3 patients	1/640	1/320
1 patient	1/320 and 1/160	1/320 and 1/30 ten days between examinations
1 patient	1/50 and 1/10	1/10 and 1/250 fifteen days between examinations

The following is a typical case:

A man aged 26, felt unwell on Dec. 17 and went to bed next day with shivering and headache. During the following week he had pyrexia, prostration, and insomnia. On Dec. 22 he had severe epistaxis, and a general practitioner was called. The patient's temperature was then 101°F but he was comfortable and had no abdominal pain. He was treated with analgesics, and his temperature returned to normal. On Dec. 27 his temperature was again raised, he complained of pains in his chest, and he became delirious. Chloramphenicol 0.5 g. six-hourly was given from Dec. 29 for five days. He then felt much better, and his temperature became normal but he felt weak and still needed rest in bed on Feb. 1 when his serum gave titres of typhoid H 1/640, typhoid-O 1/640. He had never had T.A.B. vaccine, and eight fæcal and four urine specimens taken between Feb. 3 and Feb. 15 were negative.

4 patients died. 2 of them were a man and his wife both aged more than 70 who died before the outbreak was recognised and had undergone no laboratory investigation. The man had had abdominal pain, distension, vomiting, and constipation, and died at stool thirteen days after the onset of his illness. The woman who had a previous hemiplegia, developed headache, prostration, and delirium, and died after a severe intestinal hæmorrhage the day after her husband. A woman who nursed the couple and a man who ate food prepared in the house both developed typhoid fever. The other 2 fatal cases were confirmed bacteriologically: 1 was a woman, aged 72 with chronic congestive heart-failure, who died two months after the onset of the typhoid fever. The other was a man, aged 53, who died seven weeks after the onset of his illness following an operation for intestinal perforation.

Date of Onset of Symptoms

Although typhoid fever was not suspected until the fourth week in January, the first patients became ill on Dec. 17. Between that date and Dec. 31 all 23 cases considered to have been primary had developed symptoms (see table). Infections with influenza virus B which were confirmed serologically, were prevalent just before and during the early part of the typhoid outbreak, and nearly all of the first 23 patients with typhoid fever were treated with chloramphenicol for five to ten days as cases of severe influenza. It was only when some relapsed after treatment and a complete laboratory investigation was made that typhoid fever was diagnosed.

DATES OF ONSET OF THE 23 PRIMARY CASES

—	Dates of onset (December 1954)														
	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
No. of cases	4	5	3	5	2	1	1	1	—	—	—	—	—	—	1

Affected Households

The 25 persons thought to have been primarily infected—23 with symptoms and 2 without symptoms—came from sixteen households. 1 of the patients arrived in the town on Dec. 2, another was there only from Dec. 8 to Dec. 16, and a 3rd was there only from Dec. 11 to Dec. 15. It therefore seemed probable that infection took place in the first two weeks of December and the dates of onset suggested that the patients might all have been infected on the same day.

Fourteen households were supplied with chlorinated water from the town supply, and two from another chlorinated source. The sixteen households obtained milk from five different retailers, and there was no pooling or holding of milk among the suppliers. There were no common supplies of butcher's meat, cakes, ice-cream, or bread. Groceries were obtained from two shops in the market place. The only common factor found was that in all sixteen households tongue or ham had been purchased from the same grocery shop in the first two weeks of December. Eight households bought tongue only, seven bought tongue and ham, and one ham only.

A family who bought tongue and ham on Dec. 11 clearly remembered details of the purchase. The wife was a part-time employee at the grocery shop concerned,

In England Now

A Running Commentary by Peripatetic Correspondents

ENDEAVOUR

Man's inventions and achievements
During his long sojourn on the Earth
Give us glimpses of a spectrum
At once colourful and marvellous
Skill and dexterity are begotten
Of truth and beauty;
Out of science he fashions harness for the elements;
And in the arid desert
He builds a living city
That reaches upwards to the stars
But man's exertions merge into the sublime
When, on the wings of the morning
He soars into the spacious canopy of God's universe
Into the ultra-violet zone of intellect—
Where colours fade
And things unseen
Are the things eternal

* * *

Letter from the 15-year-old daughter of a community hygienist to her mother, dated June 16, 2056

My dear Mummy,

I had a lovely day for my birthday I think Teacher must have known it was my birthday for after lunch (we had acorns and medlar cordial) we were taken to the London Museum It was wonderful First we were shown over the ancient part which we were told was in existence over a hundred years ago and then we were taken round the new People's Palace of Health and Culture You may have read that it was opened last month by the Secretary of State for Stratospheric Affairs

What we all liked best were the working models of the funny old underground railways It seems that just before they gave them up in 1988 in favour of nuclear propelled monorails they used to have white carriages and red carriages You see, that was in the days when people smoked tobacco and some people thought that it caused cancer of the lung and other people who liked smoking didn't, so the ones who didn't mind getting cancer went in the red (for danger) carriages and smoked and the ones that didn't want to get cancer went in the white ones which were labelled ' non-cancers " Of course they didn't know in those days that the underlying cause of cancer was a deficiency of guava jelly and that tobacco only hastened their end because they were going to die of some form of cancer anyway ten or twenty years later Actually the N.P monorails just came in time because all Londoners were found to be suffering from chronic emphysema, as well as cortical hypoxia, caisson disease and claustrophobia for spending so much of their time underground.

The guide was most interesting, for he was born in 1907 and was just old enough to remember the Cigarette Age, and he had actually smoked them himself He said they were horrid and a thoroughly bad habit Daddy will be amused to hear that doctors were the worst offenders, and things got so bad in 1975 that only a quarter of them didn't get cancer of the lung and survived to sign up the death certificates of the other three quarters We saw the famous Nottinghill collection of ashtrays which the old man bequeathed to the nation He was the last man to drink port and also the last man to be made a peer Some of the ashtrays he had to pay ever such a lot of money for at Christie's We also saw some amusing things called petrol lighters They caused cancer of the antrum and singed eyebrows

The guide said that when he was our age he would have been surprised to be taken round by a man aged 149, but they hadn't learnt then about the " peace of mind factor without which people used to grow old Incidentally it was once called ' the tortoise factor " because it was first isolated from the chyle of a tortoise He said that in the fifties of last century people used to do extraordinary things and get awful diseases through eating butter and margarine and meat and canned peas, and drinking milk contaminated with strontium 90 and tea, and washing their knives and forks and plates and also their undies in detergents Apparently their bread was dreadful too, and they were always having rows about it in Parliament and in the medical journals He said that for a long time Americans and Britons used to die of coronary thrombosis and everyone thought it was due to worry and eating butter and trying to get through traffic jams in a hurry (automobiles had to keep on the ground then), till someone remembered that the two nations had something else in common—*they used to eat eggs for breakfast*—just think of it, cholesterol ! No wonder their coronary arteries were all choked up Why a child would know better than that today

By the way we saw the National Collection of Alcoholic Drinks including whisky and sherry and gin in their original 20th century bottles Apparently before the passing of the Wine Restriction Act of 1990 (which followed the Abolition of Drinking Spirits Act of 1987—Teacher says I'm jolly good at history) you could buy all sorts of nasty gastric erosives and you didn't have to produce a certificate of gastronomic proficiency and submit the menu to the Ministry of Dietetics like we do now to get a bottle of wine In those days you could murder wine with bad cooking if you wanted to

I thought there was something else to tell you ; Lenina and John have been granted their permissive Licence of Procreation They said they had no trouble with the Psychiatric Board but there was a good deal of bother with the geneticist wallahs because some of Lenina's genes didn't tie up properly with his blood group but any way they passed them in the end I am so pleased about this because she is so deserving of the honour of motherhood

Remember I shall be home for the weekend after next because great-great granny is taking me on a botanical hike in the Himalayas When you make up the picnic hamper don't forget the unsaturated fats Until Friday week, your loving daughter,

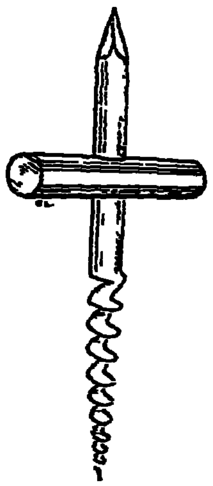
Helen

* * *

NEW INVENTIONS

A Useful Brain Biopsy Burr

Attempts to obtain brain-tissue with a hammer and chisel have not proved entirely satisfactory for routine investigation in the living subject Great advances in the technique came with the introduction of the Jones brain-biopsy burr Consisting of a spiral cutting-edge mounted at right angles to the handle, this instrument made it possible to extract adequate biopsy samples by a simple manœuvre of rotation pressure and brisk traction In the hands of Smith frequent resort to the state of the plantar responses proved an essential feature of the procedure and a sharp metal spike was therefore added to the handle This modification suffers from the disadvantage that, in order to apply the spike to the sole of the foot, the burr must be removed from the skull which is a pity



In this new modification (see accompanying figure) of the Smith modification of the Jones burr, the spike is rendered detachable by simply screwing it on and off Thus the plantar responses may be elicited without having to dislodge the entire instrument from the skull each time and it has been used in a small number of volunteers with the minimum of complications Since the spike is used solely for the feet, sterility is neither necessary nor desirable. Moreover if damaged or broken it can be replaced at a fraction of the total cost Owing to its ready detachability, the spike has also proved of value in numerous other uses about the theatre and it is ideal for prising open tin lids for anæsthetists coffee.

It is a pleasure to acknowledge the help of the research division of the Deathly Soundproofing Corporation Co., Ltd., without whose coöperation this work would not have been possible Grateful thanks are also due to Sister C[illegible] for permission to use the theatre, to the governor of [illegible] Scrubs for special facilities, and to the [illegible] for one piece of advice The instrument is manufactured by the Publican Bottle Accessories Co Potheen, C[illegible] extensors of the wrist have full function and the tendon transplant can be kept well away from the area of severe ischæmia. In the worst cases with necrosis of the median nerve, Seddon's more radical methods offer the best hope of restoring recovery.

There remains the problem of the paralysis of the intrinsic muscles of the hand which may result from ischæmia of the ulnar nerve. Parkes is at present working on a method in which the inert tendons of flexor sublimis are used to act as check ligaments to minimise clawing of the fingers, and this may well prove to be a further useful contribution to the reconstructive surgery of established Volkmann's contracture.

ADRENOCORTICAL FUNCTION IN PHYSIOLOGICAL STRESS

PATHOLOGISTS have long known that changes in certain organs are common to a great many different diseases. Conspicuous examples are the atrophy of the thymus and the loss of adrenal lipids in children dying of septic and toxic diseases. The first to formulate a definite non-specific syndrome common to many diseases was probably Widal,[1] who described the "hæmoclastic crises" characterised by a postprandial leucopenia in diseases of the liver; he compared it with the "shock-like" drop in circulating leucocytes after injection of foreign protein and with similar phenomena in paroxysmal hæmoglobinuria and allergic and infectious diseases. A more detailed description of unspecific hæmatological changes came from the work of Arneth[2] and particularly of Schilling,[3] who established the biological leucocyte curve common to many infectious diseases. He distinguished three phases: (1) the neutrophil battle phase with neutrophil shift to the left and eosinopenia; (2) the monocytic phase of resistance; and (3) the lymphocytic eosinophilic phase of recovery. About the same time, a series of investigations originated in the observation that various acute febrile illnesses had a beneficial effect on entirely unrelated pathological processes. Two familiar examples are the regression of Hodgkin's disease and nephrosis during measles. Weichardt[4] studied the effects of parenteral administration of proteins, and he referred to a general activation of the protoplasm including its enzymes.[5] Wagner Jauregg reported remissions in general paralysis of the insane after injections of tuberculin, and this observation led to malaria therapy.

There followed Selye's work[6,7] on the alarm reaction, the general adaptation syndrome, and diseases of adaptation resulting from the derailment of a physiological defence mechanism. He claimed that a great many very different stresses produced in laboratory animals an involution of the thymico-lymphatic apparatus and an enlargement of the adrenal cortex, with an increased discharge of cortical hormones in addition to liberation of adrenaline. Since cortical extracts, cortisone, or corticotrophin (A.C.T.H.) also produce atrophy of the thymus and lymphatic tissues, and since hypophysectomised animals show neither enlargement of adrenals nor thymico-lymphatic atrophy when exposed to stress, these observations suggested that the pituitary received the primary stimulus and that the adrenal was the central organ of the general adaptation syndrome. Much time was devoted to histological and histochemical changes in the adrenals in unspecific stress, and attempts were made to assess the functional state of the adrenal cortex in such conditions. Selye's ideas stimulated thorough and often critical investigations, particularly of the histological and histochemical aspects.[8–13] Much work has been done on the distribution and identification of cortical lipids, phosphatases, and dehydrogenases. But the attempts to identify ketosteroids were sternly criticised by Boscott and Mandl.[14] Depletion of the adrenal cortex of lipids was made the basis for conclusions no less dogmatic than the opposite assumption of old pathologists that adrenals with abundant lipids were hyperactive and those with depleted lipids were exhausted. Depletion of lipids may be due to rapid discharge, to exhaustion of enzymes necessary for their synthesis, or even to irreparable degeneration. There are hopes that simultaneous estimation of lipids and of enzymes of the Krebs cycle, such as succinic dehydrogenase, may lead to more conclusive results.[15]

In clinical investigations, too much significance has been attached to the Thorn test, on the assumption that lymphopenia and eosinopenia is clear evidence of increased cortical function. It has been shown, however, that adrenaline produces eosinopenia in adrenalectomised animals sustained by cortisone.[16] Moreover, a stressor which evokes discharge of adrenaline will influence the white-cell picture by vasoconstriction and by direct action on the target organs—two effects which do not run parallel.[17] Similarly, increased urinary output of 17-ketosteroids need not indicate adrenal hyperfunction since, in the adult male at least, their main source is the testis. Investigations are therefore welcome in which the effects of stress have been carefully compared with those of corticotrophin. Such investigations have been carried out for several years in Boston by a large team of workers, including clinicians, endocrinologists, pathologists, psychiatrists, and statisticians.[18–20] Members of a college boat-racing crew were studied during a four-mile race, during the intensive preparation and test trials, and on control days. The subjects examined also included coxswains, a crew manager, students presenting a clinical case for the first time, candidates for a PH.D. degree, and a mixed professional group during the showing of a documentary film of primitive tribal rites. The inquiry also included an untrained man who took part in a three-hour 17-mile run, 4 patients with Addison's disease during exercise, and a patient with bilateral adrenal cortical hyperplasia. Eosinophil counts and estimations of 17-ketosteroid, 17-hydroxycorticoid, and uropepsin excretion[21] were carried out. Psychological tests included the Rorschach test and thematic tests in which the imaginative response to pictures is evaluated. In most cases the physical and psychological stress resulted in a drop in the eosinophil count, and an increase in the urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and uropepsin; but in several cases there was a discrepancy between the drop in the eosinophil count and the rise in urinary 17-hydroxycorticoids. Loss in the sweat was suspected but excluded. Sometimes the drop in eosinophils was the only positive test. The excretion of 17-hydroxycorticoids was increased during the race but not on practice days which involved an equal amount of muscular activity. It seems that, in trained persons at least, psychological factors are more important in cortical stimulation than muscular work.

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Letters to the Editor

RADIATION HAZARDS

SIR,—The Medical Research Council report is of great interest, and many of its results must be accepted In particular it seems that the genetic damage caused by experimental nuclear explosions so far is much less than that caused by diagnostic radiology in economically advanced countries This is probably so for the world as a whole since the British figures are fairly typical for some 400 millions of human beings, though in the absence of protection from houses the danger from fall-out in the tropics may often exceed that in Britain, sometimes by a factor as high as 7, the value given on p 57 of the report

But the report seems to suffer from two defects, one of presentation and one of calculation In its table 1 D (p 93) the extra births of phenylketonurics among a generation of 20 million due to a doubling of the mutation rate are given as 5 But the total in all subsequent generations, supposing the population of England to remain steady, would be 500, and the total for the world on the same assumption, would be about 60 times this figure, or 30,000 Phenylketonuria accounts for about 1% of severe mental defect, but not all mental defect is genetically determined If two thirds were genetically determined, a doubling of the mutation rate for one generation would probably lead to the birth of about 2 million mental defectives, and also, in my opinion, of a somewhat larger number of physically defective children and a good many more abortions and stillbirths

The report estimates the increase of radiation to human gonads from test explosions as less than 1% (p 39) or less than 0 03r per generation, and the doubling dose as 30 to 80r (p 45) or 10 to 27 times the natural dose So if tests continue at the present level during one generation, their total effect would be to produce only about 2000 mental defectives or less However this may be, I think that a figure of 5 might prove unduly reassuring to a casual reader, even if a figure of 2 million is regarded as too alarming

But I believe that these figures are too low, for the following reason[1,2] Before any atomic bombs had been exploded, I calculated the probable mutation-rates corresponding to existing frequencies of congenital abnormalities The calculation was therefore unaffected by any emotions concerning nuclear warfare If a recessive gene for a character such as phenylketonuria has a frequency of 0 5% in gametes (as assumed in the report) and no phenylketonurics breed, this means that, apart from inbreeding, 0 5% of such genes meet with other similar genes per generation, so such a gene has an average "life" of 200 generations between its appearance by mutation and its elimination by natural selection But inbreeding accounts for a good many cases Of Munro's[3] 47 families containing phenylketonurics three parental pairs were first cousins two were more distant relatives and very likely another five or more were still more distantly related, the two genes which cooperated to produce an idiot or imbecile being due to the same original mutation

If, in fact 11 or 12 of Munro's families (say, 25%) were from consanguineous parents the mean "life" of such a recessive gene is reduced to 160 generations But in the middle ages and earlier inbreeding was far more prevalent than today Most people lived in villages and married neighbours Thus recessive genes were eliminated much more rapidly than today and a higher mutation-rate was needed to balance this elimination Owing to the long "life" of these genes the present gene frequency was effectively determined many centuries ago It is difficult to guess at the intensity of inbreeding in mediæval England I have assumed a figure well below that found for a Jewish community in South Germany, but above that of nineteenth century European peasantries On this basis one can very roughly calculate the mutation rate, and it turns out to be about 2 6 times that given in the report, perhaps more For rarer genes the correction is greater Thus I think that the total number of mental defectives produced by a doubling of the mutation rate during one generation would be nearer 8 million than 2 million, and might well exceed 10 million Since it is stated in the M R C report (p 90) that the principles on which mutation rates can be indirectly estimated were laid down by myself in 1932, I think that my own subsequent work, which increased the estimates by a considerable factor, might have been taken into consideration I am aware that they were stated in a rather abstract and mathematical form For this reason I have given them here in as simple words as I could achieve I may add that when the correction is made, the doubling dose for the gene for phenylketonuria if it is as sensitive as the average of 7 genes investigated by Russell[4] in mice, becomes about 36r, which is in accordance with the findings of the report (p 45) The detailed calculations will be published elsewhere

I wish to emphasise the importance of human inbreeding for another reason It is proposed to compare the frequencies of several abnormalities in different areas, in the hope of discovering or disproving a mutagenic effect of radioactive substances in the soil In the case of rare recessive conditions inbreeding in some rural areas may be expected to have a very large effect Since, on the whole, inbreeding may be expected to be higher in the more radioactive areas of Britain (e g , West Cornwall and Aberdeen) than in the country as a whole, rare recessive conditions will also be common And this might well lead to an overestimation of the mutagenic effect of radioactive minerals For this reason it is my conviction that such a survey would be a waste of public money, and what is even more serious, of the skill of the men and women who undertake it

It must also be remembered that the human doubling doses of radiation *may* be higher than for most other animals, on account of the great length of human generations Thus a human generation is about sixty times as long as a mouse generation, and a man receives 60 times as much radiation per generation But the number of nuclear divisions per generation which may also provoke mutation, is not much greater in men than mice Hence radiation may be a relatively more important mutagenic agent in men than mice, and the doubling dose correspondingly lower If so the calculated effects must be multiplied by a further factor

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[1] Haldane J B S *Ann Eugen* 1939 9 232

[2] Haldane J B S *Ibid* 1940 10 417

[3] Munro T A *Ibid* 1947 14 60

[4] Russell W L *Radiation Biol* 1954 1 825

BURNS AND SCALDS

SIR,—Your leader of May 19 and the letters from Dr Hall Smith (May 26) and Dr Leonard Colebrook (June 2) discuss the treatment to be carried out—in the home or in the surgery—of burns and scalds which are sufficiently superficial to justify non hospital treatment Dr Hall-Smith protests that your advocacy of an anti histamine ointment encourages the development of sensitisation eczemas Dr Colebrook upbraids you for neglecting the advice of Bull et al[5] to use topical penicillin Dr Hall Smith remarks that anti histamine ointment is fast replacing the topical antibiotics as the most potent cause of iatrogenic dermatitis Dr Colebrook denies that topical penicillin is likely to produce

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[5] Bull J P Jackson D M Lowbury E J L Topley E *Lancet* 1954, i 161

Public Health

AN OUTBREAK OF TYPHOID FEVER ASSOCIATED WITH CANNED OX-TONGUE

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IN December, 1954, an outbreak of typhoid fever, in which the vehicle of infection was apparently a can of ox-tongue, occurred in a market town with a population of 4150 in the North Riding of Yorkshire Because of the presence of influenza virus B infection in the area and because of the treatment of the patients with chloramphenicol in the belief that they had influenza, in the earliest cases typhoid fever was not diagnosed until more than five weeks after the onset of symptoms

The Cases

33 persons, 21 females and 12 males, aged 14–76, were affected 30 had symptoms of typhoid fever, 2 were symptomless excreters, and 1, who had no illness and from whom *Salmonella typhi* was not isolated, had agglutinins suggesting recent typhoid infection Of the 30 clinical cases 10 were confirmed by the isolation of the epidemic strain—*Salm typhi* Vi phage type El—16 were confirmed serologically, 2 had a clinical illness like typhoid fever but were not investigated in the laboratory, and 2 had an illness similar to that of many of the other patients and lived in houses where there were confirmed cases of typhoid fever, but their serological findings were not typical, and *Salm typhi* was not isolated from their urine or fæces

23 cases were primary and 4 secondary 3 cases may have been infected primarily or secondarily

The presence of typhoid-H agglutinins in persons with no history of inoculation with T A B vaccine was considered to indicate infection with *Salm typhi* All those included had typhoid H titres of 1/160 or higher, though the first serological examinations were in most instances made about nine weeks after the onset of symptoms Typhoid-H titrations are not usually considered to be of diagnostic value in persons who have been inoculated with T A B vaccine (Felix 1924) because of the possibility of anamnestic rises in H titres during non specific fevers The typhoid-O response, however, is regarded as specific, though it is impossible to distinguish typhoid from paratyphoid B fever by this titration, because of the somatic factor 12 which is *common* to the two organisms and produces agglutinins in both diseases For the sake of completeness typhoid-H as well as typhoid O titres are given in the following details of 5 persons who had had T A B inoculation

	Typhoid H titre	*Typhoid O titre*
3 patients	1/640	1/320
1 patient	1/320 and 1/160	1/320 and 1/80 ten days between examinations
1 patient	1/50 and 1/10	1/10 and 1/250 fifteen days between examinations

The following is a typical case

A man, aged 26, felt unwell on Dec 17 and went to bed next day with shivering and headache During the following week he had pyrexia, prostration, and insomnia On Dec 22 he had severe epistaxis, and a general practitioner was called The patient's temperature was then 101°F, but he was comfortable and had no abdominal pain He was treated with analgesics, and his temperature returned to normal On Dec 27 his temperature was again raised, he complained of pains in his chest, and he became delirious Chloramphenicol 0 5 g six hourly was given from Dec 29 for five days He then felt much better, and his temperature became normal, but he felt weak and still needed rest in bed on Feb 1, when his serum gave titres of typhoid H 1/640, typhoid O 1/640 He had never had T A B vaccine, and eight fæcal and four urine specimens taken between Feb 3 and Feb 15 were negative

4 patients died 2 of them were a man and his wife, both aged more than 70, who died before the outbreak was recognised and had undergone no laboratory investigation The man had had abdominal pain, distension, vomiting, and constipation, and died at stool thirteen days after the onset of his illness The woman, who had a previous hemiplegia, developed headache, prostration, and delirium, and died after a severe intestinal hæmorrhage the day after her husband A woman who nursed the couple and a man who ate food prepared in the house both developed typhoid fever The other 2 fatal cases were confirmed bacteriologically 1 was a woman, aged 72, with chronic congestive heart failure, who died *two* months after the onset of the typhoid fever The other was a man, aged 53, who died seven weeks after the onset of his illness following an operation for intestinal perforation

Date of Onset of Symptoms

Although typhoid fever was not suspected until the fourth week in January, the first patients became ill on Dec 17 Between that date and Dec 31 all 23 cases considered to have been primary had developed symptoms (see table) Infections with influenza virus B, which were confirmed serologically, were prevalent just before and during the early part of the typhoid outbreak, and nearly all of the first 23 patients with typhoid fever were treated with chloramphenicol for five to ten days as cases of severe influenza It was only when some *relapsed after* treatment and a complete laboratory investigation was made that typhoid fever was diagnosed

DATES OF ONSET OF THE 23 PRIMARY CASES

—	Dates of onset (December 1954)														
	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
No of cases	4	5	3	5	2	1	1	1	–	–	–	–	–	–	1

Affected Households

The 25 persons thought to have been primarily infected —23 with symptoms and 2 without symptoms—came from sixteen households 1 of the patients arrived in the town on Dec 2, another was there only from Dec 8 to Dec 16, and a 3rd was there only from Dec 11 to Dec 15 It therefore seemed probable that infection took place in the first two weeks of December, and the dates of onset suggested that the patients might all have been infected on the same day

Fourteen households were supplied with chlorinated water from the town supply, and two from another chlorinated source The sixteen households obtained milk from five different retailers, and there was *no* pooling or holding of milk among the suppliers There were no common supplies of butcher's meat, cakes, ice cream, or bread Groceries were obtained from two shops in the market place The only common *factor* found was that in all sixteen households tongue or ham had been purchased from the same grocery shop *in the* first two weeks of December Eight households bought tongue only, seven bought tongue and ham, and *one* ham only

A family who bought tongue and ham on Dec 11 clearly remembered details of the purchase The wife was a part-time employee at the grocery shop concerned, this sensitisation in more than insignificant numbers Here I think most dermatologists and many practitioners would differ But is Dr Hall-Smith's ointment (hydrocortisone and neomycin) itself above suspicion ?

I find it difficult to accept that 38% of the burns you consider suitable for treatment by the housewife or the general practitioner will become infected with hæmolytic streptococcus if they are not treated with penicillin cream , yet this is what Dr Colebrook would have us infer from his letter I believe he is trying to apply the results of studying the severe burns he saw at the Birmingham Accident Hospital to the more trivial ones seen on the practitioner s rounds, and I do not think one can safely do so

I have now been watching and treating the obviously superficial burn for ten years, and I am convinced (with Dr Hall Smith) that the risks of sensitisation to topical antibiotics are very real, and that they are not outweighed by the dangers of streptococcal invasion in this type of injury I have used anti histamine ointments and not seen any trouble so far—but I will heed his warning I will continue to clean these burns with cetrimide (' Cetavlon), to dry them, and cover them with tulle gras I will not be converted to topical antibiotics (having abandoned them) unless I see much more streptococcal invasion than I do at present I will arrange admission to hospital of the deeper burns, as soon as I suspect they *are* deep I will continue, I am sure, to make occasional mistakes, and to present a colleague, or my own ward, with a streptococcal wound —but not in 38% of cases And I will still be able to look the dermatologist in the eye

On reflection Dr Colebrook will probably agree that the prolongation of the old lady's disability was less likely to be due to early infection than to unrecognised full thickness damage, and unrecognised full-thickness damage brings its own infection with it Neither penicillin cream nor any other application would have done as much as a decision to send the case to hospital for early skin grafting If penicillin cream is called for every time the kettle is upset, it will do more harm than good

Sunderland   T G LOWDEN.

DETENTION OF THE MENTALLY HANDICAPPED

SIR,—Medical superintendents of hospitals for the mentally handicapped must be somewhat bewildered at the moment If they keep patients too long in hospitals they are criticised, and if they license them out they are liable to be accused of subjecting the general public to risks from violence

The question as to the suitability of a patient for release to the community is surely a matter for experienced medical superintendents who have had these patients under their continual observation

The high grade mental defective is probably quite able to perform remunerative tasks and may appear on the surface to be suitable for discharge Yet personal histories may reveal tendencies to persistent immorality, thieving, indecency and inability to conform to normal standards of living Instances of inability to cope and plan (typical of the high-grade *defective*) are well known , many of them are far happier in the institution atmosphere where their occupations and social activities are arranged for them Medical superintendents required to give evidence in courts of law have their hands tied and cannot reveal confidential case histories which might embarrass relatives , it is unfortunate that dispensers of the law are so ready to make comments and give views on superficial examination without specialised knowledge of the problem It is doubtless true that there have been cases of wrongful diagnosis and certification, but I suggest that such cases are few and that there is no need for panic measures

The recent circular of the Board of Control[1] has been viewed with concern by local authorities, who have always taken an impartial view of recommendations for discharge from institutions, since sooner or later they may have to provide further care and supervision for these cases I agree with the view expressed by the medical superintendent of a large hospital[2] that eighteen months is insufficient time in which to judge whether a patient is stable enough to be at large in the community

Fitness for discharge should be decided on the individual merits of each case One step that may help to solve the problem is the provision of sheltered day workshops, combined with residential hostels giving a certain amount of liberty coupled with kindly discipline and supervision

Z P FERNANDEZ
Chairman Leeds Mental Health
Services Subcommittee

PAIN IN PEPTIC ULCER

SIR —Your leading article of June 16 omitted one of the principal considerations It is clear that all pain is conditional upon the state of the higher levels of the brain Further, it has long been established that the movements and secretions of the stomach are adjusted by conditioned reflexes which pass through the cerebral cortex , and conditioned responses have been obtained from painful stimuli It is thus reasonable to suppose that there is a process of interaction between stomach and cortex—a supposition supported by the prominent rôle of psychological factors in peptic ulceration Account must therefore be taken of those changes which Pavlov showed to occur in the functional derangement of cortical cells, especially pathological inertia and the paradoxical phase

I venture to suggest that attempts to explain the pain of peptic ulcers mechanistically in terms of local factors alone do not correspond to the clinical problem On the other hand, a study of the local pathology in relation to the pathophysiology of conditioned reflexes might be more rewarding

Sheffield   C H FOGGITT

TUBERCULIN-TESTING OF SCHOOL-CHILDREN

SIR,—It is five years since MacDougall et al[3] reported the results of tuberculin-testing of school-children as a method of detecting sources of tuberculous infection Independently a similar scheme was started in Ipswich in 1950, and since then 752 children have been referred by the school medical service to the chest clinic for investigation 688 (91%) children and their families and other home contacts have been seen As a result 42 cases of tuberculosis, including 8 of active disease, have been discovered among the children, and 39 cases, including 6 of active disease, among the contacts This is not a great harvest compared with the results of others, but it has been a worth-while experience from which we would draw the following conclusions

1 The shorter the interval between the infection and the tuberculin testing the greater the likelihood of success At a residential school we discovered 4 active cases among 13 converters tested at an interval of a year

2 A very thorough search of all home contacts must be made At least 3 active cases came to us through other sources within a short time of the tuberculin testing of the children

3 All home contacts must be interviewed It is humiliating to discover the proportion of infections that can be traced to known sources (50–60%)

4 In an area where bovine infection has been recently present the results of testing can be most confusing, but with experience past and present bovine sources can be identified and fairly accurately dated

5 The tuberculin jelly test using flour paper, gives a high rate of false positives (20%) in 5 year old children compared with the Heaf multiple puncture or Mantoux tuberculin tests

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[1] See *Lancet* April 7, 1956 p 379

[2] *The People*, June 10 1956

[3] MacDougall I A Milhall J R Tattersall, W H *Med Offr*, 1951 86 253 *Brit med J* 1953 i 64

her duty was to make up orders for delivery Having a cold on Dec 10 she stayed in bed on Dec 11 and arranged for her mother to come from a neighbouring town and look after her from Dec 11 to Dec 15 On Dec 11 her husband bought the last $^1/_2$ lb of a can of unsliced tongue and some sliced ham The wife ate *all the ham but only tasted the tongue, which was eaten* by her husband and mother on Dec 11 and 12 Her husband and mother developed typhoid fever on Dec 17 and 20 respectively, while she was unaffected

The housewife who bought only ham bought it on Dec 11 She ordered $^1/_4$ lb of tongue, which was sliced with a knife, wrapped in grease proof paper, and weighed Meanwhile she found that ham was considerably cheaper than tongue and asked the grocer to give her $^1/_4$ lb of ham instead The ham was cut with the same knife It was eaten by 3 persons for lunch on the day it was bought 2 *of them ate a small amount and were* unaffected, but the 3rd, who ate most of it, developed typhoid fever twenty days later In this case there was an opportunity for contamination of the ham from the tongue by the use of the knife used for slicing both products

Tongue was bought every Saturday in December by nine households three bought it only on Saturday, Dec 11, and three bought it in the first two weeks in December but could not remember the exact date Tongue was therefore a common factor among all the patients but one, and this patient ate ham which may have been contaminated by a knife from the tongue The evidence suggested Dec 11 as the date of infection In some enteric fever outbreaks the occurrence of gastro enteritis soon after the time of infection helps to confirm the date of infection, but in this outbreak none of the affected persons had had any gastro intestinal illness in the four weeks preceding their enteric illness

The Ox-tongue

The tongue sold on Dec 11 came from one 6 lb can and was bought by a score or so of households, the average quantity purchased being about $^1/_4$ lb Typhoid fever developed in fifteen of these households The high proportion of affected households indicates that *the tongue must have been extensively contaminated*

The grocer was certain that tongue was never left over from one day to another, and that there was no possibility that tongue from a can opened on Dec 10 had been sold on Dec 11 The can sold on Dec 11 was opened in the shop on Dec 11 by the grocer and was of normal appearance taste, and odour It was the custom to slice part of the tongue on the bacon-slicing machine ready for the earlier customers, and this may have been done on this day The remainder was cut with a knife for each order The knife was also used for slicing ham and sometimes for cutting up packs of sausages, but sausages were usually sold packed, and on many Saturdays the knife was not used for sausages at all

Inquiries were made in the factories producing the ham and the sausages sold on Dec 11, but there were no findings to suggest that either of these foods was contaminated

The Food Handlers in the Shop

On Saturday, Dec 11 three men and one woman in the shop may have handled the tongue One man had been in France in 1914 but gave no history of a typhoid illness Serological and bacteriological tests on him and his family, including sewer swabs in the drains of his house, were negative In the case of another man, who had never been out of the country similar tests were negative The third man and the woman, his daughter, had eaten tongue but not ham from the shop for luncheon on Dec 11 Serological examination and the examination of this man s urine and fæces were negative His daughter however, became ill on Dec 17, went to bed on Dec 18, and next day had nausea, slight diarrhœa, thirst, insomnia, and rigors She was *treated with chloramphenicol* 0 5 g six hourly for ten days, her temperature became normal on Jan 3, 1955, and she was convalescent on Jan 9 She had never had T A B vaccine The agglutination titres of her serum on Feb 12 were typhoid H 1/640+, typhoid O < 1/10 Nine specimens of fæces and five of urine did not yield *Salm typhi* She is considered to have been a victim of the outbreak

The Can

All the evidence therefore suggested that the can was *contaminated before being opened in the shop* It was manufactured overseas and had been packed in June, 1954, and shipped in July It was of double seam soldered construction with cap and bridge The top collar and bottom of the can were double seamed on to the body flanges, which had been pre dipped in solder After double seaming heat had been applied to the seams to sweat the solder and to make a complete seal This method of construction reduced the risks of leakage to a minimum (T E Bashford, personal communication) However, small self sealing leakages can develop in a small proportion of such cans, and these leaks may allow the entry of a drop or two of fluid before resealing takes place (Townsend and Esty 1939, Braun 1953) In these circumstances no change may be noted in the partial vacuum in the can Leakage is most likely to take place when the cans are being cooled in water at the end of the canning process

The Canning Factory

The suspected can was one of 35,000 produced in the same factory in 1954, and no complaints about other cans were received by the producers The factory was situated on the bank of a deep fast flowing river Two supplies of water were used in the factory Both were drawn from below the surface of the river downstream from the outlet of the city sewage treatment plant One supply was filtered and chlorinated, and the other was untreated The untreated water was used for cooling the sealed cans in the retorts at the end of the canning process Treated water was used for all other operations in the factory After cooling, the cans were washed and then incubated at 92°F for fifteen days before they were labelled and shipped

If the can was contaminated in the factory, contamination probably took place during the cooling process, in which untreated water was used Sandiford (1954) isolated *Salm typhi* from a can of cream, but two hundred and twenty five other cans of the same batch were negative These cans had been cooled with water from a contaminated source However, with the type of can we have described, the possibility of leakage and the chances of examining a contaminated can are slight Only two unopened cans of tongue of the same batch were investigated They were examined by the Food Hygiene Laboratory and were found to be sterile The cans were sound

Discussion

The use of untreated river water for cooling cans in the retorts at the canning factory suggests, even though the cans were of double seamed construction, that the most probable source of contamination was in the factory *but there can be no certain proof of this* Sandiford (1954) showed that a similar state of affairs occurred with canned cream, but it must happen rarely A contaminated can might pass through the incubation test if it contained only non gas producing organisms, and *Salm typhi* does not produce gas The risk that a can will leak momentarily and in that moment will absorb an enteric non gas producing pathogen must be

6 *The incidence and annual rate of infection at specific age groups are valuable guides to the incidence of tuberculosis in the community*

In certain districts of Norway annual tuberculin-testing of school children has been practised for many years When conversions do occur which may be at intervals of three or four years, a diligent search, which rarely fails is made for the source

REGINALD LEADER
Medical officer of health
CHARLES J STEWART
Ipswich Chest physician

PASSION AND CONTROVERSY IN SCIENCE

SIR,—I was very interested to read Professor Polanyi's article (June 16) May I point out the slight error in the spelling of Prof J H van't Hoff's name ?

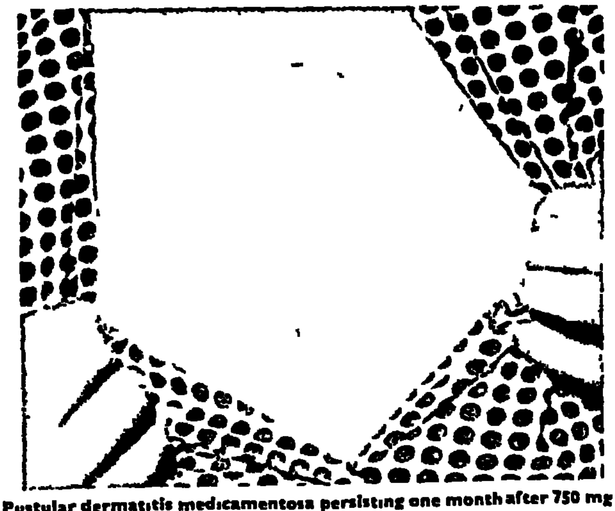
Westminster Hospital,
London S W 1
WALTER VAN'T HOFF

NOVOBIOCIN DERMATITIS

SIR,—Your comment of May 5 on Dr Pellerat's objection to restriction of new antibiotics induces me to suggest a generalisation that may serve to waive authoritarian action in this regard Although Dr Pellerat and a growing literature point to the emergence of resistant staphylococci, this is still being encountered chiefly in hospital populations (human and bacterial), and geneticists who are familiar with bacterial mutation are still reluctant to predict dangers to those undosed by antibiotics Strong independent opinion exists in this country that our gravest problem is in the indiscriminate use of penicillin and the "panallergenisation" to that antibiotic, an incidence that has been estimated at as high as 10%[1]

The wide use of the cationic mycin antibiotics (streptomycin the tetracyclines, and the carbomycins) did not result in comparable sensitisation True, these particular streptomyces derived antibiotics are potent contact dermal sensitisers, but appear to be weakly allergenic in the injectant or ingestant phase In fact certain hypersensitivity states have been treated by their administration[2] An explanation of this contrast between the cationic mycins and the anionic penicillin may be found in a rule pieced together from researches at the Canadian Red Cross Hospital in your country,[3] on the haptenic specificity of sulphated dextrans and those carried out in the United States on vaccine adjuvants[4] This rule has been enunciated as "macroanions enhance antigenicity (of an immunising substance), macrocations diminish it"[4]

Believing in the validity of this rule, I have prescribed the recently introduced anionic mycins for my own patients Several months ago, however, a housewife who had had a severe protracted urticarial reaction to penicillin ten years ago and who has had several bouts of recurrent purulent lymphadenitis, yielding in turn to the tetracyclines or carbomycins to which she is not sensitive was given the still experimental streptonivicin ('Albamycin') because her wound flora, a carbomycin oxytetracycline resistant staphylococcus was found markedly sensitive to it The third 500 mg dose was followed by such an intense generalised erythema and pruritus that it was discontinued and another, supposedly dissimilar, antibiotic (Pfizer PA 93) was obtained Naturally enough, since this is now known to be a novobiocin, the staphylococci proved susceptible in vitro Two weeks after the administration of the streptonivicin, PA 93 was given, on the second day it was evident that the abscess was reacting well but the patient poorly A maculopapular rash evolved over the next week, covering the scalp, cheeks, and torso finally becoming pustular in the fashion characteristic of a dermatitis medicamentosa One month after stopping PA 93 and two weeks after the eruption began to subside pustules were evident on the chest (see accompanying figure)



Pustular dermatitis medicamentosa persisting one month after 750 mg of oral novobiocin

Allergic dermatitis has just been reported[5] as a common complication of novobiocin So has urticaria[8] and other skin rashes[9] These have arisen during observations on small series and notes of caution have been sounded[10] These are perhaps not as yet convincing as to the validity of the rule about anionics[5] as applied to new antibiotics, but we should all dislike a repetition of the penicillin story

Laurelton Long Island
N Y U S A
ROBERT D BARNARD

FIRST-AID MANUALS

SIR,—"First aid" must interest many of your readers, and yet it is surprising how seldom it is mentioned in your columns The quick and widespread reaction to the exchange on the "three quarter prone" position in head injuries[11] has prompted me to write this letter, in the hope that it may perhaps provoke a similar response

Those of us who are required by law to train and appoint first aid men in industry, or at least to supervise their training and appointment, are often in the embarrassing position of having to use a textbook whose teaching we regard as out of date and sometimes dangerous

The transport of unconscious patients on their backs has already been commented on, but this is surely less undesirable than the treatment of wounds advised in the latest (1951) edition of the St Andrew's Ambulance Association handbook, which says that "the edges should be gently sponged with some antiseptic solution such as diluted lysol, carbolic lotion (1 to 40), a weak solution of iodine (Liq Iodi Mitis B P 1932) or methylated spirit Some of the antiseptic used for cleansing the edges may be wrung out of a clean swab into the wound in order to complete the cleansing"

One feels that even Ambroise Paré would have disagreed with this, and yet it has continued to appear through seventeen editions

This is perhaps the worst of several passages in this particular manual which should have been altered long ago In the light of modern work on "surgical shock" and the improvement in the technique of accident surgery, passages in all the current textbooks need revision Furthermore I suggest that the revision should be supervised by people competent to assess

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1 Barnard R D, Fox H L N Y *State med J* 1953 53 2820
2 Barnard R D N Y *Physician* 1951 36, 2
3 Glynn, L E Holborow E J, Johnson G D *J Path Bact* 1951 48 205
4 Takemoto K K Personal communication
5 Freeman M D Stanton R I Barnard R D Goldman B *Ann Allergy* 1956 14, 82
6 Limson B M Romansky M J *Antibiotic Med* 1956 2 [illegible]
7 Milberg M B Schwartz R D Silverstein I A *Ibid* p 256
8 Kessler L A Personal communication
9 Freeman M D Personal communication
10 David N A Burgner P R *Antibiotic Med* 1956, 2 219
11 *Lancet* 19[illegible] i [illegible]

infinitesimal, and complete proof of its occurrence is almost impossible to obtain because only one in some thousands of cans is likely to be affected On general principles, however, it seems unwise for canners to use potentially contaminated water for their cooling processes

In the past twenty years there have been four outbreaks of typhoid fever associated with meat

In 1938 there were two such outbreaks, each affecting seventeen to twenty households (Ministry of Health 1938) Both were connected with grocery shops selling cooked canned meats, and the vehicle was thought to have been food, but no particular food was suspected In one shop the staff were negative bacteriologically and serologically, and in the other a girl who did the cleaning had a high content of antibody in her serum, but there was no evidence that she was a carrier

In April, 1948, an outbreak due to *Salm typhi* Vi phage type E1 at Crowthorne, investigated by Moore (1949), affected 41 persons The vehicle was thought to have been canned corned beef, and no carrier, symptomless excreter, or other source of contamination of the meat after the can was opened was found

Peters and Clutterbuck (1942) described a typhoid outbreak in Glasgow where 35 persons were affected and where meat was suspected of being the vehicle of infection No particular meat was common to all the primary cases, but the shop sold a high proportion of canned and processed meats A month after the suspected date of infection the butcher became ill with typhoid fever

Summary

An outbreak of typhoid fever due to *Salm typhi* Vi phage type E1, affecting 33 persons, is described Except for 1 woman, who ate ham which seems to have been secondarily contaminated, the primary cases were in patients who had eaten ox-tongue from one 6 lb can

The can of tongue was probably contaminated in the factory, after processing by sewage-polluted river-water used for cooling

The outbreak was unrecognised for five weeks because of a simultaneous outbreak of influenza B and the wide use of chloramphenicol

We wish to thank Dr E S Anderson and the staff of the Central Enteric Reference Laboratory and Bureau for Vi phage typing, Dr H G M Smith, of Bradford, for the influenza complement fixation tests, Dr Betty Hobbs of the Food Hygiene Laboratory, for the examination of food and water, Mr T E Bashford, of the Metal Box Company, for the examination of cans, Dr N J Hessian, of Yearsley Bridge Hospital, for details of his cases and Dr Kenneth Froome, of Scarborough Hospital, for some bacteriological results

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DETERGENTS

A committee was appointed three years ago by the Minister of Housing and Local Government to examine and report on the effects of the increasing use of synthetic detergents and to make any recommendations that seem desirable with particular reference to the functioning of the public health services" Its report[1] contains a wealth of technical information which will be useful in the management of public waterworks and sewage-disposal plants, and it also covers many aspects of the problem which are of topical popular interest

The use of these household washing powders does not seem to have led to any significant increase in the incidence of dermatitis in housewives and laundry-workers Even in normal concentrations, however, they are capable of causing dermatitis in the susceptible and the risks are increased if they are not used in a sensible way Similarly they can have a deleterious effect on certain types of domestic plumbing If the housewife could strike a balance between sales resistance and casually extravagant use of detergents, a lot of interests at the other end of the sewer would feel much less anxiety

When crockery is slipped, without rinsing, from the foaming sink to the labour saving drying-rack, some traces of synthetic detergent inevitably remain to be swallowed with the next meal Whether this is harmful, and if so how the risk compares with those attached to cigarettes, diesel fumes, radioactive fall out, and the bizarre chemicals nowadays sprayed on our crops, remains to be discovered The committee says that long-term study is needed to see whether there are any ill effects

The production of massive foam at sewage-works is more than an embarrassment to the operators and a detriment to the purification process, the sewage-contaminated foam is liable to be picked up by the wind and blown across the countryside, which is not only unpleasant but a danger to public health Foaming extends into many of our main rivers and adds fresh hazards to the life of fish, which are already battling (for survival and oxygen) with sewage and industrial wastes When the same river becomes the public water-supply to downstream communities, the problem returns to the housewife

A majority of the committee fear that conditions may deteriorate and recommend the Government to consider whether control powers should be prepared in advance Four members, however, contend that the difficulties are being exaggerated, and hold that in any case the public health authorities ought to be clever enough to find the remedy Unfortunately the report does not disclose whether or not the four optimists happened by any chance to be the four representatives of the trade interests involved We like to know such things.

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[1] H M Stationery Office 1956 Pp 60 3s

WESTERN EUROPEAN UNION

As a result of administrative arrangements which have just come into force, the member States of Western European Union now form a single territory for health control of sea and air traffic, thus extending the scheme operated by the five-power Brussels Treaty Organisation.

Under the new arrangements, health control regulations at airports no longer apply to aircraft coming from any of the seven countries of the Union, and the maritime declaration of health is no longer required from vessels of member countries plying only between those ports of the seven countries included in the scheme

An information exchange service has been organised so that the health authorities in member countries can keep in constant touch and can supply each other with information about all disease covered by international health regulations, or any epidemiological incident which would be of interest to the other countries

OCCUPATION CENTRES FOR THE MENTALLY DEFECTIVE

"The nurturing and training of mentally defective children in occupation centres is one of the most important and useful activities of a local health authority" Dr R W Elliott, medical officer of health for Bolton, expresses this view in his report for 1955 But, he adds Bolton's centre deals only with those up to the age of sixteen, and there is an overwhelming need for the centre to be extended so that all age-groups can be constantly guided and trained, to prevent social deterioration

All the excellent training which has been given before the age of sixteen years is completely nullified if at that age they have to leave us and become once more flotsam tossed about on the sea of life " the value of the advice offered from the points of view of ease of teaching practical application to the recently injured, and conformation to the requirements of the receiving hospital For this purpose I suggest the appointment of a committee composed of industrial medical officers and practising surgeons experienced in the treatment of accidents

National Coal Board,
Scottish Division
Lothians Area Edinburgh

C E WATSON
Area medical officer

GENDER OF -ITIS

SIR,—Your peripatetic correspondent wandered a little too far last week The U are particularly strong on Latin grammar, and would prefer to speak of "polyarteritis nodosa"

Folkestone, W

F I CAIRD

MEDICAL EDUCATION

SIR,—Most essays on "medical education" excite the profession's interest, and I hope I have sympathy in airing a disappointment that Dr Ellis (June 2 and 9) should review so competently in his first article and then drift into platitude with his second He knows well what is wrong but has obtained little satisfaction by arguing himself back to "essential steps"

I suggest that the foundation fault is contained in his title The word "education" is by tradition limited to the developing adolescent mind and would be better avoided for any process applied over the age of 21 Thus, "further education" is really "further information," "postgraduate education" is "postgraduate revision," and medical education is a technical training—no more, no less

I ask readers to imagine what would happen if other professions adopted our attitude What kind of a man would a lawyer be, if he began his studies at 16 ? Or a priest ? Surely, better doctors would be produced by a shorter but very intensive and resident course, to be given to minds of proved general ability, and not to be commenced before the age of 20 or 21

Manchester

A F

PHENYLBUTAZONE IN THE TREATMENT OF PROLAPSED INTERVERTEBRAL DISC

SIR,—I have read Dr Steer's valuable letter (June 16) in which he reports favourably on the treatment of prolapsed intervertebral discs with oral phenylbutazone

For the past $2^1/_2$ years I have treated such cases with this drug, and I am now preparing a detailed account of my experiences Approximately twenty-five patients have been given this drug either orally or by injection and the results compared with the previous twenty five cases treated by conventional methods

At first 600 mg of phenylbutazone by mouth was given daily for a week, after which the dose was reduced to 300 mg daily for as long as necessary I found that, although initially most of the cases responded satisfactorily, some showed a tendency to relapse or took a long time to recover During the past 6 months I have been more successful with intramuscular injections of 600 mg every third day for 6 weeks All those receiving the drug in this way left hospital within 10 days and continued to receive the injections from the district nurse In all the patients the relief from pain was rapid and the condition was usually cured by the end of the 6 week period In one instance an operation which had been advised for relief of pain of three years' duration has been avoided

It can be concluded therefore that this method of treatment may be superior to those in present use, but lengthy controlled clinical trials are necessary to establish its true value

Dudley Road Hospital
Birmingham

R O GILLHESPY

ANÆMIA IN PREGNANCY

SIR,—In your leader of June 2, the possible need to supplement dietary iron in pregnant women is considered entirely in terms of hæmoglobin, as though the only metabolic rôle of iron in the body was to provide part of the hæmoglobin molecule Furthermore no differentiation is made between nullipara and multipara Changes in the observed values for mean corpuscular hæmoglobin concentration and hæmoglobin mass may result from depletion of the iron store of the body, but neither is a measure of the size of this store There is no satisfactory way of measuring this in man at present

Surely the question of supplementary iron in pregnancy should be related to the problems of whether the mother, at her first menses after pregnancy and lactation, has a total body-iron content as great as when she conceived as a nullipara, and of whether her iron stores are replenished by the time she conceives again

There is little experimental evidence on this aspect of iron metabolism, but observations on rats by Widdowson and McCance[1] give a hint that the iron stores of a woman might still be depleted at her first post-pregnancy menses Such depletion might be prevented by supplementary iron during pregnancy

Department of Chemical Pathology
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D MARRACK

FOOD-POISONING AND DETERGENTS

SIR,—To combat the constantly rising incidence of food-poisoning and other infectious gastro intestinal complaints, the newly introduced Food Hygiene Regulations aim at improving the cleanliness of food-handling premises and the personal hygiene of food-handlers These requirements will cost the catering trade large sums Is there any certainty that they will reduce the incidence of these conditions ?

These diseases have become more prevalent in the past ten years despite great efforts by health departments in raising standards of personal hygiene in food-handlers and improvements in equipment methods, and cleanliness in food handling premises It is therefore unlikely that any material benefit will accrue from further efforts in these directions

If, after all the attention given over the past ten years to personal hygiene and cleanliness in food premises and even homes, the incidence of food borne *infections* is still increasing, it suggests to me that we are *not* attacking the problem at all and some other factor or factors must be involved In an effort to find other possible contributory factors it is worth considering what other changes have occurred in our way of life simultaneously with the increased incidence of food poisoning, and one stands out clearly —namely, the introduction of powerful, non bactericidal, synthetic detergents as a substitute for soap and their widespread use over the past ten years in homes and particularly in catering establishments

Is there a connection between the use of detergents and the increase in food poisoning ? Because of the widespread use of detergents for cleansing crockery, and the difficulty even with special care and attention of removing every trace of these, we must all be ingesting small amounts of detergent every day from our eating and drinking utensils especially when the more usual perfunctory methods of washing up are employed Detergents lower surface tension and can thus presumably affect cell permeability In solution they are excellent solvents and could presumably interfere with the normal protective mechanism of the gut lining, thus facilitating absorption of toxins and even the penetration of the mucosa by bacteria

Is it possible that the distribution among the community of the food poisoning organisms is unchanged and that before the introduction of powerful detergents we obtained relative natural immunity by the ingestion of small doses of organisms with which our normal protective mechanism could cope and also that small doses of ingested food poisoning toxins did not penetrate the gut-lining in sufficient quantity to give symptoms ? Such a possibility is not referred to by the

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[1] Widdowson E M McCance, R A *Biochem J* 1948 42 577

The Casualty Department

III A COMPREHENSIVE ACCIDENT SERVICE*

T G Lowden
B M Oxfd, F R C S
CONSULTING SURGEON, SUNDERLAND GROUP HOSPITALS

THE previous articles have described how the reception of emergencies, the disposal of accident cases, and the treatment of diverse minor conditions whose only common feature is that they are ambulant, are gathered into one department of the hospital This association has grown fortuitously, mainly because the arrival of all these patients is unpremeditated, but partly also because the disposal of accidents is only now, and only to a limited extent, being separated from the disposal of other emergency cases

Most of the country is so populated that only a few large cities can *support a system* where *all accident cases*, major and minor, can be dealt with at a centre whose periphery has a conveniently short radius Many industrial areas of 150,000–300,000 inhabitants cannot afford to provide for themselves a comprehensive system with fracture clinics, general surgical wards, head injury and burns units, and a staff to give a 24-hour cover The problem cannot be solved by making the largest casualty department the centre and closing down the rest, because this would reject very many of the minor injuries The question arises, on the other hand, whether *it is necessary* for every hospital to have a complete casualty department, and whether a redistribution of its three *main* functions could not make for greater efficiency and improved clinical results

If the medical and surgical emergencies which are to be considered for admission are assessed by the inpatient staff, their reception and early treatment pass at once into the hands of those who will follow their definitive treatment In many hospitals this system is already in operation, and the casualty officer's function is often confined to informing the R S O or R M O of their arrival In very large hospitals admissions are so frequent that it is an advantage to have someone whose main duty is to receive them, but in smaller ones there seems *to* be *no* valid objection to a system where the inpatient houseman is *called to see the case* he *will very soon* have to examine anyway, and there would be advantages *in* him carrying out examinations in the privacy of an admission room instead of after admission to the ward Putting responsibility for these cases upon the senior resident staff of the receiving hospital, and for accident cases on the accident service, would distribute among a number of doctors a medicolegal responsibility which is becoming too much for a single junior to bear

More of the "sorting-house" work can be avoided, if cases are referred direct to their special clinics instead of through the casualty department Radiological diagnoses should be made in the X ray department, general-practitioner work should be referred to the family doctor (now that everyone has a doctor), minor specialist procedures in such departments as E N T and skins should be done in the departments concerned

If an accident service could be organised in areas with a twenty mile radius, most of the remaining casualty work in all the related hospitals and clinics could be associated with it *under centralised supervision* but without bringing every patient to the centre itself

The Outposts

A perfect accident service starts at the accident itself, and a system of outposts, closely associated with a central hospital, would avoid calling every *minor* case to the centre Many such outposts in the industrial medical service, the medical units of nationalised industries, the school medical service, and the out patient departments or casualty rooms of the smaller hospitals have an independent existence already If the treatment of thousands of cases seen in these units can be integrated with the casualty department in a central hospital, a great step forward will have been made—and at the same time a mechanism will have been created for the more rapid and accurate reference of major accidents to their proper place of treatment

Those who have acquired extensive experience in the management of acute injuries would be the first to agree that orthopædic problems play much less part in it than is generally supposed The treatment of shock and of burns, the care of multiple injuries (especially the association of head injuries with injuries to other parts), problems of infection, plastic surgery, and special anæsthetic technique require an accident service that can call upon a team rather than an individual It is important *that an early decision should be made on whether* such a team is likely to be wanted The periphery of a casualty service must be capable of making such a decision with a high degree of reliability All parts of it should have a clear idea of the type of definitive treatment likely to be given at the centre, so that first aid, transport, and what has been called "second aid," are in line with the treatment the patient will ultimately receive

In this conception many of the smaller casualty departments, after being relieved of much of their responsibilities for the reception of inpatients and disposal of outpatients will cease to be part of the hospital in which they are housed They will become representatives of the accident service, and fulfil a function similar to other accident service outposts in large industrial concerns They will treat those cases which can be dealt with on the spot and refer those which require attention at the centre Their equipment can then be simplified, and in particular it will not be necessary for them to maintain outpatient operating theatres On the other hand, their facilities for administering first aid and shock therapy, and for organising rapid reference of major accident cases must be considerably improved They will be in constant communication with the main casualty department at the accident *centre They will always have power to admit* cases to the hospital where they are situated if it is felt that further travelling will be dangerous for the patient

The Centre

The central casualty department can cover an area of a thousand square miles It needs consultant surgeons and must be able to provide a day and-night medical cover It also needs enough doctors for one to visit each of the outposts daily Its establishment must include clerical assistance and the services of an adequate bacteriological laboratory It will have complete control of a short stay ward, and X *ray* facilities devoted primarily to its own needs It will have first call on the services of an anæsthetist It will be situated in the same hospital as the inpatient accommodation for the accident service, and will work as *part of that* service Its medical staff will be in constant touch with the emergency bed bureau and the other receiving hospitals of the area It will act as an information centre for all questions on the admission and disposal of urgent cases, its doctors will also be coordinating officers, and its senior doctor on duty will be in charge of casualty services

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* The last of three articles dealing with some of the difficulties facing casualty departments of non teaching hospitals and outlining a scheme for a more comprehensive accident service

Committee on Detergents, whose final report appeared last week.

Unfortunately as a whole-time medical officer of health I have not the time to investigate myself these suggestions in the laboratory and I therefore offer the idea to any research-worker who may be interested.

Doncaster H. L. SETTLE
Medical officer of health

NOT OXFORD

SIR,—Many other Oxford men will join with me in applauding the initiative of the distinguished band of Cambridge medical men who, as reported in your last issue, realised the error of their ways just in time and took their degrees in the University of Oxford.

As a traditionalist, however, I feel I must protest against certain departures from precedent. No notice of a congregation on June 7 was given, and we were thus deprived of the opportunity of attending and welcoming our professional brethren appropriately. No witnesses can be found, nor has any mention of the conferment of these degrees appeared in the *O. U. Gazette*. Can it be that the silent Roman Emperors outside the Sheldonian were the sole spectators of some secret nocturnal ceremony?

Most deplorable of all was the use of English in the proceedings. Can the banal "By proxy" compare with the euphonious syllables of "In absentia"? One can only surmise that the vice-chancellor sanctioned this departure from traditional practice as a special concession, well knowing that Cambridge men would be untutored in the liberal arts.

Finally, Sir, what of the future? Are the lemmings on the move?

Westminster Medical School
London, S.W.1
ANDREW SHERRINGTON

*** We regret that last week (p. 1021) graduates of the University of Cambridge on whom the degrees of M.D. and M.B. had been conferred were shown as having gained the D.M. and B.M. of the University of Oxford. Otherwise our announcement was, we hope, correct. An amended notice will be found on p. 1078.—ED. L.

METHYLTESTOSTERONE

SIR,—Oral methyltestosterone has been used in clinical practice since its introduction by Foss in 1939,[1] both for its anabolic and for its androgen effects. It was not until 1947 that Werner[2] suggested that its use might occasionally be associated with jaundice. Other reports followed.[3-5]

The hepatic lesion found in cases of jaundice following methyltestosterone therapy was not associated with the laboratory findings usual with severe parenchymal damage or biliary obstruction: the cephalin flocculation reaction was negative, the serum-alkaline-phosphatase only moderately elevated, and the serum-bilirubin increased. Werner thought it improbable that methyltestosterone was a markedly hepatotoxic agent, since the syndrome was rare, despite the widespread use of this hormone. Further, in two patients who had recovered, renewed administration of this methylated compound failed to reproduce jaundice.

Since testosterone has not been so implicated, some pharmaceutical literature has given this as a reason in favour of sublingual or sublabial tablets of testosterone. Though testosterone when given orally is ineffective, owing to deactivation by the liver, the makers and others claim that given by the sublabial route it is as effective as parenterally administered esters.

Methyltestosterone on the other hand is effective both when swallowed and when absorbed sublabially, although it is slightly more efficient by the latter route.[6] It would seem, therefore, that methyltestosterone is less wasteful, as some of the hormone from the sublabial tablet of testosterone is bound to be swallowed in the saliva, particularly from the sublingual site. The metabolism of these two hormones is indeed different in that methyltestosterone (*a*) increases creatinuria and (*b*) does not increase the 17-ketosteroids. Although not directly related to the problem, it is perhaps of incidental interest that Lloyd-Thomas and Sherlock[7] used methyltestosterone to relieve the distressing pruritus of obstructive jaundice.

In a fairly extensive use of methyltestosterone, with doses ranging from 5 mg. daily to 150 mg. daily over long periods, we do not happen to have come across a case of jaundice. Since for practical purposes it would be a pity to omit the use of methyltestosterone, we should like to know whether any physicians in this country have noted jaundice which they attributed to methyltestosterone therapy.

Bristol G. L. FOSS
London W.1 S. LEONARD SIMPSON

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[1] Foss, G. L. *Brit. med. J.* 1939, ii, 11.
[2] Werner, S. C. *Amer. J. Med.* 1947, 3, 52.
[3] Kinsell, L. W. *Gastroenterology*, 1948, 11, 672.
[4] Werner, S. C., Hanger, F. M., Kritzler, R. A. *Amer. J. Med.* 1950, 8, [illegible]
[5] Wood, J. C. *J. Amer. med. Ass.* 1952, 150, 1484.
[6] Foss, G. L. *J. Endocrin.* 1956, 13, 269.
[7] Lloyd-Thomas, H. G. L., Sherlock, S. *Brit. med. J.* 1952, ii, 1289.

ELUTION AND MICRO-ESTIMATION OF 5-H.I.A.A.

SIR,—The new colorimetric method of Udenfriend et al.[8] for the quantitative estimation of urinary 5-hydroxyindole-acetic acid (5-H.I.A.A.) is based on the older Gerngross reaction with 1-nitroso-2-naphthol and is simpler but less specific. It is, moreover, liable to serious error if "metabolic" keto acids are not completely removed with 2 : 4-dinitrophenylhydrazine, before the final extraction. Further, in all methods involving extraction if the extraction time, if quoted, is not strictly adhered to, quantitative results will not be obtained. These inherent weaknesses in the Udenfriend method can be overcome if the urine containing pathological amounts of 5-H.I.A.A. is directly applied to the paper for chromatographic separation and estimation. In normal urines, however, where the concentration of 5-H.I.A.A. is much less (1 to 5 µg. per ml.), it is still necessary to extract the 5-H.I.A.A. with ether, and evaporate to dryness in vacuo. The quantitative estimation of 5-H.I.A.A. by means of one-dimensional paper chromatography depends on a clear-cut separation of the spot, especially if an elution method is used; and whether the total colour in the spot can be quantitatively determined by photometric evaluation of the spot area and intensity, or by elution followed by colorimetric estimation; and whether Beer's law holds for the colour reaction employed and for the subsequent elution.

A semi-quantitative method for the estimation of 5-H.I.A.A. can also be used by assessing visually the amounts of 5-H.I.A.A. contained in the spots as regards area and intensity of colour of the spot given by the urine and spots obtained with standard amounts of 5-H.I.A.A. This method could be used in the clinical sideroom. But I am not aware of any *detail method* where a micro-analytical technique, using paper chromatography has been fully described in relation to urinary 5-H.I.A.A.

The method is based on the simple expedient of cutting out the spot of the developed chromatogram which contains the 5-H.I.A.A., eluting it from the paper, and determining the amount of 5-H.I.A.A. in the eluate. It was *found that the* coloured product formed by staining the chromatogram with Ehrlich's reagent could be quantitatively eluted and its concentration determined colorimetrically. This was done by applying 5 µl. aliquots of a standard solution containing 2 µg. per 5 µl. 5-H.I.A.A. to Whatman no. 1 filter paper using an Aimer automatic ultra-micropipette (0·005 ml. capacity).

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[8] Udenfriend, S., Titus, E. O., Weissbach, H. *J. biol. Chem.* 1955, 216, 499.

in an emergency with functions such as are defined in the Birmingham scheme.[4] The centre will provide a mobile team, such as is recommended for attendance at "major disasters".[5] The provision of a private telephone network with all its outposts should receive consideration.

Contact Between Outposts and Centre

No economy in medical man-power would be effected if it were proposed to staff each outpost or even such outposts as are at peripheral hospitals, with a casualty officer. The majority of minor injuries seen in casualty departments can be treated effectively by an experienced nurse, and indeed many of them are so treated at the present time. A clinic held by a doctor once a day for reassessment and supervision will make it unlikely that any important complication is missed. One doctor can thus control five or six outlying clinics. Although immediate medical attention to every trivial complaint or injury would not be given, the total medical cover would be increased, because more establishments treating such conditions would be supervised by the accident service. The medical cover, furthermore, would have some continuity of direction and policy, and, one hopes would be capable of making clinical advances.

Cases of acute superficial sepsis would be treated in their early stages at the outposts, but seen daily by the doctor "on circuit" who would decide when or if operation is indicated. He would be followed around by an ambulance which could pick up operation cases and take them to the casualty centre.

Injuries of a more serious nature such as extensive lacerations or obvious fractures would be referred to the centre. Major injuries would normally be taken there direct from the accident but occasional cases would have to be "staged" at outposts for first aid or even held at the peripheral hospital if unfit to travel farther. On such occasions the accident service should be prepared to send a doctor to the outpost, though every hospital, whether equipped to deal with accidents or not, should be prepared to hold those few cases which arrive unheralded and are obviously unfit to be transferred.

In this way the obviously trivial cases which constitute 90% of the casualty department's work, are filtered off. The doubtful acquire medical cover promptly, and transport is burdened only with those who need it.

Most important of all every outpost, whether situated at a peripheral hospital a clinic, or an industrial concern should be in constant touch with the casualty centre so that advice is always available and the chances of error in disposal are reduced to a minimum. Every doctor in the accident service, from consultant to junior house surgeon, should take turns in going 'on circuit, so that he is continually reminded of the problems in the catchment areas. No accident service can regard itself as complete if it sits in a department and waits for its cases to be brought to it.

A working knowledge of the local authority's services (police, ambulance, fire brigade) and of other organisations, such as pit rescue-teams, first aid societies, and N.H.S. reserve and Civil Defence Corps and an active attempt to make them aware of the proper disposal of accident cases will do much to send the injured straight from the incident to their right destination. There must also be a free exchange of nurses between outposts and the casualty centre, so that they are made aware of any advances in treatment. The attendance of voluntary or local authority employees concerned with the administration of first-aid should be encouraged. Industrial medical officers, having the care of a large number of workers, should be invited to bring their own first-aid posts into the scheme.

The Staff

The Nurses

An accident service designed on these lines will depend very much on the ability of its nurses, and there is no reason why this should not be so. A properly trained nurse is as skilled a dresser, and as accurate at skin suture, as a doctor, and she commands, or can command, as much respect. If a nurse can be trusted to bring us into the world, she can be trusted to sew up our cuts. In many areas there is no difficulty in recruiting for part-time duties, though there may be scarcity in resident nurses. Such part time nurses would appreciate the stimulus of close association with a medical centre, they would be proud to be members of its team, and they would welcome the opportunity to cooperate in the improvement of the medical services.

The Doctors

I believe that if one could offer young doctors membership of an efficiently organised and clinically satisfying section of the hospital system, with the prospect of teaching and support from more senior colleagues, there would be less difficulty in recruiting them for casualty posts. At present the casualty officer is very often left in isolation, and this should be remedied.

General practitioners should be brought into the service, not as stopgaps for a weak part of the hospital system but with benefit to themselves and to the service. Many of the proposed outposts could be supervised by them, as part-time members of the staff, and arrangements could be made for them to attend at the central hospital as well, so that they can keep themselves up to date in this type of work.

SUMMARY

1. The work of casualty departments in non-teaching hospitals is reviewed.

2. Many difficulties arise from lack of continuity in medical care, from shortage of medical staff and from the several unrelated duties that fall upon the casualty department.

These difficulties have only partially been overcome by enlisting the help of local practitioners by appointing senior casualty officers, and by making consultants "responsible on paper" for the work of the department.

As a result there are serious shortcomings at present, both in the standard of medical care and in administrative efficiency.

3. A plea is made for the establishment of comprehensive accident services and a scheme for such a service is outlined.

It would consist essentially of a central casualty department—housed in a hospital with facilities to treat all major accident cases either as outpatients or as inpatients—and of a number of outposts in close contact with the centre.

If the responsibility for receiving medical and surgical inpatients, for distributing outpatients to special departments, and for dealing with major accidents, were removed, the chief reasons for continuous medical cover in the smaller casualty departments would cease to exist.

Minor accident cases could be treated at the outposts by trained nurses under regular but not continuous supervision by doctors from the centre.

An efficient system would ensure the prompt transfer of all major cases to the central casualty department.

The requirements of such a centre are discussed, and particular stress is laid on the need for maintaining a general surgical rather than a purely orthopædic character.

A closely knit accident service would allow its medical and nursing members to keep abreast of advances in treatment, and it would provide opportunities for

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[4] *Lancet* 1955, i, 298.

[5] *Ibid* 1954, i, 1225.

The spots were dried after each application, and the chromatograms developed for three hours by the ascending technique in the following solvent system *n* butanol acetic acid water (4 1 5 v/v)[9] The chromatograms were then air dried and drawn through a solution of Ehrlich's reagent,[10] and the blue colour allowed to develop for eighteen hours The stained areas were then cut out as rectangles, allowing a suitable margin and choosing a size suitable to all concentrations One stained area of similar dimensions was taken from a position adjacent to one of the standard spots, and used as a solvent blank Each of the areas was then extracted with 3 1 ml of 50% acetone in 10% HCl at 30°C for twenty four hours and kept in the dark The extracted colour appears to be quite stable, even if exposed to light for several days

The absorption curve for the blue colour was established on a Unicam SP 600 spectrophotometer using 10 mm fused-glass cells, and by choosing a wave length of 610 mμ, a calibration curve was established which obeyed Beer-Lambert's law over a range of 0–20 μg 5 H I A A with an optical density of 0 223 for 20 μg The law was also obeyed by non chromatographed standard spots over the same range

Clinical Research Laboratory
Department of Obstetrics and Gynaecology,
University of Edinburgh
F J SCANDRETT

BREAD

SIR,—I had hoped to see much correspondence concerning the proposed further reduction of the extraction-rate of wheat

Present day brown bread is not palatable I have heard complaints about this from many districts, and I myself have failed to procure any really good brown bread Even those firms which formerly provided delightful brown bread now produce a spongy sticky loaf Can it be due to a new method of baking?

Has the work of Sanderson Wells and of McCarrison so soon been forgotten? We of the older generation remember the beautiful nutty flavoured bread of our youth During the war I made delicious brown bread with yeast and stone-ground wholemeal flour, made from wheat grown on composted ground Several colleagues tell me that they have reverted to that practice, which produces a palatable loaf

London, W 1
AGNES SAVILL

SIR,—In the House of Lords debate on bread[11] the possible dangers of using chlorine dioxide as a flour improver were discussed, and the case against it failed However, no mention appears to have been made of its possible rôle in hypersensitive individuals Sheldon and Yorke[12] showed that flour treated with agene or chlorine dioxide was undoubtedly very harmful to their hypersensitive patient Their case resembles in many respects the syndrome of headache, insomnia, and depression following infections that I described recently[13] If further work shows that this syndrome is as common as I believe it is, and in some way is related to the "improving" of flour as I think it may be, then the present Government policy towards "improvers" should be reviewed In the meantime, I shall advise my patients to eat only untreated bread and flour if they wish to be on the safe side If such an attitude were to become a popular health fashion, "improvers" would soon disappear without any Government action

Hove Sussex
GUY DAYNES

SIR,—In the recent discussions on the composition of bread, insufficient attention seems to have been paid to certain aspects of the Food and Drugs Act

Section 1 makes it an offence for any person to abstract from food any substance so as to make it injurious to health The Act says nothing about the proportion of the population at risk, or about re balancing the diet to counteract the effect of processing—it is concerned with the right of "a person," in the singular, against another person Although most of the Act is concerned with the local authorities and their duties, this section can be used by any purchaser who complies with simple requirements on sampling No local authority, Ministry panel, or committee stands between the purchaser and the courts He must have the will, the money, and the evidence, but need wait upon nothing else The purchaser need not be the consumer

Hadley Wood
Barnet Hertfordshire
R MAXWELL SAVAGE

THYROTOXICOSIS

SIR,—It may help the busy clinician, in the "office" differential diagnosis of an anxiety state from slight thyrotoxicosis, to make the patient breathe deeply while the pulse is counted and note whether this produces a sinus arrhythmia

Sinus arrhythmia is mediated through vagal reflexes, which are suppressed by heightened sympathetic tone—at least at the level of cardiac innervation—in hyperthyroidism Though I have often noticed the appearance of sinus arrhythmia in patients as they become euthyroid after medical or surgical treatment of thyrotoxicosis, I have yet to meet a thyrotoxic patient who exhibits sinus arrhythmia I have met many anxious people who do

Italian Hospital Queen Square
London W C 1
E MONTUSCHI

PARTHENOGENESIS IN HUMAN BEINGS

SIR,—In a recent lecture by Dr Helen Spurway,[1] the possibility of parthenogenesis occurring in human beings was mooted Moreover, some of the criteria by which such a birth might be recognised were put forward This led the *Sunday Pictorial* to inquire whether there were any mothers who genuinely believed that they had given birth to a parthenogenetic child It was stated that any such child would be a girl (Spurway later pointed out[2] that the possibility of parthenogenetic male offspring could not be ruled out, but they would be expected to be perhaps a hundred times as rare as parthenogenetic females, and in addition they would be defective)

Nineteen claimants presented themselves At this stage we were approached by the Editor of the paper with the request that we subject these claims to scientific investigation

In planning these investigations, two possible mechanisms of parthenogenesis were considered

(1) *Budding from somatic cells of mother*—In this case mother and child would resemble each other as much as monozygotic twins because the genotypes would be identical, not only for their blood groups, but also for all genes including those giving rise to the tissue antigens responsible for skin-graft compatibility

(2) *Autofertilisation*—In this case mother and child would not necessarily be alike, as the child might not have all the genes possessed by the mother although she could not have any additional genes A skin graft from the child would be expected to take on the mother, but one from the mother would not necessarily take on the child

Whichever of these mechanisms would be operative, the child could have no antigens which the mother did not possess

Of the nineteen pairs of mothers and daughters who presented themselves, eleven pairs were eliminated at the preliminary interview They were under the impression that a hymen which remained intact after conception had occurred, was what was meant by a "virgin birth"

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[9] Erspamer V *J Physiol* 1955 127 118

[10] Jepson J B Smith I *Nature Lond* 1953, 172 1100

[11] See *Lancet* June 16 1956 p 956

[12] Sheldon G C Yorke A *Ibid* 1953 i 577

[13] *Ibid*, Feb 18 1956 p 296, see *Ibid* Feb 25 1956, p 303

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[1] See *Lancet* 1955 ii 987

[2] Spurway, H *New Statesman and Nation*, Nov 19, 1955 p 651

further improvements It would help to solve problems which are at present created by a shortage of casualty staff, and ensure the more economical and more efficient care of patients both with trivial and with serious injuries

I should like to thank many casualty officers and nursing sisters in my own and other hospitals who have given time (which could ill be spared) to show me their departments, to discuss these problems, and to produce most of the information

Medicine and the Law

The Limits of Friendship

ON July 5, 1948, the Liverpool Radium Institute, formerly a voluntary cancer hospital conducting research as part of its work, was vested in the Minister of Health under the National Health Service Act, 1946 In September, 1948, people who before the vesting day had been associated with raising funds locally and in the North-west for the hospital, met to form a new unincorporated association, called the Friends of Liverpool Radium Institute The agenda and minutes of the foundation meeting stated that the object of the new body would be "to enlist support for research and scientific and medical developments as well as additional comforts and amenities for patients" Appeals were made as before, a series of leaflets were distributed to the public, and at the date of these proceedings the funds of the charity amounted to *£110,000*, *but in 1953* a divergence arose on the committee between those who thought that the object of the trust should be limited to activities connected with the institute itself and those who thought it extended to the wider use of the funds for cancer research generally or at least in the North west area To test the matter the committee resolved to make a payment of £800 to the University of Liverpool for a cancer research fellowship The trustees of the fund then asked the Court for a ruling, and on Jan 25, 1956, the Vice Chancellor of the County Palatine Court of Lancaster made an order which in effect declared that the funds could be donated to the wider purposes The institute appealed

Lord EVERSHED, the Master of the Rolls, said that though the formation of the new body and the framing of its object and rules had been rather informal, the words stating the object in the "foundation documents," the agenda and minutes of the inaugural meeting, made it clear that in their context the objects were limited to those directly concerned with the institute The minutes showed that the new body was to be a reconstitution of friends of the old hospital who would do for the hospital what the hospital as a nationalised institution could no longer do itself, the 'comforts and amenities for patients" must be limited to patients of the institute, and the words 'research development" did not mean development throughout the United Kingdom or the world, but were limited by the title Friends of the Institute," which was a cancer hospital "Research and development" therefore meant "cancer research and development" logically including the institute

His Lordship did not agree with the Vice Chancellor who had held that leaflets issued to the public appealing for funds showed that the primary purpose of the association was to collect money for cancer research generally, for anyone who gave attention to the leaflets would see that they were an *invitation by this body* formed in September, 1948, whose object was that for which it had been founded

The Court declared that the object was "for the purposes of cancer research and medical and scientific developments at, by, or under the direction of the Institute" The appeal should be allowed, and accordingly the resolution to devote £800 to the University of Liverpool for a cancer research fellowship was outside the scope of the powers of the trustees or the committee His Lordship expressed the hope that this decision would end the local dispute, for these funds were subscribed to use and not to hold, but if the differences continued, the Attorney-General for the *Duchy would no doubt* apply for a scheme

Lord Justice JENKINS and Lord Justice HODSON agreed

Shields v The University of Liverpool and Others—*Court of Appeal* Lord Evershed *M R* Jenkins and Hodson *L JJ* June 1 1956 Sir Lynn Ungoed Thomas *Q C*, *and Joseph Turner* (Walker & Co, Liverpool) Lionel Edwards Q C and W Lyon Blea (Alsop Stevens & Co, Liverpool) William Geddes (Bateson & Co), *Attorney General for the Duchy of Lancaster* (F Wilmer Holland, Q C), and Eric Griffith (Garnett, Tarbet Lindsay and Ellsworth for the Solicitor to the Duchy)

M M HILL
Barrister at Law

Special Articles

SOME HEART-MURMUR SIMILES

GEOFFREY BOURNE
M D Lond, F R C P
PHYSICIAN, ST BARTHOLOMEW'S HOSPITAL, LONDON

THE quality of some cardiac murmurs is a key to their type and origin Lewis years ago said that recognition of the presystolic murmur of mitral stenosis was analogous to the instant realisation that the bark heard was that of one's own dog This statement implied two things the difficulty of accurate description, and the necessity for listening so frequently to typical mitral presystolic murmurs that auscultatory diagnosis became automatic

I have for some time, in teaching, used certain similes in the description of murmurs A belief that such similes have been helpful is the stimulus for these few poetico clinical remarks

Diastolic murmurs, in rheumatic heart disease, may be caused by aortic regurgitation or by mitral stenosis and when differentiation between these seems difficult the quality of the murmur is often of great diagnostic value The diastolic aortic murmur, heard best in most cases down the left sternal border and to the apex, has the high pitched rushing and persistent quality of water escaping under pressure from a hose, over a weir, or from a leaky lock gate The diastolic murmur of mitral stenosis—not the presystolic—has the low pitched rumbling quality of a wooden wheelbarrow trundled over cobble stones Either of these murmurs may be loud and easily heard or distant and elusive, but the weir may be distant too, and the wheelbarrow in the next garden but one The quality of the sound is unchanged in both types of sound whether remote or near, *bucolic* or pathological

A less rural simile is applicable to the forcible harsh brief, systolic murmurs caused by the powerful ventricular expulsion of blood through a rigid and narrowed valve Examples of this are found in aortic stenosis pulmonary stenosis, and coarctation of the aorta The sound here suggests the deliberate forceful and short blasts of steam given off by the *Scottish express* starting from rest at King's Cross The sound may be heard from the other end of the station, or from farther off still, and may vary correspondingly in volume, but the character of *both steam blast and murmur* is very similar When this same type of murmur is due to coarctation of the aorta it is naturally much fainter than in the *other* two conditions

The so called "*machinery*" murmur heard in many cases of patent ductus arteriosus again suggests the Scottish express, but this time the sound is that heard by

The blood-groups of the remaining eight pairs were then examined with the following results

Mrs Alpha	A1	Rhesus phenotype c̄dec̄de
Daughter	A1	,, ,, c̄dec̄de
Mrs Beta	A1	,, ,, CCDee
Daughter	O	,, ,, CCDee
Mrs Gamma	O	,, ,, CCDee
Daughter	O	,, ,, CCDee
Mrs Delta	A	,, ,, Cc̄Dee
Daughter	A	,, ,, c̄dec̄de
Mrs Epsilon	A2	Rhesus positive to anti D
Daughter	A2B	,, ,, to anti D
Mrs Zeta	O	Rhesus phenotype c̄c̄DE
Daughter	O	,, ,, Cc̄Dee
Mrs Eta	O	,, ,, CCDee
Daughter	O	,, ,, Cc̄DE
Mrs Theta	O	Rhesus positive to anti D
Daughter	A1	,, ,, to anti D

Further blood-group studies were carried out on four of these pairs, and the results are shown in the accompanying table

—	M	N	S	P	Lu	Le^a	Le^b	K	Fy^a
Mrs Alpha	+	+	−	+ +	−	−	−	−	−
Daughter	+	+	−	+ + +	−	−	−	−	−
Mrs Beta	+	−	+	+ + +	−	−	−	−	+
Daughter	+	−	+	+	−	−	+	−	+
Mrs Gamma	+	+	−	−	−	+	−	+	−
Daughter	+	+	−	+	+	+	−	+	−
Mrs Delta	+	−	+	+ + +	−	−	−	−	+
Daughter	+	−	+	+ + +	−	−	−	+	−

Although the Betas could not be excluded on the blood group results (since the A1 antigen is known to tend to suppress Le^b) they were nevertheless eliminated on the colour of their eyes, the mother having blue eyes, and the daughter having dark brown eyes[3] One pair, Mrs Alpha and daughter, were selected for special tests as follows

(a) *Tasting of phenyl thiocarbamide* —Both were "tasters" and could taste this substance at the same threshold value of 2 54 mg per litre

(b) *Test for secretors* —Both mother and daughter did not secrete group A substance in the saliva, and identical titres against A2 cells were obtained after incubating treated saliva from both against a known anti A antiserum

(c) *Direct filter paper serum electrophoresis* —Mother and daughter gave identical patterns

Following these tests, skin grafting between mother and child was performed The graft from daughter to mother was shed in approximately four weeks, and that from mother to daughter remained apparently healthy for six weeks before showing signs of devascularisation It was then completely wiped off by means of damp cotton wool

It will be of interest to workers in related fields that, despite the complete identity of blood groups, there was still graft incompatibility This raises the problem of how far we can now accept earlier assumptions as to the behaviour of grafts in parthenogenetic pairs

In the case of the Alphas the probability of so good an agreement between mother and daughter, if the daughter had a father, is less than 1 in 100 It was 0114 on the blood groups The data on taste brings it below 01

It is clear that a very much higher degree of probability must be attached to a claim made by a mother who could not possibly have any pre knowledge of the results of these special investigations In certain cases this absence of pre knowledge has been taken by the courts to constitute proof of the rightness of a claim

No further tests were undertaken because it was considered that such evidence as might be forthcoming would not materially affect the final estimate of probability

The significance of the skin grafting operations is obscure Thus, while Spurway would expect that at least the graft from the child to mother would take, Folley[4] would apparently not be satisfied that such a result would be conclusive

In such a case as this, rigorous proof is impossible, but it remains that all the evidence obtained from serological and special tests is consistent with what would be expected in a case of parthenogenesis The absence of the pre knowledge factor, although not capable of precise statistical evaluation, adds greatly to the probability of such a claim being well founded Thus, this mother's claim must not only be considered seriously, but it must also be admitted that we have been unable to disprove it

It is desirable that all who undertake investigations of this sort should publish the results, for in the long run the evidence can only be fully assessed if negative and inconclusive as well as positive results are available for criticism

My thanks are due to Prof J B S Haldane, F R S, for permission to quote his statistical evaluation of the serological data, to Mr David Wynn Williams for undertaking the skin grafting investigation, to Dr Sidney Shaw, of Charing Cross Hospital, for carrying out the pathological investigation, to all these for permission to quote their results and opinions, and to Dr A E Mourant, director of the Blood Group Reference Laboratory of the Medical Research Council, for samples of the rare blood group sera I should also like to thank Dr Bernard Camber, of Charing Cross Hospital clinical research department, for his invaluable help and constant advice during this investigation

An investigation of this kind was made possible only by the publicity given by a mass circulation journal

London, W 8 S BALFOUR LYNN

VITAMIN K

SIR,—I have been interested in the effects of the two commonly used vitamin K analogues—acetomenaphthone and 'Synkavit'—for the past ten years The following notes on my experience in their use may be relevant to the current discussion in your columns of the dangers of overdosage with these substances, following the report (May 19) by Dr Bound and Dr Telford

For a number of years, I have used the above vitamin K analogues extensively for their apparent antibiotic effect,[5][6] resorting only occasionally and in special circumstances to the use of the popular and better known antibiotics I have consistently found the optimum oral dose of either to be 10 mg daily or, when supported by vitamin E and "vitamin P" ('Rutin'), 5 mg only, larger doses than these appear to have the reverse effect in many cases of infection and other conditions

In view of this limited range of dosage and also an apparent conditioned deficiency of nicotinic acid often accompanying their use, possibly analogous to that induced by the sulphonamides, I have come to the conclusion that the vitamin K analogues, given orally, may have a bacteriostatic effect on intestinal commensals, possibly by interfering competitively with their metabolism of natural vitamin K and thus lowering the synthesis of nicotinic acid as well as of bacterial toxins Significantly, I have found the foods reputedly most abundant in natural vitamin K[7] to be the most powerful in counteracting the observed favourable effects of oral vitamin K analogues

For these reasons and for fear of interference with the vitamin K metabolism of the host, I have studiously avoided the parenteral use of the analogues Moreover, it is possible that vitamin K may be involved in metabolic processes other than that of synthesis of prothrombin

The ease with which liver metabolism of natural vitamin K might well be disrupted by excessive parenteral dosage with synthetic analogues is suggested by the small dose (0 5-1 0 mg) of menaphthone (the naphthoquinone nuclear moiety of natural vitamin K[8]) quoted by Professor Capon and his colleagues (June 16) as adequate for the correction of hypoprothrombinæmia a passenger sitting in the train as it coasts downhill and with brakes off through the tunnels towards King's Cross

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[3] Gates, R R *Hum Genetics* 1946 1, 88

[4] Folley S J *New Statesman and Nation* Nov 26 1955 p 70[illegible]

[5] Evans D M *Practitioner* 1946 157 391

[6] Evans D M *Ibid* 1948 160 305

[7] Bicknell F Prescott, F Vitamins in Medicine London, 1946 p 504

[8] *Ibid* p 798

The lub dub of the heart sounds corresponds to the coupled sounds made as the carriage rolls over the joints between successive pairs of rails, and the roar of the tunnel mimics the continuous murmur of the lesion, but the windows are shut and the sound is not too loud The roar seems to be intensified at each sound cycle, as the new pair of rails is reached, but this is an auditory fallacy In the heart lesion the systolic accentuation of the continuous murmur is real and not apparent The rhythm and the basic succession of sounds, in many cases of patent ductus recalls this picture, but here again the volume varies, in some cases being loud, in others moderate, and in yet others very distant

Another sound—a rarity—heard when an aortic valve cusp is severely ruptured, perforated, or perhaps even everted, as a result of syphilis or subacute bacterial endocarditis, is a diastolic croon This murmur closely mimics the coo of a near by and rather hoarse wood-pigeon which has been restricted to one rhythmic falling note instead of the usual three or four The murmur may be so loud as to be audible by the unassisted ear at a distance of several inches from the chest

A final simile, this time from the dance hall, is applicable to the friction rub of pericarditis

The drum beat of a dance-band playing a two step is a measurable fraction of time in advance of the shuffle of the dancers' feet upon a well chalked floor The double rub of the pericardial surfaces is similarly appreciably delayed behind the beat of the first and second heart sounds Sometimes the rhythm of the friction instead of being to and-fro is triple, and, to modify the metaphor, the dance becomes a waltz, not a two step, the third sound of the triplet being caused by auricular systole Once more it must be stressed that the quality and timing of the sounds are the important points The volume varies The shuffle of the dance may be quite loud, or if the ballroom door be shut may be heard only by close attention

CONSULTANTS' CONFERENCE

A CONFERENCE of over 300 consultants and specialists, organised by the central and regional consultants and specialists committees, was held in London on June 20 It was the first conference of its kind, and it was attended by members of the central committee and by representatives appointed by regional committees Mr A M A MOORE was in the chair After a private session in the morning, the conference heard an address by Sir RUSSELL BRAIN, chairman of the Joint Consultants Committee

THE DOCTOR'S POSITION TODAY

Sir Russell spoke of the present paradoxical situation in which the demand on hospital beds and outpatient departments was as great as ever, despite the striking medical progress of recent years which had enabled us to cure or control many diseases There was still more work for more doctors But, Sir Russell went on, the doctor could not get on with his job satisfactorily unless certain conditions were fulfilled He must be free to do his work without interference on matters for which he was personally responsible The task of the Government and all lay authorities was to create the conditions in which doctors could do their best work—" so far as possible, to give us the tools and leave us to get on with the job " Perhaps it was not generally realised, Sir Russell remarked, that this involved a new pattern of social organisation State services were usually hierarchical, and in medicine we had to combine a State organisation with individual freedom This was not an easy task, but Sir Russell believed we should succeed He thought there was a need to emphasise that the doctor occupied, and must continue to occupy, a unique place in the Health Service Medicine today was increasingly a matter of team work, but there must be a captain, and surely it was obvious that the more complex medicine became the more important it was that the responsibility for the patient should be in the hands of a single person—the consultant in hospital and the family doctor outside We were grateful, Sir Russell said, for the help which a growing army of technical experts gave to medicine, but it was the doctor in charge of the patient who must always decide how their services were to be used

When Parliament set up the National Health Service, it made itself responsible for the economic status of most doctors, and the present economic situation meant not only real hardship for those in the lower salary range but for all a deterioration in economic status relative to some other occupations, which, if we did nothing at all, might well be permanent This had not happened as the result of anyone's design but as the by-product of other people's actions and unchecked economic tendencies We faced here, Sir Russell declared, a challenge to the future of the profession But we must not let the difficulties of the times blind us to what had been achieved He believed that historians of the future would look back with astonishment at the establishment of the National Health Service between 1946 and 1956—a minor social revolution in which they would say, he hoped, that Britain, with characteristic wisdom, welcomed the new ways while conserving all that was best in the old

HOSPITAL MEDICAL STAFFING

At the afternoon session, Prof G I STRACHAN, chairman of the committee which reported last year on hospital medical staffing, told the conference that the plain fact was there were too many senior registrars Barring some such scheme as his committee had suggested, there were no alternatives but other employment or, to put it bluntly, unemployment The Joint Consultants Committee is now discussing this subject with the Ministry of Health, but, as the central committee's report puts it, " in view of the complexity of the problem early agreement is not to be expected "

Mr G WARING ROBINSON, chairman of the S H M O s' group executive committee, urged that there should be an expansion of the consultant establishment which should first absorb existing S H M O S Most S H M O s, he declared, were now doing consultant work A total of 10,000 consultants would not be too liberal an allowance for the population of this country, yet at present there were only about 6000 consultants and rather less than 3000 S H M O S Mr A STAVELEY GOUGH emphasised that Professor Strachan's committee had had no intention of worsening the present position of the S H M O , but he called this motion an irresponsible one It was nonsense to suppose that all S H M O S were doing consultant work When Mr Waring Robinson's motion was amended to read " absorb existing *suitable* S H M O S " it met with the conference's approval

After discussing other matters dealt with in the Strachan report, the conference agreed to the following motions

(1) " That this meeting is opposed to the introduction of any new career grade where the holders of such posts carry out work which should be carried out by consultants " (carried after a recount)

(2) " That in the event of the *reforming of the* structure of hospital medical staffing the grade immediately below consultant should be linked with the consultant grade and should be regarded as part of the senior medical staff "

It is surprising that the knowledge gained from study of the bacteriostatic action of sulphonamides, *p*-aminosalicylic acid, and other antibiotics has not been applied, long ere this, to the question of administration of vitamin-K analogues Incidentally, to swing the axe in another direction, this point is also relevant to Dr Schlesinger's allusion last week to over-prophylaxis against rickets The substance commonly used for this purpose is vitamin D_2 (calciferol), a synthetic analogue of natural vitamin D, and, in view of the above considerations relating to vitamin-K analogues, equally deserving of a more critical examination I described several years ago[6] some of its effects, short of idiopathic hypercalcæmia

Merioneth
North Wales

D Marcus Evans

PARAPLEGIA FOLLOWING SPINAL ANÆSTHESIA

Sir,—I hope that Sir Francis Walshe's verbal pyrotechnics do not blind your readers to the fact that the only opinion I have expressed on spinal analgesia (under the above heading) is that it is dangerous to store ampoules of the local anæsthetic solutions in antiseptics

Oxford

R Macintosh

Sir,—Sir Robert Macintosh (June 16) replies to my letter of June 9 by questioning the training, skill, and experience of the anæsthetists to whom I referred For his information I would point out that they were specialist or graded anæsthetists R A M C, I M S, or I A M C Ashley Daley in the *Medical History of the Second World War, Surgery* (p 221) details the training to which they were subjected

Sir Robert's reference to the unknown unaccounted dead of ill-administered general anæsthesia is apt. Death, however, is recognised as a hazard of general anæsthesia Patients about to be anæsthetised are conditioned to the possibility that the end-result may be death I doubt, however, whether any patient would opt for spinal anæsthesia if it was explained to him that the horror of paraplegia was a possible fate in store

I venture to say, Sir, that, in these days of efficient relaxants, there is no place in our armamentarium for spinal anæsthesia Before many years have passed this will come to be accepted by all surgeons and anæsthetists It is time the leaders of our profession abandoned the practice and teaching of this outmoded technique

London S W 3

L H Lerman

Sir,—This problem seems to have two parts

The first concerns the sequence of events which brings about disaster, and especially the possible rôle of phenol We know that phenol when placed intrathecally will generally have a destructive effect upon nerves but we also know that it may not always do so (Haxton, June 23, Steel, June 9) At the moment we can only say that, where phenol is involved, it may be, but is *not* necessarily, the cause

The second concerns the justification for the continued use of spinal anæsthesia

Dr Lerman proposes the all too easy solution of abandoning it With all respect I disagree with this We cannot be sure that there will never be a combination of circumstances which will make spinal anæsthesia the method of choice, and it would be unwise to restrict the doctor's freedom to choose what will best serve the interests of his patients We can no more solve this problem as Dr Lerman suggests than we can solve that of inhaled vomit in operative obstetrics by issuing an embargo upon general anæsthesia As Professor Macintosh has pointed out, the latter is by no means free from risks or complications nor is any form of anæsthesia thus blessed We should not forget that anæsthetic hazards, regional and general, are essentially secondary, since they spring from the primary hazard that the patient has already suffered—that of becoming a person requiring operative treatment Without running the gauntlet of these secondary hazards, it may be impossible to overcome the primary misadventure It is our duty on some occasions to undertake these remote risks in the hope that the patient may thereby benefit

I submit that spinal anæsthesia is, in some circumstances, a wholly justifiable procedure

London S W 15

G C Steel

Sir,—For some years I have been impressed by the possibility of neurological complications following spinal anæsthesia, and I now rarely employ the technique Nevertheless, in spite of the condemnation of several writers, I am convinced that the method will continue to be used because, in some circumstances, it can rationally be judged the safest, even though the occurrence of neurological complications be admitted If this be so, then the important matter is to try to make the procedure as safe as we can To this end no doubt research is needed, as has been suggested, but so is reasonable thinking

Sir Francis Walshe (June 23) regards the injection of "an anæsthetic substance" as the salient common factor in the ætiology of these complications and charges an unnamed fellow medical man with being "completely simple" in ignoring this proposition It seems to me that the problem is by no means so straightforward, and I would like information on the following questions

1 Can we assert with assurance that "neurological complications" never follow upon spinal puncture for diagnostic purposes, without the injection of anything? It seems to be difficult to be sure of this, for such a puncture is usually done in the presence of real or suspected disease of the nervous system and the rare occurrence of a complication could be confused with the developing effects of disease

2 If, however, we assume, as Mr Haxton (June 23) carefully puts it, that "the risk is inherent in the injection" then is the deleterious factor (*a*) some physical effect of the injection of fluid, (*b*) the anæsthetic solution, remembering that these are chemically various and may very often be injected without damage, or (*c*) an accidental *contaminating* substance of which an infective agent, a skin disinfectant, or the carbolic solution provide examples?

3 Is it likely that there is a single causative mechanism or are there probably several? In general, the diagnosis of the location and extent of the lesion of the nervous system *does not necessarily* determine its nature, much less its cause

The research, both experimental and by study of clinical experience, needed to solve this problem will be complicated and lengthy Meanwhile we must concentrate on the most likely dangers, and wisely to select these requires calm thinking and ordinary courtesy toward varying viewpoints

Department of Anæsthetics,
The Medical School
Newcastle upon Tyne 1

E A Pask.

EPHEDRINE POISONING

Sir,—In the following case of chronic ephedrine poisoning the patient had taken large doses of this drug for a long time

On Jan. 6 this year a 49-year-old man was admitted to a surgical ward with a diagnosis of Graves's disease He had had symptoms referred to the nose and throat since the age of 20, and of asthma since the age of 24 He had had pneumonia five times, and had twice been operated on for adenoids In 1947 he had been tested with various kinds of pollen and grain, and had been vaccinated without effect The patient had for some years been taking ephedrine and, in severe attacks adrenaline In the past five years his asthma had increased in severity He had spontaneously increased the dosage of ephedrine until, in the past two years, he had been taking 1–1 5 g of the drug daily This dosage had caused palpitations, which had become more pronounced He had become nervous and restless and his hands trembled He had attacks of hot flushing, especially at night, and he sweated profusely He had lost 8 kg in weight despite a large appetite He felt as if his eyes were being pressed out of their sockets, and had a constant sense of tightness round his throat

(3) 'That in any hospital restaffing the number of senior assistants should be strictly limited in order not to exploit the grade'

(4) 'That, in view of the disparity in consultant establishments in various hospitals, a minimal standard of consultant staffing in relation to the number of hospital beds should be recommended'

MEDICAL ADVISORY MACHINERY

Dr A **ROWLAND HILL**, deputy chairman of the central committee, said the committee had consistently pursued its policy of seeking to improve the medical advisory machinery at all levels in the service But the position was not satisfactory and he feared the domination of lay advice, hospitals, it seemed, had an attraction for those with a love of power One proposal aimed at improving matters was put before the conference the suggestion that there should be a medical advisory committee to each regional hospital board was approved The majority of members of this committee should be elected by the consultants and SHMOs in the region

MILEAGE ALLOWANCES

After considering the adequacy of the present ca mileage allowances, the central committee decided th there was not a sufficiently strong case for seeking an improvement in the rates But the conference di agreed and held that "in view of the increased rat of depreciation in car values and the need on ground of reliability for consultants *to maintain reasonabl* modern cars," the time had come for an increase in th mileage allowance

POWER OF THE CONFERENCE

The conference was asked to say that resolution passed by it and future consultants' conferences shoul be binding on the Central Consultants and Specialist Committee Mr T **HOLMES SELLORS**, chairman of th committee, said the original idea was that the conferenc should be advisory and not policy making, and he wa reluctant to see that principle changed at present Th conference voted in favour of remaining an adviser

CONSULTANT AND OTHER SPECIALIST STAFF IN HOSPITALS

THE Ministry of Health and the Department of Health for Scotland last year issued figures for consultant and other specialist staff in National Health Service hospitals up to the end of June, 1954[1] These Departments have now carried the figures forward a further year

In table I (not reproduced here) they show the age-distribution of consultants and senior hospital medical officers in each specialty and the number of paid session undertaken by those in each specialty for each year o birth

Table II shows the number of consultants in each o the specialties year by year from 1949 The corresponding figures *for SHMOs are not available*

Table III shows the number of senior registrars in each specialty on June 30, 1955, at the various levels o training

TABLE II—NUMBER OF CONSULTANTS IN EACH SPECIALTY AT VARIOUS DATES SINCE DEC 31, 1949 (GREAT BRITAIN)

Date	General medicine	Diseases of the chest	Mental health	Neurology	Pædiatrics	Radiology	Radiotherapy	Physical medicine	Pathology	Infectious diseases	Dermatology	Venereology	Ophthalmology	General surgery	Anæsthetics	Neurosurgery	Plastic surgery	Thoracic surgery	Orthopædic surgery	Ear, nose, and throat surgery	Obstetrics and gynæcology	Total
Dec 31 1949	755	216	419	53	166	337	85	49	495	50	127	89	331	927	498	37	30	49	252	312	424	5719
Dec 31, 1950	821	250	504	53	202	378	93	57	526	52	136	101	341	944	602	39	32	57	269	328	439	6213
Dec 31 1951	857	266	532	59	208	400	101	61	541	48	135	99	342	918	655	42	33	66	293	341	449	6176
Dec 31 1952	904	310	566	61	214	414	108	70	581	51	142	97	351	980	714	44	36	81	320	339	474	6862
Dec 31 1953	905	340	595	67	222	436	112	75	631	60	145	94	342	982	748	46	44	80	328	346	473	7079
Dec 31 1954	924	314	616	68	226	447	116	74	640	59	146	93	340	987	782	48	48	91	335	350	485	7225
June 30 1955	932	316	633	69	228	455	120	73	659	58	146	93	341	988	797	49	50	93	339	353	493	7315

Consultants practising in more than one specialty have been included under each This table includes honorary consultants

TABLE III—SENIOR REGISTRARS IN GREAT BRITAIN ON JUNE 30, 1955

Specialties	Training plan 1st yr	2nd yr	3rd yr	4th yr	Total	Others*	Grand total
General medicine	44	40	20	21	125	80	205
Diseases of the chest	16	17	13	3	49	11	60
Mental health	29	33	14	11	97	18	115
Neurology	6	1	4	2	13	1	14
Pædiatrics	7	8	5	5	25	14	39
Radiology	21	22	11	4	58	2	60
Radiotherapy	7	4	5		16	1	17
Physical medicine	4	3	2		9	2	11
Pathology	16	18	20	6	60	39	99
Infectious diseases	1		1		2	3	5
Dermatology	5	3	5	6	19	13	32
Venereology	1	1	1		3	5	8
Ophthalmology	22	13	6	11	52	7	59
General surgery	41	41	28	13	123	80	203
Anæsthetics	21	19	9	2	51	9	60
Neurosurgery	5	3	3	2	13	7	20
Plastic surgery	5	1	3	3	12	6	18
Thoracic surgery	6	7	7		20	0	20
Orthopædic surgery	19	11	12	7	49	18	67
Ear, nose, and throat surgery	12	10	10	3	35	15	50
Obstetrics and gynæcology	24	20	9	13	66	38	104
Totals	325	275	188	112	900	377	1277

* Includes those holding transitional posts and 91 honorary and 34 part time

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1 See *Lancet*, 1955, i, 448

When examined in the medical outpatient department on Jan 13, he was nervous and restless, his hands trembled, skin moist, warm, and shiny, eyes slightly protruding, pulse rate 100 per minute, blood pressure 180/100 mm Hg The right lobe of the thyroid gland was slightly enlarged There were clinical signs of emphysema Total serum-cholesterol 228 mg per 100 ml Measurement of radioactive iodine (^{131}I) uptake showed 45 9% uptake in twenty four hours Basal metabolic rate 129%

After treatment with ephedrine was stopped all signs of hyperthyroidism disappeared

No similar case has, to my knowledge, been recorded This case may be of some interest in elucidating the ætiology of Graves's disease

Rikshospitalet, Oslo, Norway ANTON E ODEGAARD

MEDICAL CARE OF THE AGED

SIR,—It was of interest to learn, from your review of June 2, that Dr Homburger's book was illustrated by that celebrated Hibernian artist Raoul "Duffy" We can now look forward to medical illustrations by his equally famous Celtic colleague MacTisse!

Department of Medicine,
State University of New York MILTON PLOTZ

THE HEBERDEN SOCIETY

SIR,—In your report (June 16) of the recent meeting of the Heberden Society we are quoted as having said that an antibody prepared by immunisation with synovial tissue reacted with reticulin, whereas an antibody to renal glomeruli did not In fact we reported that antibody to glomeruli had been found to react with two groups of tissue elements—basement membranes and material present in the media of vessels forming one group, and reticulin the second Antibody to synovial tissue, on the other hand, reacted only with the second

Stoke Mandeville Hospital
Aylesbury, Bucks

D G SCOTT
A G S HILL

INFANTILE PYLORIC STENOSIS

SIR,—In your very interesting editorial of May 19, the rôle of the ethnographic factor in the ætiology of this disease has been omitted

Wallgren[1] cited Eckhaus from Turkey, showing that hypertrophic pyloric stenosis was rare in that country Field[2] reported likewise about Malaya It is believed that this disease is rare among Negroes[3] In 1953 we made a survey in Israel[4] and found that the incidence of infantile pyloric stenosis in the Jewish population was much lower than that reported from Sweden[1] or England[5]

Further surveys of the incidence of this disease in the whole population of a given area, performed in different parts of the world and in areas with a population of mixed extraction, could help to clarify this challenging part of the question

Department of Pædiatrics,
University of Pittsburgh
Pennsylvania ZVI LARON

MEMORIAL TO SIR JAMES SPENCE

SIR,—The friends and colleagues of Professor Sir James Spence in the University of Durham and the Teaching Hospital of Newcastle upon Tyne are anxious to commemorate his name and perpetuate his memory in ways which he himself would have appreciated To this end it has been decided to appeal for funds for the following purposes

To award a medal for outstanding contributions to pædiatric knowledge—The award would be made from time to time by the British Pædiatric Association, usually, but not exclusively, to persons working in the United Kingdom or in any country of the Commonwealth who have made outstanding contributions to the advancement or clarification of pædiatric knowledge within the fields of clinical and social pædiatrics, clinical science, epidemiology, and family practice

To establish an annual prize in pædiatrics for the students of this medical school—This would consist of a sum of money and a volume of James Spence's collected writings to be awarded to the student submitting the best essay on any pædiatric subject which has excited his interest and led him to personal inquiry during his clinical training

To provide a sculptured portrait head to be cast in bronze—This would be placed eventually in the new Children's Hospital which we trust will be erected within the precincts of the Royal Victoria Infirmary

We feel that these proposals will prolong his influence in ways which will commend themselves to his many friends We would add that the university is being invited to rename the chair he held with such distinction "The James Spence Chair of Child Health"

Donations will be received by Dr A W Sanderson, House Governor and Secretary, the Royal Victoria Infirmary, Newcastle upon Tyne

URSULA RIDLEY
Chairman of the Babies Hospital House Committee
C I C BOSANQUET
Rector of King's College
R B GREEN
Dean of Medicine
R MUCKLE
Chairman of the Board of Governors
S D M COURT
Newcastle upon Tyne Professor of Child Health

The Editor of the *Medical Directory* writes "The accuracy of the directory depends on the return of the annual schedule, which has recently been posted to members of the medical profession Should the schedule have been mislaid I will gladly forward a duplicate upon request The full name and year of qualification of the doctor should be sent for identification" The directory is published by Messrs J & A Churchill, Ltd, 104, Gloucester Place, London, W 1

Parliament

QUESTION TIME

Thermonuclear Weapons

Mr ROY MASON asked the Secretary of State for Foreign Affairs whether, in view of the Medical Research Council's report on the hazards to man of nuclear and allied radiations and its findings regarding the danger of strontium 90, he would now seek international agreement with the major Powers concerned at least strictly to control all future atomic and thermonuclear tests

Mr A D DODDS PARKER replied, The Government are prepared to discuss methods of regulating and limiting test explosions which take account of their position and that of other Powers and will seek every opportunity to put this policy into effect The Government have already put forward proposals which will, no doubt, be considered by the Disarmament Commission next month

Mr KENNETH YOUNGER Would the Foreign Secretary agree that the white paper and the corresponding medical reports of a similar nature which have been published in the United States are of a rather alarming nature, indicating, in particular, that scientists have very little idea what the medical effects are likely to be? There is a great lack of precise knowledge Does not that indicate that some action rather more urgent than that contained in the Anglo French proposals is now required? Mr SELWYN LLOYD One must form an individual judgment as to these reports I should have thought that, on the whole, the reports were rather reassuring

Fall-out of Radioactive Particles

Mr MASON asked the Lord Privy Seal what research was being conducted into the possibilities of controlling radioactive fall out over the United Kingdom—Mr R A BUTLER

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1 Wallgren A Amer J Dis Child 1941, 62 751
2 Field C E Lancet 1951 ii 452
3 Nelson W E Mitchell-Nelson Textbook of Pediatrics Philadelphia 1950 p 816
4 Laron Z Acta pædiat Stockh 1955 44 40
5 Davison G Arch Dis Childh 1946 21 113

displayed laterally A pack is then inserted, gowns and gloves are changed, and the patient is placed in the Trendelenburg position Node dissection and dislocation of ureters is performed as usual, but division of the parametrium is then greatly facilitated since the operator can pass a finger from rectum to bladder beneath the specimen to be removed and thus display more clearly the uterine ligaments

No claim to originality is made for this procedure, which is the logical result of the solitary operator attempting to apply the excellent principles laid down by Mr Howkins It has worked well enough in 5 recent cases and, somewhat modified, in a similar number of patients with carcinoma of the uterine corpus It certainly allows a clear decision to be made at the beginning of the operation regarding the amount of vagina to be removed, it gives better access for the control of bleeding points deep in the pelvis, and it makes excision of the parametrial tissue safer and more radical for the less experienced surgeon

Birmingham W G MILLS

CLINICAL PATHOLOGY

SIR,—One may read with enthusiasm the report, printed in your issue of Dec 31, of the presidential address by Dr Allott to the Association of Clinical Pathologists The vision, balance, and broadmindedness shown in his description of the future laboratory service, particularly with regard to chemical pathology, would be near perfect but for the unfortunate fact that there is not the slightest real indication that administrative change is in the direction to which Dr Allott points

He speaks of necessary expansion Before any would-be trainee or aspiring registrar in chemical pathology binds his future to this specialty he should note that the trend during the past few years has been, not towards expansion, but towards contraction Since 1948 there have been fewer than 18 posts, including "turnover posts," in chemical pathology advertised, and of these, at least a third have either been changed subsequent to advertisement to non-medical biochemist, or, in a few cases, withdrawn altogether and no appointment made

The would-be aspirant in chemical pathology would therefore be well advised to note that, as things stand, his chances of a hospital post are small—indeed almost negligible Furthermore, human nature being what it is, he will seldom be more than S H M O—however good his work is admitted to be

S H M O (chemical pathology)

ECZEMA VACCINATUM

SIR,—Dr de Salles Gomes and his colleagues, describing in your issue of Dec 17 a case of eczema vaccinatum, mention that they have not been able to find any published report of such strict localisation as was found in this case—i e, limitation of the lesions to the eczematous patches My experience and that, I believe, of other workers in this country is that such localisation is not so much the exception as the rule Of ten cases reported by Sommerville, Dick, and myself[1] the eruption was limited to the eczematous areas in eight, while in the ninth it affected an area of acne and in the tenth an abrasion

The Brazilian workers favour the hæmatogenous spread of the vaccinial infection, with entry through the respiratory tract, whereas in the article quoted we give reasons in support of direct inoculation of the virus A point of significance is the frequent appearance of enlarged tender glands at the sites draining the infected area, such as is mentioned in the case-report from Brazil "a hard painful lymph-gland in each crural region" Surely this indicates infection travelling inwards and not outwards

Infectious Diseases Hospital,
Paisley WILLIAM NAPIER.

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[1] Sommerville, J, Napier W, Dick, A *Brit J. Derm* 1951, 63 203

INGUINAL HERNIORRHAPHY

SIR,—May I supplement Mr Doran's article of Dec 24?

As an alternative to suturing the conjoined tendon to the upper edge of Poupart's ligament, I reflect an elliptical flap of the anterior rectus sheath with its base on the outer edge of the rectus sheath, and suture the free turned-down edge of this to the upper edge of Poupart's ligament with interrupted nylon sutures I have used this method on adults for twenty years and have been satisfied with it An added refinement, which I have not tried, would be to suture the conjoined tendon to Poupart's ligament, leaving the ends of the interrupted nylon sutures long, reflect a flap of rectus as already described, and pass the long suture ends through the free edge of the turned-down flap

Longtown Cumberland ROBERT RUTHERFORD

MODIFIED QUECKENSTEDT TEST

SIR,—It has long been recognised that occlusion of the internal jugular vein by manual compression slows absorption of cerebrospinal fluid and so causes the pressure in the ventricles and spinal canal to rise Such manual occlusion is applied *in the Queckenstedt test* Raising the venous pressure by crying or coughing has the same effect

Compression of the internal jugular vein is commonly not done effectively by nurses, and it causes considerable discomfort to the conscious patient An efficacious alternative is to ask the patient to inspire and then forcibly expire against the closed glottis In all cases in which I have used this method at lumbar puncture, and compared the effect with that of compression of the internal jugular vein, the rise and fall in cerebrospinal-fluid pressure has been identical This method is not only more comfortable for the patient, but does not require the cooperation of an assistant

Nelson New Zealand C H BELTON

"BURNS" IN THE ABSENCE OF FIRE

SIR,—Last year Sir Harold Whittingham and his colleagues described the injuries in the Comet aircraft disasters[1] In the Elba Comet disaster, changes with the appearance of burns were found in the skin but there was no singeing or burning of the clothes or hair Several possible causes were discussed, and it was concluded that the most likely one was fire starting after the bodies had fallen into an area of sea covered by a kerosene film and that scalding occurred Fryer has since declared that the skin changes "were found to be due to" this cause[2] This touch of finality is perhaps not justified In the original article it was stated that this type of "burning" was not familiar to forensic pathologists It is worth recalling, therefore, the Senghenydd coal-mine explosion in South Wales in 1913, which was the worst disaster in British mining

Of 458 men working in the western side of the mine, 440 were killed and 18 were rescued and survived Some of the survivors showed areas of what appeared to be burning, but they came from a part of the mine where there had been no fire In the Elba Comet disaster, 14 of the 15 bodies showed skin damage simulating burns, and in 13 the injury was on the back or buttocks In the coal-mine disaster, of the 18 men rescued, skin lesions resembling burns were found in 9, and the buttocks likewise were the commonest sites, 5 were affected on the right side and 3 on the left, and in 1 the buttocks escaped In several of the men there were also lesions over bony prominences, such as the ischium The mine survivors were suffering from carbon-monoxide poisoning, and Davies[3] concluded that it was the main cause of the skin changes, and that local pressure from sitting or reclining was a contributory cause In the Comet cases some of the affected areas were traversed by bands of apparently undamaged skin, suggesting that some local condition of the skin surface influenced the development of the lesions

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[1] Armstrong J A, Fryer, D I, Stewart, W K Whittingham H E *Lancet* 1955, i 1135
[2] Fryer D I See *J clin Path* 1955 8 348.
[3] Davies I J *Brit med J* 1914, ii 57

Other instances of burn-like lesions with carbon-monoxide poisoning have been recorded, and it may well be that other forms of anoxia could have similar effects Perhaps some of the "burns" in babies with asphyxia are due to anoxia and not to hot-water bottles

In writing this letter I do not wish to suggest that the Comet "burns" were caused in the same way as those in the mine but rather to draw attention to mysterious "burns" in circumstances where it is known that there has been no fire

Institute of Pathology
Royal Infirmary, Cardiff

J GOUGH

Medicine and the Law

Death of Patient with Artificial Pneumothorax

A WOMAN, aged 46, with a long history of pulmonary tuberculosis died soon after an attempt to refill an artificial pneumothorax No air-space had been found with short refill needles A longer one was tried without success, and the operation was then abandoned Soon afterwards the patient became unconscious, and she died about an hour later Necropsy showed that the intrathoracic structures had been distorted by the long-continued pulmonary disease and that the aorta had been punctured by a needle A verdict of death by misadventure was recorded [1]

Osteopath Criticised at Inquest

The possibility of a verdict of manslaughter was mentioned at an inquest into the death of a young man following treatment by an osteopath [2]

The dead man was Frank Marsden, a 24 year old bank clerk, of Ossett, near Huddersfield Marsden suffered from curvature of the spine and pains in the feet which he attributed to rheumatism, and he consulted Mr Leonard Redfearn Carter, described as an osteopath and naturopath After examining him, Carter gave a hopeful report and prescribed dietary treatment Marsden had kept rigidly to these diets over a period of fifteen months to the day of his death

Dr W L Rose, who conducted a post mortem examination, said that the cause of death was malnutrition due to inadequate food intake "In my opinion," he said, "to keep this boy on these diets for a long period was absolutely criminal" Giving evidence, Carter said that he took up his present practice nearly thirty years ago after passing examinations He was firmly of the opinion that the diets he had prescribed would cure the rheumatism, but he admitted that they supplied only 1500 calories a day

The coroner told the jury that, if they thought that Carter had been so negligent as to cause death in a criminal way, that would be a question of manslaughter, but the evidence did not seem as strong as that The jury returned a verdict of death by misadventure

A Patient 30 Miles Away

Worcestershire Executive Council has decided that it was unreasonable for a Birmingham doctor to include in his list a patient living at Pershore,[3] on the ground that the doctor could not, from 30 miles away, fully comply with the terms of service It was stated on behalf of the doctor that he expected the patient to return to Birmingham, where he had formerly lived, and that he had in fact treated the patient in Pershore The chairman of the council is reported to have said "We can't prove the doctor could not render service," but the council decided to advise the patient to attend a local doctor

Obituary

WILLIAM GILCHRIST PATTERSON

M D Edin, F R C P, D P H

Dr Patterson, who died on Jan 5 at the age of 55, was the first senior administrative medical officer appointed under the National Health Service, and was often the spokesman for his colleagues. His previous work as medical officer of health for Surrey had given him unusual knowledge of the planning and management of hospitals, and in his eight years with the Newcastle Regional Hospital Board he won respect and admiration by an administrative ability based on intelligence, understanding, and courage

He was the second of three brilliant sons of George Patterson, who in his later years was headmaster of Whitburn School in West Lothian, and much of his youth was spent in the Lothians countryside At George Heriot's School in Edinburgh, where he was dux and played for the first fifteen, a distinguished future was forecast for him, and, after serving for a short time in a combatant regiment, he continued to win honours at Edinburgh University, including the Ettles scholarship for the best student of his year He qualified in 1924 with first-class honours, held various house-appointments in general hospitals and mental hospitals, and then had a period in general practice before concentrating upon a career in public health

Patterson's first public-health post was that of medical officer of health for the Chertsey combined district, and this was followed by appointment as M O H for the county borough of Barnsley From Barnsley he returned to Surrey as deputy to Dr James Ferguson This was the time when some of the major local authorities were going rapidly ahead with new hospital services, and Patterson, whose heart was in this from the first, took a big share in the Surrey schemes by which many hospitals were upgraded and a new one was built at St Helier The Surrey system differed from the neighbouring one in Middlesex in that it gave more scope for part time consultants though Patterson thought that hospitals gained by having a medical superintendent, who should be one of the senior clinicians, he held that, in appointing consultants, they should secure the best men they could get, and not limit the field by asking whole-time service Under Ferguson's inspiration the Surrey policy was one that made a particular effort to preserve, in the municipal hospital, part of the pattern of the voluntary hospital, and association between these two kinds of hospital was closer in Surrey than it generally was elsewhere

Owing to the war, and the additional strains it imposed on the county organisation, Ferguson's retirement was deferred and Patterson did not succeed him as M O H till 1946, when the county was already about to lose its hospitals altogether No doubt it was because of the closing of this chapter in hospital administration that he went in 1947 to Newcastle upon Tyne to help in opening another

Newcastle was certainly fortunate in his being available and wishing to move to the North The region was not an easy one to organise some of the municipal hospital services had been developed exceedingly well, but bed provision and standards in many areas were lagging a long way behind Long before the appointed day Patterson had made a detailed tour of all the hospitals in the board's area and had met most of the senior staffs Once he had made his surveys he could see things remarkably clearly, and as a result the board's programme for development was skilfully and fairly laid down in accordance with his advice If, through his strength and knowledge, he was a somewhat dominating personality, the relations between the board and its officers were as good as anywhere else in the country Moreover, he soon made a name and created a respect for himself in the region among members of all the various health services He was intensely interested alike in the general practitioners, in the consultants and in the medical nursing, and hospital staffs, and he never lost his sincere interest in the public-health service Nothing pleased him more than when he, a senior

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1 *Southend Standard* Dec 21 1955
2 *Yorkshire Post* Jan 2 1956
3 *Birmingham Post* Dec 29 1955

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When involved in these decisions ?—Miss HORNSBY SMITH Jan ' Thirty projects at a total estimated cost of £340,000

skin EDITH SUMMERSKILL In view of the fact that the minister showed sympathy with the Guillebaud report, the chief recommendation of which was to provide capital expenditure for hospitals, can the hon Lady say why this attitude is adopted at this stage ?—Miss HORNSBY SMITH The Guillebaud Committee repeatedly laid down the principle that, whilst many items might be desirable, they would have to conform to the general economic circumstances of the country, and that is the principle we are following here

Social-security Reciprocity with Sweden

Replying to a question, Mr J A BOYD CARPENTER, Minister of Pensions and National Insurance, said that an agreement had been reached with Sweden on reciprocity in social security Besides covering the benefits provided by the schemes of National Insurance, Industrial Injuries Insurance, and National Assistance in this country and the corresponding benefits in Sweden, the agreement would enable British families to draw Swedish family allowances as soon as they became civilly registered in Sweden Legislation at present before the House would enable this country to make a corresponding concession in our scheme of family allowances An important feature of this agreement was that British nationals who visited Sweden would be able to make full use of the Swedish health services Agreements with other European countries had enabled British nationals to use the health services of those countries if they were working there, but Sweden was the first country outside the Commonwealth to offer full reciprocity with the United Kingdom by making its health services available for all British nationals, including tourists The agreement required ratification, and the date of its operation would be announced later

Protection of Children

Replying to a question, Major GWILYM LLOYD GEORGE, Home Secretary, said that the terms of reference of the committee which he proposed to appoint[1] would enable it to study the problem of preventing or forestalling the suffering of children through neglect in their own homes and to make recommendations for any change in the law Meanwhile he was arranging, in consultation with the Ministers of Health and Education, for a survey of the existing arrangements for coordination, and as a first step local authorities would be asked for up to date particulars of the arrangements operating in each area

Mr G S DE FREITAS Is it not right that we should take account of the recent findings of the British Medical Association and the magistrates that family welfare work has been hindered by the number of people and organisations concerned ?—Major LLOYD GEORGE Coordination is the better way to deal with this Many local authorities have had coordinating committees, which have done good work I entirely agree that coordination is most important, and I hope that the work of local authorities will be coordinated

Replying to a further question, Major LLOYD GEORGE said that, as at present advised, he would not feel justified in proposing in the case of this offence the quite exceptional step of raising above six months the term of imprisonment which magistrates had power to impose From long experience he knew that the powers were sufficient but often were not utilised

Health Education and the Effects of Alcohol

Replying to questions, Mr DENNIS VOSPER, parliamentary secretary to the Ministry of Education, said that the Ministry s handbook of suggestions on health education designed for teachers and parents contained a passage on alcohol, and he had no doubt that most pupils received advice on this matter The Minister of Education agreed with the Royal Commission that Teachers should be left free to handle it as they thought best The handbook was about to be reissued, and this would contain a new passage referring to alcohol

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[1] See *Lancet* Feb 11 1956 p 280

Appointments

BROWN ELIZABETH L M B Edin senior registrar in chest medicine Norwich and East Norfolk areas

[illegible] A M M D Lond M R C P F F R D M R T consultant radiotherapist Middlesex and Mount Vernon Hospitals Northwood

WALL G A M B N Z F R C S registrar in plastic surgery, regional plastic surgery and burns unit West Norwich Hospital

WATTERS J H M D Camb M R C P part time consultant physician Hospital for Tropical Diseases London

Obituary

ALFRED HOPE GOSSE

T D , M A , M D Camb , F R C P

Dr Hope Gosse, consulting physician to St Mary s Hospital and to the Brompton Hospital, died on June 23 He was 73 years of age and was in his usual health until a fortnight before He had lately remarked on his good fortune in being granted a bonus of three years over the allotted span of three score years and ten

Alfred Hope Gosse received his early education in South Australia, but his later training was at Caius College Cambridge, where he took his B A in 1907 He spent the clinical years of his medical course at St Mary's Hospital, which he entered as a student in 1908 and from which he qualified in 1910 After filling the post of house-physician he became medical registrar in 1911 When war broke out in 1914 he spent a year or two as registrar to the 3rd London General Hospital (Territorial), but in 1916 he volunteered to go to Mesopotamia with 40 B G H He was soon appointed officer commanding the officers' hospital at Beit Naama, where he ran a very efficient unit He was thrice mentioned in despatches and was promoted brevet-major

On his return home in 1919 he was elected physician to outpatients at St Mary's Hospital He had done some work with Sir James Mackenzie, and from the start he decided to specialise in diseases of the heart and lungs This was furthered by his election to the staffs of the Brompton Hospital and of the King Edward VII Sanatorium, Midhurst He was elected F R C P in 1923 Between the two world wars Gosse carried on a large consulting practice, though he never let it interfere with the faithful discharge of his hospital duties He was a careful and accurate clinician, and a very acceptable teacher Large numbers of students used to attend his clinic at the Brompton Hospital, where his clear and dogmatic teaching was much appreciated During the late war he spent a large part of his time at St Mary s Hospital, doing a great amount of teaching and encouraging the students by his example and advice Though working in the Emergency Medical Service he refused to take any remuneration In 1917 he retired from active hospital work, but he continued in private practice till three years ago

In his prime Gosse was one of the leading cardiologists in this country His care and conscientiousness inspired confidence in his judgment, his kindness and sympathy gave the patients hope His long connection with the Medical Sickness Society gave him an unrivalled knowledge of the incidence of disease among doctors, and the few papers he wrote on that subject are of exceptional value

In 1933 he was made president of the Harveian Society but he took an even greater interest in the Medical Society of London, of which he was president in 1912 and had acted as honorary treasurer for the last 22 years A good mixer, he was an oarsman and tennis player in his youth and in later life he enjoyed watching a match at Lord's or spending a day at Goodwood

One of his friends has written " in a long life I have never met a more fair-minded, entirely upright man " Another, T C H , speaks of his clear purpose and integrity

' Few physicians in London can have had a greater number of true friends than he, and his complete honesty and sincerity made all who knew him trust him to the full He was always on the look out to help others and always careful to do so unobtrusively Kindness and hospitality were part of his very nature and there are many of his juniors who owe

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him much both in practical ways and for his interest in their welfare and his common sense advice and guidance Gosse had a direct and clear approach to problems His way of brushing aside non-essentials often seemed at first too simple and blunt, but in the end often proved to be the best He had despite his forthright opinions and firm way of making decisions a sensitive and even diffident nature, and he could be easily hurt and distressed if he thought he had been unfair to others or had been treated with discourtesy or dishonesty He was incapable of deception himself and hated it in others His modesty made him a man who did not like outward show and he could never tolerate hypocrisy. He was afraid of giving others trouble of any sort, but would go to any length to do things for them As a physician he had a clear idea of what he meant to achieve, and he did not allow too many doubts to weaken his conclusions, so that he was able to give his opinion with a clearness and force that was greatly appreciated both by patients and doctors His teaching was direct and his handling of patients set an example of gentleness and humour which his students remember with gratitude"

In the words of Sir Zachary Cope, to whom we are indebted for much of this memoir, he was "a most faithful absolutely reliable friend, a man who scarcely ever spoke ill of anyone, a man to whom one could trust one's last penny and one's reputation There are many who will feel that some virtue has gone out of them, now that Gosse has departed."

IAN MURRAY BURDON

M.B Glasg, F.R C S.E

Mr Ian Burdon, visiting surgeon to the Victoria Infirmary, Glasgow, died in hospital on June 16 He was in his 56th year.

He received his early education at the Glasgow High School and graduated in medicine at Glasgow University in 1923 After house-appointments at the Victoria and Western Infirmaries he returned in 1926 to the Victoria Infirmary, where he remained, becoming surgeon in charge of wards, in 1947

A colleague writes

During his earlier years Ian Burdon worked with Mr Robert Carslaw, the late Mr Robert Tennent, and the late Mr Norman Davidson, all accomplished general surgeons, and during his thirty years' association with the Victoria Infirmary he similarly kept his surgical interests wide, though the field of biliary surgery claimed his special attention and study Before the inauguration of the health service, he did a great deal of emergency surgery in the smaller hospitals in the West of Scotland such as Dunoon and Rothesay, while in addition he was surgeon for a number of years to the Glasgow Homœopathic Hospital

His surgery was characterised by great facility, for he had the artistic temperament and was a superb craftsman. He was not so much an innovator as an improver and refiner of existing methods, and his results could hardly be bettered His opinion was widely sought throughout Glasgow and the West of Scotland He published little, but he turned his artistic talent to account in his *Atlas of Anatomy for Nurses* published in the 30s He was also one of the first surgeons in Scotland to realise the importance of the cine camera in recording operative procedures and teaching students Many of his films were demonstrated before the Southern Medical Society, of which for a time he was president, and they will be long remembered

He was a modest, kindly man with a quiet, charming manner and a great capacity for friendship His death leaves a wide gap in the surgical ranks in Glasgow, where he was honoured and loved

Mr Burdon leaves a widow and two children.

Births, Marriages, and Deaths

BIRTHS

JAGO—On June 21 at Charing Cross Hospital London to Dr Margaret Jago wife of Douglas Hewitt a second son—Adrian

MARRIAGES

HOPKINS—WOOLNOUGH—On June 16 at St Luke's Church Duston Northampton Denis Hopkins M.B to Hilda Woolnough of Woodlees Weedon Road Northampton.

Notes and News

THE M.R C

THE Medical Research Council, like a well rooted tree, has ramified prodigiously since, in 1920, it was planted in the plot occupied since 1913 by the Medical Research Committee The luxuriant foliage on most of its branches conceals from most eyes the supple wood beneath Those who would like to see more of this may turn to a pamphlet [1] just published, which shows the structure in simple outline

REMUNERATION OF SENIOR HOSPITAL MEDICAL OFFICERS

COMMITTEE B of the Medical Whitley Council has agreed that, in accordance with an Industrial Court award,[2] the remuneration of S H M O S shall be increased by £75 a year as from April 26 this year The new scales are as follows

Main scale—£1575 × £50 to £2025
Scale for those appointed at age 30 or less—£1475 × £50 to £2025
Scale for those appointed at age 31—£1525 × £50 to £2025

ST THOMAS'S HOSPITAL THROUGH EIGHT CENTURIES

THE history of St Thomas's Hospital, London, is illustrated by an internal exhibition of archives in the grand committee room of the hospital which continues until 1 P.M this Saturday The records of the hospital begin in the 13th century and they include early maps and deeds, accounts minute-books, and photographs On show are autographed letters from Queen Elizabeth, Oliver Cromwell, and Charles II that from Oliver Cromwell recommends, in curious grammar, the appointment of "a man thoroughly tried in ye service of ye state, & found able & faithfull in his profession," but despite this testimonial the candidate was unsuccessful A salary book, 1657–77, contains the signature of Thomas Hollier, who operated on Samuel Pepys. The Treasurer's weekly accounts in 1704 include the payment of 3*s* 4*d* to Mr Ferne, one of the surgeons, for taking off a leg, and "Paid the Helper in the Kitchen as usual 3*s* 4*d* There are the orders for "cubbs" drawn up on Feb 12, 1702 (Old Style) The more official title was "covenanted servants," but students were first mentioned as "cubbs" towards the end of the 17th century (in 1699 the rule was made that they were not to keep their hats on in the wards), and the regulations of 1702 mark the formal beginning of the medical school Intending "cubbs" had to produce a testimonial that they had served a surgeon for five years and that they were of sober life and conversation One cannot imagine the side whiskered earnest young men receiving their awards in a print of an early 19th-century prize-giving, being other than sober in life and conversation But among the fine pewter tankards on display are those of the students' hall.

The clerk's diary records the first patient to die in the hospital "from the effects of chloroform"—on Oct 10, 1849 A letter from Florence Nightingale in 1875 expresses strong disapproval of a proposal that ward rounds should be made in the afternoon In pride of place, of course, is the Letters Patent of Edward VI in 1551, but most fascinating are the lesser records such as the survey of farms owned by St Thomas's in 1774, which describes one tenant as "a Sot" The exhibition has been arranged by the Archivist

NEOHIPPOCRATIC MEDICINE

THE third International Congress of Neohippocratic Medicine was held on May 20–23 at Montecatini and Florence, under the presidency of Prof C Frugoni (Rome) The object of this congress, as of the previous ones, was to study the combination of modern technical medical advances with the perennial Hippocratic principles of consideration of the whole man as a person in his internal dynamism and his special environment

The first day was devoted to a review of the constitutional factors of predisposition to cardiovascular disease, tuberculosis, and cancer

The second day was devoted to the treatment of disease by methods acting on the "whole man"—the old "Airs, waters and places" of Hippocrates Papers were read on the systemic, constitutional action of mineral waters, various physical procedures, and the psychological organisation of health resorts

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[1] Medical Research Council Constitution and Functions Published by the council 38 Old Queen Street London S W 1 Pp 16

[2] See *Lancet* May 12, 1956 p 699

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The third day was devoted to the personality, duties, and social rôle of the physician The congress expressed the wish for a more general application of the Hippocratic oath at graduation and for the creation of chairs of history and philosophy of medicine, with the object of helping the synthesis of medicine and the humanistic outlook in the practice of the physician

More than four hundred physicians attended the congress British participants were Sir Horace Evans, who read a paper on the constitutional predisposition to cardiovascular disease, and Prof A P Cawadias, vice president of the congress, who reported on the developments in the science of constitutional types—biotypology

At the end of the congress a permanent International Committee of Neohippocratic Medicine was instituted Much of the success of the congress was due to the energy of the president and to the activities of the secretaries, Prof J Delore (Lyons) and Prof D Scalabrino (Montecatini)

University of Cambridge

At a congregation on June 7 the following degrees were conferred

M D—*A C Elithorn Rodney Finlayson, W D Foster *I W de D Gregory, H E Lockhart Mummery, P K Robinson C E D Taylor

M B—M H Heycock, D L Miller, Helen J Pegg

* By proxy

University of London

Dr K R Hill, professor of pathology in the University College of the West Indies, has been appointed to the chair of pathology tenable at the Royal Free Hospital School of Medicine

Professor Hill graduated B SC with first-class honours in the University of London in 1932, and qualified M R C S from Westminster Hospital in 1937 He subsequently graduated M B in 1943 and M D (pathology) in 1946 Throughout the 1939–45 war he served in the R A M C as a specialist pathologist with the rank of major He held a Rockefeller fellowship in 1947–48 He was appointed assistant pathologist to the Royal Victoria Infirmary, Newcastle upon Tyne and lecturer in pathology at King s College University of Durham Before going to the West Indies he was on the staff of the pathology department of Johns Hopkins Hospital Baltimore He is a member of the W H O Expert Consultants Panel on Treponematoses His publications include accounts of work on yaws and on liver disease in Jamaican children

The title of professor of human metabolism has been conferred on Dr C E Dent *in respect of his post at University College Hospital Medical School*

Dr Dent graduated B SC in 1931 and PH D in 1933 in the University of London He engaged in research work in organic chemistry at the Royal College of Science from 1931 to 1934 and with Imperial Chemical Industries from 1935 to 1937 In 1939–42 he undertook secret chemical war work and in 1942 he was consultant in chemistry to the War Office He qualified M B from University College Hospital in 1944, gaining the M R C P in the same year After qualifying he was house physician to Sir Thomas Lewis, and for the next two years he was assistant on the medical unit at University College Hospital Medical School In 1946–47 he held a Rockefeller travelling fellowship in the U S A Returning to his appointment in London he was elected Foulerton research fellow of the Royal Society, and in 1949 he graduated M D In 1951 he took up his present post of reader in medicine at University College Hospital Medical School He was elected F R C P in 1951 Dr Dent's many investigations have been concerned predominantly with the metabolism of calcium and of amino acids

University of Bristol

At the final examination for the degrees of M B CH B the following were successful

Pauline F Haswell D H Wright (with second class honours) Miriam M Alderwick, Babatunde Oladipo Amure Elizabeth M F Andrews J H Andrews J C Bailey F P Beck W F Benney B T A Clarke, Ruth E A Coles H F Cramp J D Davison K M Evans Irene F Gibbs P M Gill C L G Hale A F Hickson A L Horton Rachel M Hulbert A T Lloyd, Sheila M McClements June M McLeod Terence Morley R W Morris Anezionwu Nwankwo Okoro, K M Parry Weekakkodige Fredrick Perera C K Protheroe M J Rose W J Stephen S J Strong J P Telling M J Watson A H F Williams Mary B Wilson C H Wood

University of Liverpool

As a tribute to Sir Henry Cohen professor of medicine in the university, the family of the late Sir Montague Burton has given £50,000 to the appeal for £500,000 which the university launched on June 27

Ministry of Health Appointment

Dame Enid Russell Smith has been appointed deputy secretary to the Ministry of Health in succession to Sir Frederick Armer, who is to retire next November

General Medical Council

The next session of the Medical Disciplinary Committee is to begin on Tuesday, July 17 at 10 30 A M

Institute of Child Health

The Alex Simpson Smith lecture for 1956 will be given at the Hospital for Sick Children on Tuesday, July 17, at 5 P M by Dr William T Mustard, of Toronto, whose subject will be the Surgical Correction of Total Anomalous Pulmonary Venous Drainage Tickets may be had from the dean, Institute of Child Health, Hospital for Sick Children, Great Ormond Street, London, W C 1

More Mental Nurses

Mr R H Turton, the Minister of Health, speaking on June 23 to the Association of Hospital Matrons, said that in the first quarter of this year there was an *increase of 270 nurses* in the mental hospitals and 175 in the mental deficiency hospitals The most welcome feature of all in his view, said the Minister, was the increase in student nurses In mental hospitals there were 143 (10%) more male student nurses, and 109 (5%) more female student nurses In mental deficiency hospitals, *the increase in male student nurses* was 16 (6%) and of female student nurses 36 (8%) These increases had occurred before the recent salary settlement

Royal Society of Tropical Medicine and Hygiene

At this society's annual meeting on June 21, Prof R M *Gordon, the president, presented the Manson medal to the* widow of the late Brigadier J A Sinton, F R S, awarded in recognition of his outstanding work on malaria and other tropical diseases while serving in the Indian Medical Service Sir Leonard Rogers, F R S, received the Laveran gold medal of the Societé de Pathologie Exotique for his pioneer work—*also* while in the Indian Medical Service—on such fundamental studies as the treatment of amoebiasis with emetine, the treatment of leprosy with chaulmoogra derivatives, and the epidemiology and control of leishmaniasis

Mental Deficiency Laws and Administration

At a conference to be held by the National Council for Civil Liberties on Saturday, June 30, a report will be given on the council's six years' work on legal aspects of the care of mental defectives Reference will be made to cases of lengthy detention brought to an end by the council s intervention, and proposals will be put forward "to deal with the position of a large number of people whose detentions would appear to be illegal, in consequence of the High Court decision in the Kathleen Rutty case" The sessions will take place at the Beaver Hall, Garlick Hill, London, E C 4 at 2 30 P M and 6 P M, and the opening paper (What is Mental Deficiency ?) will be given by Dr Bruce Cardew

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Diary of the Week

JULY 1 TO 7

Monday, 2nd

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road W 12
4 P M Dr T E Lowe (Melbourne) Management of Congestive Cardiac Failure

Tuesday, 3rd

UNIVERSITY COLLEGE Gower Street, W C 1
5 15 P M Dr D A Denton (Melbourne) Regulation of Sodium Ion Content in Sheep with Parotid Fistulæ

Wednesday, 4th

ROYAL COLLEGE OF SURGEONS Lincoln s Inn Fields, W C 2
5 P M Mr F G Slesinger Sir William Arbuthnot Lane—A Tribute (Arbuthnot Lane lecture)
POSTGRADUATE MEDICAL SCHOOL
2 P M Dr R W Riddell Mycology

Thursday, 5th

ROYAL COLLEGE OF PHYSICIANS OF LONDON Pall Mall East S W 1
5 P M Dr Ivan de Burgh Daly F R S Some Intrinsic Mechanisms of the Lung (Bertram Louis Abrahams lecture)
ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 30 P M Prof W V Mayneord D SC Recent Scientific Development in Radiotherapy
UNIVERSITY OF LONDON
5 P M (University College Hospital Medical School University Street W C 1) Dr Naguib Mahfouz (Cairo) Urinary Fistula in Women
INSTITUTE OF NEUROLOGY National Hospital, Queen Square W C 1
5 P M Dr J D Spillane Developmental Abnormalities in the Region of the Foramen Magnum

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administrative medical officer of a regional hospital board, was elected president of the Northern branch of the Society of Medical Officers of Health in 1953

In national and international spheres and on central advisory committees Patterson s advice was often sought On any committee he was a tower of strength he had always read the papers and formed his own view, which he put forward clearly and persuasively, often ending with a charming smile and a diffident question as to whether he had expressed accurately his colleagues' views His contributions none the less could be outspoken, and he had no hesitation in joining the unpopular side when he thought it the right one To the North-East region—which felt itself in some danger of being overlooked—it was a great satisfaction that its chief hospital officer should enter the lists so strongly for a reasonable allocation of central funds, and not without success, as was his wont

Though to some he may have appeared a somewhat lonely figure, and others may have thought that his intense concentration on the matter in hand left little time at work for casual or "off record" conversation, Patterson had a "second personality ' reserved for his home and family life He was above all a family man, and those who were privileged to see him with his wife and children in their home saw happiness and a family unit at its best He and his wife were friends from childhood, and she has five children—a married daughter, and two older and two younger sons

He died suddenly when attending a hospital meeting in Sunderland Some of his friends had noticed that he looked tired during the last few months, but there had been no diminution in the vigour of his mind, nor had he ceased to throw himself heart and soul into any task which confronted him The personal notes which follow are taken from tributes received from associates

* * *

Dr Patterson had a strong and independent mind and was fearless in deviating from the "official" line, whether of the Ministry or of his own group, if he thought differently His approach was logical and practical, he was a shrewd judge of human beings, and he sought means that he knew from experience worked He made his contributions in debate in a quiet voice, with a smile upon his face and with a roving eye which twinkled as he saw approving glances on the other side of the table On the rare occasions on which I have heard him on the platform he held his audience by logic, fairness of mind, and force of personality

Since 1948 I have had a number of official "field days" with him in the territories of his board

He would prepare a programme of visits and of topics to discuss The visits were to sites for new hospitals, say for West Cumberland at Whitehaven or for the new town at Peterlee, or to existing hospitals where extensions were pending or where new buildings deserved study as at Carlisle or Durham or Shotley Bridge However well prepared he was, and confident that his proposal was sound, he valued the criticism or opinion of any knowledgeable person, and he prudently sought by such means as this to gain informally the official viewpoint so as to avoid delay or foundering later of the schemes he was promoting for his board The hospitals and sites were always inspected but there was never enough time for the discussion of the many subjects of policy and practice within the National Health Service on which he offered reflections and sought those of others

These days with Patterson were always a delight His interest in all aspects of his "charge" was deep and lively, his judgments on people when not generous were just and restrained, he had an optimistic and forward-looking mind, his courtesy was unexceptionable, his humour of the Scottish sort, quiet and pawky We should be thankful for the example of such a man

C T M

I had the privilege of seeing Dr. Patterson at close quarters over a sixteen-day period when we were both among the delegates sent by the United Kingdom Government to a course organised for *fonctionnaires* of the Brussels Treaty (now Western European Union) governments in France last summer

We were both members of a group that studied the organisation of hospital services we visited a number of French hospitals and enjoyed much generous French hospitality I do not think that Dr Patterson was altogether in his element under these conditions—I suspect that his good Scottish soul would have preferred something a little more austere in the eating and drinking for instance, and none of us British were at home with the language—but he rose above these difficulties splendidly, and I think the whole of our group conceived a very real affection, as well as admiration, for him before the course was over. I specially admired his dogged refusal to allow himself to be swept away by the rapid pace of the French *exposés* to which we listened, and by his frequent interventions, with forefinger uplifted and that little smile at the corner of the mouth, to clarify, in slow, simple French with a pronounced Scottish accent, some point which he felt had not been properly covered, or to explain how much better these things were ordered in the Newcastle region At the very outset of the course he made his mark, at the session when each of us was called on to introduce himself—in French "Mon nom est Patterson" he announced, "je suis écossais, mais je travaille depuis vingt ans (or was it more ?) dans le pays de mes ennemis" I should like to feel, as I am sure would the rest of the *stagiaires*, that we could all, national *ennemis* of the past and international colleagues of the present, claim his personal friendship

A R. W B

His appointment was the first act of the Newcastle Regional Hospital Board, and a most fortunate decision it proved A Scot educated in Scotland, an administrator whose professional life had been lived in the South of England, he came as a stranger to the North-East But so thorough was his method and so quick his apprehension that in a very short time he was so much at home with the region and the people in it that it was difficult to think of him as belonging anywhere else He was admirably fitted, both by temperament and training, for the responsibilities of his office He was never timid either in what he did or what he advised On the contrary, he was bold and decisive and the event has proved his wisdom Human, conscientious, and highly intelligent as he was Patterson addressed himself to his duty with something of a fervour of dedication with the result that, under his impulse, a great deal of reorganisation and expansion, particularly in the consultant services, was very rapidly achieved for a relatively small expenditure But he was always insistent that only heavy capital expenditure could bring real relief and improvement to those parts of the hospital service most in need of them, and he chafed sorely, as others have done under the severe financial restraints which prevented them Happily, he served long enough to see the fruits of his early work and the commencement of some at least of the larger projects he had proposed

Although he had made the deliberate choice, at an early stage, of a career in administration rather than in clinical medicine, the choice had clearly not been an easy one As his academic record and professional distinction showed, he had high intellectual gifts, and to visit a hospital with him was to know that he had a real compassion for the sick But he had chosen a remoter field and was resolved to make it beneficent That he succeeded there could be no doubt The inspiration of his work came from a compassionate heart and his skill in execution from an acute and cultivated mind tempered by long experience One of his gifts was a remarkable memory stored both with the kind of information for which other people have to refer to their files, but which he could mobilise at a moment's notice and with much else besides In conversation with him it soon became clear that, at one time or another he had read widely in general literature and remembered what he had read In his professional field there was none better at presenting a case with clear and cogent reasoning supported by all the relevant facts, which he had immediately at command This is not to say that he had no prejudices he would have been more than human had that been so. But, once convinced, he discarded them in a disarming way Although he knew how to delegate duties without loosing grip or authority over the field of action as a whole, he could never for long relax the pressure on himself This was the forfeit he paid for enthusiasm. To his abilities experience and knowledge he added great charm of manner These qualities of mind and heart made him not only a fine administrator, the admirable chief officer that he was, but the well-loved friend of those whose fortune it was to work with and learn from him and who have now to mourn his untimely death

E F C

Cicero in *The Offices*, referring to public officials, wrote

> “But he who takes on him a public trust, should see that he himself be qualified for the management of it, in considering which there is a double extreme to be carefully avoided, that he neither despair through mean timidity, nor yet be over confident through eagerness of desire, and lastly, in whatever he sets about, let all things be diligently and carefully put in order, before he goes on to the execution of it”

This reference to characteristics held to be desirable in a public official could not be illustrated by a finer example than the personality and work of William Patterson All things were diligently and carefully put in order before he went on to the execution of his duty As a result, his work will live for many years to come

W S W

ETHELBERT REST FLINT

M B Leeds, F R C S

Mr E R Flint, emeritus professor of surgery in the University of Leeds, died at Leeds on Jan 5, after a long illness

Born in 1880 at Scarborough, and educated there, he received his medical training in the Leeds School of Medicine and qualified in 1905 After holding a house-appointment at the Norfolk and Norwich Hospital he returned to Leeds in 1907 as house-surgeon at the General Infirmary He spent the next four years in general practice, an experience which he always regarded as of the greatest value In 1911 he was appointed resident casualty officer at the General Infirmary and in 1912 resident surgical officer The same year he took the F R C S On the outbreak of the 1914-18 war he was commissioned in the R A M C, but in fact all his service was done in the Infirmary Owing to the absence of the honorary surgeons on war service he shouldered a tremendous burden of work and in two years he did 6140 operations on civilians and wounded soldiers M J S recalls that “for weeks on end Flint was never out of the hospital (except that he slept out—on the roof of the Infirmary porch, where he had a protective awning erected) or out of surgical attire by day All or nearly all the house-surgeons of the war period were undergraduates, and the weight of responsibility which he bore would have crushed a lesser man To him, it was but a stimulant to increased effort”

Photo Press (Leeds)

The war over, he presently resigned his joint office of surgical registrar and tutor to become private assistant to Sir Berkeley Moynihan He held this post until 1926, but meanwhile, in 1922, he was elected an honorary assistant surgeon to the Infirmary, and, in 1933, full surgeon He was also consulting surgeon to the Marguerite Hepton Orthopædic Hospital, Thorp Arch, to Batley and District General Hospital, to Malton Cottage Hospital, and to the General Hospital, Halifax In 1940, after he had joined the consulting staff of the General Infirmary, he again undertook important surgical duties at the Clayton Hospital and Pinderfields Hospital, Wakefield He was also a member of the Leeds and West Riding Medico-Chirurgical Society for over forty years, an original fellow of the Association of Surgeons of Great Britain and Ireland, a fellow of the Royal Society of Medicine, and a member of the Moynihan Chirurgical Club

Flint was thus fully and usefully occupied in the clinical field, but he also did excellent work on the academic side In 1922 he had been appointed clinical lecturer in surgery in the University of Leeds and for some years he was an honorary demonstrator in physiology He also from time to time carried out research in other departments, including investigations into the ætiology of biliary-tract infections and a study of liver function in cholecystitis and cholelithiasis He investigated the abnormalities of the right hepatic, cystic, and gastro-duodenal arteries and of the bile ducts, and he published several papers with colleagues in the departments of pathology and bacteriology He was Arris and Gale lecturer in the Royal College of Surgeons in 1923 and again in 1930, and a Hunterian professor in 1933 In 1934 he was appointed to the chair of clinical surgery at Leeds, which he gave up on his appointment to the chair of surgery two years later In 1940 he was made emeritus professor

Outside his professional work Flint was a distinguished athlete, and represented his county and the North of England at hockey for many years As a good golfer he also enjoyed this game He won the Moynihan golf cup in 1914 and again in 1919, and continued to play until he was over 70

Of his work in the operating-theatre G A writes “He will always be remembered as a general surgeon of outstanding brilliance and dexterity Although most actively engaged in abdominal surgery, there was no field in which he was not proficient, possessing quite remarkable talent and instinct, always calm and unruffled, he could make up his mind quickly and act promptly He possessed a tremendous capacity for work, as evidenced by his lengthy operating-lists which he carried out so expeditiously and without any apparent fuss He was very modest, quiet, and reserved, but when he did engage in discussion he contributed something valuable and worth listening to As a colleague no-one could have been more loyal His services were continuously at the disposal of his colleagues and many have cause to be thankful to him.”

M O also writes of Flint's remarkable dexterity which “seemed to make him almost independent of an assistant, and sometimes of an anæsthetist when he used spinal anæsthesia During the 1914–18 war he had acquired an exceptional surgical experience and astounding technical ability, and his great experience, especially of abdominal surgery, enabled him to work much faster than most people For instance he performed a partial gastrectomy usually in about 40 minutes He was a kindly man, not given to saying unnecessary words, and was always rather shy of the limelight He was gentle and quiet with his patients and helpful to his assistants He will be remembered throughout Yorkshire for his kindness, his hard work and great surgical skill”

“As a medical colleague,” writes, C W V, “I treasure the memory of the quickness and dexterity with which he carried out the operation for infant pyloric stenosis—a relatively insignificant operation when put against the background of major surgery His disposition was inclined to be shy and reserved, but behind this attitude he was gentle, kindly, and friendly and one who was never hurried or ruffled under the stress of work Our feelings of sorrow, pity, and loss are the more poignant because the last years of his long and arduous life in the service of others were clouded by disability which denied him the enjoyment of a happy and restful retirement which no man could have more deserved”

In 1918, Professor Flint married Miss Alicia Bay Farrer, who survives him with three sons

JOHN PUNNETT PETERS

M D Columbia

Dr Peters, who died on Dec 29 at the age of 69, had been John Slade Ely professor of medicine at Yale University since 1927 He will be remembered, as a scientist, for his pioneer work on the application of chemical observations to clinical medicine, as a doctor, for his concern that medical care should be accessible to the whole community, and, as a citizen, for his

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Queen's University, Belfast

At recent examinations the following were successful

M D—R L Turner (with commendation)

Ph D—R W M Strain

M B B Ch, B A O—J S Armstrong J F Caskey G R Cocks, John Colville John Cooper, J C Cronhelm B S Douglas, J A Gilmore J E Glassberg H D Hall Lilian M Hamilton, Lorna K Hogg, Irene C Hooks Crawford Hull, D A C Johnston, Sarah D Killough H C S Leitch J H McCauley, L C McKenna, W R McKibben, Anne T Mathews, J K Millar, Christabelle R Mutthumani W M Pillow, K B Sloan, W F Speers A W Wilkie, M J Wright

D.P.H—John Tohill

University of Cape Town

Dr L H. Wells, reader in physical anthropology in the University of Edinburgh has been appointed to the chair of anatomy

Order of St John of Jerusalem

The Queen has sanctioned the following promotions in, and appointments to, this Order

As Knights—Colonel G G L Stening, F R C S, E M Humphery, M B

As Commanders—E Parry M B E F R C.S, Lieut -Colonel C G F Morrice F R C S, Sir Harry Sinderson, K.B F C M G, M V O, M D, D H Kinmont, M.B, Cecil Heygate Vernon, F.R.C.S.E, R S Steel O B E, M R C P, A L Dawkins, O B E, F R.C S H W Ward, M.B, D D McCowan M B, Air Commodore T K Lyle, C B E, F R C S, Lady Wakeley, M B

As Officers—J G Mackereth M B, Hector Munro, F R C S E, C M Willmott, M R C S Harold Fallows M B, R J Maule Horne M B, K A Boughton Thomas M B, W C Lyons M B, Major T M Wilks, O B E T D, M R C S, G M S Smith M.B, H S Brown M D, D J Martin F R C S, C B Ball M B E, L M S S A, W E George M B, I O Thorburn M.D, D W Montgomery, F R C S I, Lieut Colonel George Gregg, O B E F R C P I Laura K Maule Horne, M B, Clara Stewart, M B

St George's Hospital, London

Postgraduate demonstrations in neurology and psychiatry are being held at the medical school at 5 P M on Thursdays from Jan 12 to March 15 They are open to doctors without fee

Social Medicine Research Unit

The Social Medicine Research Unit of the Medical Research Council has been transferred to the London Hospital Letters should be addressed to the unit at the London Hospital Research Laboratories, Ashfield Street, London, E 1 Tel Stepney Green 5257

Royal Northern Hospital Centenary

On June 26 the Duke of Gloucester is to preside at a dinner for past and present members of the consultant and resident staff of this hospital and their wives The dinner will be held at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W C 2 Those who hope to attend should write to the hon secretary, Staff Dinner, Royal Northern Hospital, Holloway Road, London, N 7, as soon as possible

British Society for Research on Ageing

On Friday, Jan 20, at 2 30 P.M, a meeting on connective tissue and its changes with age will be held at the General Infirmary, Leeds Further particulars may be had from Mr G H Bourne, D SC, hon secretary of the society, London Hospital Medical College, E 1

Runwell Hospital, Essex

The sum of £10 000 has been granted by the Peel Trust, under the ægis of the Mental Health Research Fund, to Runwell Hospital for research on the incidence of temporal lobe epilepsy in epileptic colonies and mental deficiency institutions The work is to be carried out under the direction of Dr D W Liddell with the help of a full time research fellow A new electro-encephalograph is being supplied by the Fund

Dr. G D Fraser Steele has been appointed whole time consultant psychiatrist to the hospital, Dr J H Margerison whole time research assistant in the senior registrar grade (Peel Trust), and Dr J E Boulding whole time clinical research fellow

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The booklet on the Allocation of Pension under the National Health Service Superannuation Scheme has been revised to accord with the National Health Service (Superannuation) Regulations 1955 (H M Stationery Office Pp 25 1s)

Diary of the Week

JAN. 15 TO 21

Monday, 16th

Hunterian Society

8 30 P M (Mansion House E C) Dr J J Nuboer (Utrecht) Lung Resection in the Treatment of Pulmonary Tuberculosis

Tuesday, 17th

Royal College of Physicians, Pall Mall East S W 1

5 P M Dr J R Ellis Changes in Medical Education (First of two Goulstonian lectures)

University of London

5 30 P M (King's College, Strand, W C 2) Prof B Folkow (Gothenburg) Quantitative Aspects of Some Mechanical, Nervous, and Humoral Factors Controlling the Cardiovascular System (First of two lectures)

Royal Army Medical College Millbank, S W 1

5 P M Prof George Macdonald Recent Developments in Malaria Elimination and Control

St Mary's Hospital Medical School, Paddington, W 2

5 P M Dr Leslie Williams Thrombophlebitis

Institute of Dermatology, Lisle Street, W C 2

5 30 P M Dr Brian Russell Lupus Erythematosus

South West London Medical Society

8 30 P M (Bolingbroke Hospital) Sir Charles Dodds, F R.S Modern Endocrinology and the General Practitioner

University of Liverpool

5 15 P M (Medical School) Sir Geoffrey Keynes Myasthenia Gravis and the Thymus Gland

University of Edinburgh

5 P M (University New Buildings Teviot Place) Dr H J Deuel (University of Southern California) Fat as an Essential Component of the Diet (Macarthur lecture)

Wednesday, 18th

Royal Society of Medicine, 1, Wimpole Street, W 1

8 15 P M *General Practice* Dr L Dulake, Dr Stanley Rivlin Ulceration and Varicose Veins

Institute of Diseases of the Chest Brompton S W 3

5 P.M Dr J Smart Chronic Bronchitis

Institute of Dermatology

5 30 P M Dr J O Oliver Pathology of Lupus Erythematosus

Eugenics Society

5 30 P M (Royal Society Burlington House, Piccadilly, W 1) Dr Elizabeth Tylden Dr Mildred Creak, Mr S G Singleton Personality Characteristics of Parents of Promising Children

Hypnotherapy Group

8 P M *(1 Wimpole Street W 1) Dr George Newbold* Recent Experiments in the Hypnotic State

Royal Faculty of Physicians and Surgeons 242, St Vincent Street Glasgow, C 2

5 P.M Dr Alexander Brown Hæmolytic Anæmias

Thursday, 19th

British Institute of Radiology, 32, Welbeck Street W 1

8 P M Dr J B Fawcitt Dr H E Parry A Review of the Radiological Changes in the Chests of Children with Whooping-cough and Measles

Royal College of Surgeons of England, Lincoln's Inn Fields W C 2

5 P M Mr J H Peacock Raynaud's Disease Raynaud's Phenomenon and Acrocyanosis in the Upper Limb

Royal College of Physicians

5 P M Dr Ellis Changes in Medical Education (Second of two Goulstonian lectures)

Royal Society of Tropical Medicine and Hygiene *Manson House, 26 Portland Place W 1*

7 30 P M Prof A W Woodruff, Dr A P D Adams Treatment of Human Amœbiasis

West London Medico Chirurgical Society

7 45 P M (White Lion Hotel Putney) Dr Roger Bannister Physiology of Muscular Effort

University of Liverpool

5 P M Sir James Paterson Ross The Craft of Surgery (William Mitchell Banks lecture)

Friday, 20th

Royal Society of Medicine

5 P M *Epidemiology and Preventive Medicine* Dr A L Cochrane Field Surveys of Chronic Disease in South Wales

8 15 P M *Radiology* Mr H H G Eastcott, Dr David Sutton, Prof Charles Rob Diseases of the Major Arteries

Faculty of Radiologists 45 Lincoln's Inn Fields W C 2

5 P M *Radiodiagnosis* Dr P H Whitaker Pneumoconiosis in Tin workers Prof Jethro Gough Pathology of Tin workers Lung

Institute of Dermatology

5 30 P M Dr S C Gold Lupus Erythematosus

Sir Horace Evans has been appointed medical consultant to the London Transport Executive in succession to the late Lord Horder

On his retirement from the post of principal medical officer to Bristol City Council Prof P H Parry has been appointed visiting professor in public health to Yale University for six months

A digest of statistics of pneumoconiosis in the mining and quarrying industries in 1954 has been published by the Ministry of Fuel and Power (H M Stationery Office Pp 27 2s 6d)

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"*Look around for some subject on which we are all agreed, and start thinking for yourself You will find you are on virgin ground*"

As far as I am concerned, when I have talked about the orthodox, I have in fact meant little more than the views I hold myself Let me apply the acid test What did I consider orthodox and heterodox twenty five years ago?

I described an operation I had invented myself for the treatment of right sided abdominal failure—right hemicolectomy, with transplantation of the ileocæcal sphincter, carrying its nerve and blood-supply, into the transverse colon I was very pleased with this operation then The fashionable London surgeon of the day approved of it, and did fifty in the next six months I have never done it again, and I have, like most surgeons, steered entirely clear of the right sided abdominal failures Those that are fortunate enough to escape the underworld of surgery who still make a living out of pexy operations, now go to the psychiatrists or to Christian Science, which is much the same thing Yet in the *Medical Annual* of 1930 I find that one surgeon reports one hundred and fifty nephropexies, and many surgeons advocate colopexy My operation was very much better

In the surgery of peptic ulceration I praised gastrojejunostomy and I criticised the Billroth-I operation Today I could not agree less Though I still love doing a gastrojejunostomy, I ceased to regard it as a rational procedure twenty years ago I doubt if I have done half a dozen since the war On the other hand, I regard the Billroth-I gastrectomy as one of the best operations in surgery when the duodenum is normal (that is, in gastric ulcer), and one of the worst operations in surgery when the duodenum is scarred (that is, when done for duodenal ulcer)

I criticised the Billroth I twenty five years ago, on the following grounds

> The pyloric end of the stomach and first part of the duodenum are poor surgical material, thick, friable, and vascular, they must be mobilised for approximation, and are pulled from their natural line and under tension after suture, they are not readily controlled by clamps When an anastomosis is made between them bleeding is troublesome at the time, leakage is not uncommon afterwards, and the finished operation is seldom a really satisfactory craftsman's job"

Those were the criticisms by a young surgeon of a technique he had not yet mastered The gastroduodenal anastomosis can be done with complete safety, and is a perfect craftsman's job if the material is good A stoma, like a sphincter, should be perfectly mobile It should be free to move with the movements of peristalsis, or with the displacement of its component parts or of its neighbours When the resection has been done for duodenal ulcer the stoma is not mobile, for the distal component is tethered by its fusion with the head of the pancreas and by the entry of the common bile duct

To one who takes the long view—and I am sorry to say that I am now able to do that—the Billroth I operation is following today the path that gastrojejunostomy followed in 1920 The operation gives such excellent results when it is done for the proper indications that it is being applied wholesale to cases for which it is entirely unsuitable The bad results are already accumulating, but they are as yet known only to the few, for no surgeon ever reports bad results, certainly not his own When they are known sufficiently widely, I fear that the Billroth-I operation may be condemned as gastrectomy is condemned in some quarters today—not because it is a bad operation, but because it is done badly

Pause and Progression

For my peroration I must once again quote my former Chichester talk

"A barge making its way up the Thames from London to Oxford does not proceed at a uniform rate At times it is moving forward, at times it remains stationary in a lock, but while it is in the lock, water is flowing in from the higher streams, till finally a new level is reached and a fresh advance is possible Thus, by alternate pause and progression, it finally mounts to the highest levels So the advance of knowledge must be wayward the locks are periods of orthodoxy, the advances, of heterodoxy"

I wish that I could be as certain today of the inevitability of advance It appears too often that a surgical advance is like a wave rather than a river, a change of form in which there is little true forward motion The wave rises from the expanse of water, it mounts, for a brief period it towers above its surroundings, then at last it collapses in a welter of foam We must watch the waves of knowledge We must try to keep on the rise and avoid the backwash

EFFECT OF CHLORPROMAZINE ON CONVULSIONS OF EXPERIMENTAL AND CLINICAL TETANUS

R E KELLY
M D *Lond*, M R C P
PHYSICIAN TO NEUROLOGICAL DEPARTMENT, ST THOMAS'S HOSPITAL, LONDON, AND CONSULTANT NEUROLOGIST, MOUNT VERNON HOSPITAL, NORTHWOOD

D R LAURENCE
M D Lond, M R C P
SENIOR LECTURER IN APPLIED PHARMACOLOGY AND THERAPEUTICS, UNIVERSITY COLLEGE AND UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL, LONDON

THE treatment of tetanus convulsions is attracting much attention There are two principal methods the use of sedatives and mephenesin, and the use of neuromuscular-blocking agents with light anæsthesia The ability of anæsthetists to keep patients completely paralysed yet alive for long periods has been amply demonstrated, but treatment by paralysis, quite apart from other disadvantages, must be impracticable in any country where tetanus is common and skilled anæsthetists are few, and a simpler alternative must be sought

There is need for a drug or combination of drugs which will abolish the muscle spasm without affecting respiration or abolishing consciousness Mephenesin has some of the qualities of such a drug, but it has serious clinical disadvantages including apparent inability to control the most severe cases The readiness with which physicians have invited anæsthetists to paralyse their patients is a sufficient indication that mephenesin is thought to be inadequate or dangerous

With this need in mind, one of us examined the effect of both old and new drugs on experimental tetanus in the hope of finding a substance more effective than mephenesin So far the only drugs of any promise are chlorpromazine and promethazine, which have similar chemical constitutions

Technique

Rabbits were given an intramuscular injection of tetanus toxin into one hindleg, the dose being adjusted to cause pronounced resting tetanus in the injected leg the other being minimally affected or unaffected and so acting as a control Electromyographic records were taken from both hindlegs of the conscious animal, which was supported in a canvas sling Drugs being tested were injected intravenously and their effect on the tetanus spasm observed This technique is based on that described by Wright et al (1952)

A standard afferent stimulus, consisting in dropping a weight on to the metal frame supporting the rabbit sling, was used to give a rough measure of the completeness of abolition of the tetanus

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(mg per day) being 75, 180, 220, 200, 155, 225, 285, 275, 330, 250, 215, 300, 240, 115, 50, 30 The child had a slow but uneventful convalescence

We are not here concerned with general aspects of treatment, but the following features are important

1 The child was fed by stomach tube from the first He never vomited

2 A small blood transfusion, given to correct anæmia, was followed by the transient appearance of bile pigments and salts in the urine

3 Oxygen was given by a nasal tube for cyanosis due to the spasms This was thought to do more harm than good by provoking spasms and was soon abandoned

4 An intravenous drip was kept going throughout the period of chlorpromazine administration The solutions were at first 5% dextrose and then half strength Hartmann's solution (sodium lactate compound injection *B.P*), of which about 500 ml was given each day

5 The electrolyte balance was carefully controlled (Dr E Jepson), and close attention given to oral hygiene (Mr B W Fickling)

6 Considerable intravenous thrombosis occurred and was attributed to the chlorpromazine solution (25 mg per ml) despite the fact that it was diluted ten times before being injected into the tubing of the drip near the patient 10 mg of heparin was added to each bottle of intravenous infusion

7 Large doses of tetanus antitoxin were given at the start of the illness

8 Penicillin was given to prevent respiratory complications

9 Every effort was made to deprive the patient of provocative afferent stimuli

10 Very severe abdominal distension occurred towards the end of the period of chlorpromazine administration The distension subsided At the same time an erythematous rash developed on the back and scalp It never became generalised and was attributed to excessive sweating That the drug might have played a part in these cannot be denied, but it seems unlikely

Discussion

Brooks et al (1955) investigating the mode of action of tetanus toxin, found that it caused " a large development of polysynaptic reflexes " and suggested that this might be due to " the depression of inhibitory synaptic action on the interneurones " involved in these reflexes Tetanus toxin acted by suppressing synaptic inhibition only , it did not convert inhibition into excitation

Experimental work has shown that mephenesin acts mainly by depressing the spinal-cord internuncial neurones (Berger 1947) and the brain-stem reticular formation (Henneman et al 1949) Dasgupta and Werner (1955) have shown that chlorpromazine almost certainly has similar actions

In clinical medicine mephenesin is known to be active against tetanus muscle spasm (Belfrage 1947) and against spasticity and parkinsonian tremor (Schlesinger et al 1948)

Chlorpromazine is also effective against spasticity and parkinsonian tremor (Basmajian and Szatmari 1955, Kelly and Laurence 1955) and against rabbit tetanus, as described earlier in this paper

It was therefore reasonable to suppose that chlorpromazine would be effective against tetanus in man The dose of mephenesin effective against local rabbit tetanus is 12 mg per kg body-weight, which is comparable to that known to be effective against tetanus in man (Davison et al 1949, and many other reports)

Pentobarbitone will reliably abolish rabbit tetanus only in doses which cause loss of consciousness (unpublished observations), and this finding agrees with clinical experience of barbiturates in tetanus

It therefore appeared likely that chlorpromazine, in the dosage which is effective against rabbit tetanus (1 0 mg per kg body-weight), might be useful in the treatment of human tetanus either alone or in combination with other drugs Infused carefully, 1 mg per kg body weight is not an excessive dose to give intravenously to man

In addition to the central effects of chlorpromazine Burn (1954) reported that 3 mg per kg body weight had a direct depressant effect on skeletal muscle of cats Such an effect could play a part in producing the results reported here

While these experiments were being made, Hougs and Andersen (1954) published observations on the effect of chlorpromazine and promethazine on local tetanus in anæsthetised rabbits The results recorded here substantially agree with theirs

The present case is reported, not because it is thought that the outcome of one case can provide conclusive evidence of the value of a drug but because it was a treatment chosen in the light of experimental evidence. It is our opinion that, if uncontrolled, this child would have died , but no doubt he could also have been treated successfully with thiopentone (with the concurrent disadvantage of unconsciousness), with neuromuscular blocking drugs (with the necessity for continuous anæsthesia as well as artificial respiration), or with mephenesin (which is short-acting and has the disadvantage of having to be given in very large volumes of fluid by vein to avoid the hæmolysis which strong solutions cause) Chlorpromazine was used since it offered a possibility of controlling the convulsions without any of these disadvantages

Possibly the most effective method will be to use a mixture of drugs, but it would be difficult to find two people agreed on the composition of the mixture This situation is due to the absence of information on the relative efficacy of individual drugs against tetanus convulsions , and without this information the ideal combination is unlikely to be found

To have given other drugs with the chlorpromazine would have prevented any definite conclusion as to whether the drug was capable of arresting tetanus spasm The knowledge that chlorpromazine is more effective against tetanus in rabbits than are other drugs such as mephenesin, and the belief that there is no significant difference between animal and human tetanus, justified the very large doses

We conclude that chlorpromazine is capable of controlling tetanus in man but offer no opinion on what place it may have in routine treatment If the effect reported here is confirmed in other cases this drug might then be tested in combination with other drugs of known action against tetanus—e g , barbiturates, mephenesin and promethazine

When treating severe tetanus boldness may be required in pressing drug therapy to the limits of safety If the physician is not ready to do this he is liable to find himself at critical moments either changing from one *drug to another, adding different drugs,* or resorting prematurely to neuromuscular blocking agents

Forbes and Auld (1955) report the successful use of ' constant intravenous infusion " of thiopentone, succeeded, as the patients improved, by oral paraldehyde or another barbiturate They treated fifteen patients, sometimes using a different sedative drug as the principal agent There were no deaths and it was never necessary although some cases were severe, to proceed to the use *of neuromuscular blocking agents* They aimed at the abolition of severe convulsions and opisthotonos, but not at complete flaccidity This technique, effective though it proved, must inevitably result in long periods of unconsciousness (Forbes and Auld give no information on this point), and this may account at least partly for the high rate of respiratory complications (ten patients required tracheotomy)

It is by work such as this, in which treatment was virtually *confined to* the use of barbiturates, that the efficacy of drugs against tetanus convulsions can be compared, and by such comparisons the reign of chaos over tetanus treatment may be ended

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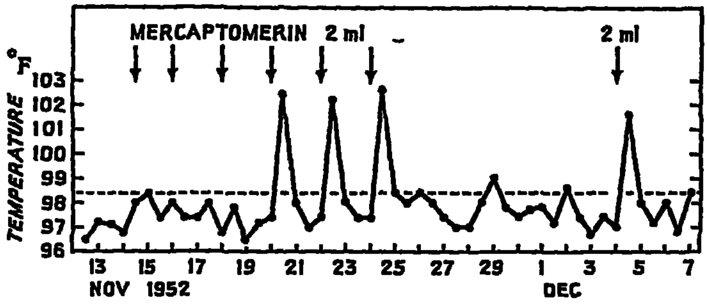

Fig 1—Pyrexia after mercaptomerin in a woman of 70 with congestive failure

one year, swelling of the ankles for one month, and attacks of nocturnal dyspnœa for three weeks She had had pernicious anæmia, treated regularly and adequately with 'Anahæmin,' for sixteen years Two months before admission her appearance and behaviour suggested myxœdema and subsequently she had thyroid (gr 2 daily) without obvious effect There was no personal or family history of allergy and she had not previously had any organic preparation of mercury

She had severe orthopnœa and cyanosis with signs of congestive failure including moderate subcutaneous œdema Pulse 100, regular Blood pressure 170/110 mm Hg Heart size uncertain because of obesity E C G showed left bundle branch block Urine normal

Treatment in hospital initially included bed rest, morphia, and digitalis folia (gr 3, reduced later to gr 2, daily) When dyspnœa and œdema were unrelieved, mercaptomerin was started (2 ml on alternate days subcutaneously) The resultant diuresis, though small, was considered worth while and the treatment was continued After the fourth injection she became febrile but without symptoms or other physical signs About one hour after each of the fifth and sixth injections she had rigors followed by about twelve hours of fever (maximum 102 4°F) (fig 1) Each was accompanied by some *increase in cyanosis, which was generalised, and by malaise* and anorexia, the sixth injection causing more subjective upset than the fifth None of these three upsets caused concern to nurses or doctors, and twenty-four hours after each of them recovery appeared complete At the time of the third reaction the white cell count was 14,800 per c mm (polymorphs 88 5%, eosinophils 0 5%, lymphocytes 10 5%, monocytes 0 5%) No malaria parasites were found on repeated examinations

At this point it was recognised that the febrile upsets were probably related to the mercurial drug Other patients in the ward who were receiving the same batch of drug did not react in this way, and the readily available literature on mercaptomerin gave no reference to febrile reactions

On *Dec 4* the seventh dose of 2 ml was given subcutaneously This was followed after one hour by rigor, extreme malaise, and cyanosis (temperature 100 6°F, pulse 126, regular, small volume, and at times impalpable, blood-pressure 90/60) Later that day she vomited twice and passed six fluid stools

On *Dec 5* she was afebrile but still drowsy and cyanosed with evidence of peripheral circulatory failure (blood pressure 60/35) Adrenaline by injection appeared to increase the cyanosis Blood chemistry Na 310, Cl 342, K 21 5 mg per 100 ml No more than 1–2 oz of urine was passed, incontinently During the day she had oral cortisone (150 mg in three divided doses) and was kept in an oxygen tent She received no other corticoid The drowsiness and signs of peripheral circulatory failure lessened during the day, the pulse volume improved, and the blood pressure rose to 90/60 The 24 hour output of urine was 18 oz

On *Dec 6* the slow improvement was maintained Blood-pressure 100/70 Urine output 12 oz E C G no change since admission

She continued to improve slowly though blood-pressure remained low and on Dec 19 was only 150/85 At no time during the stay in hospital was any preparation of liver, vitamin B_{12}, or thyroid given to her

Case 2 —Mr H H, aged 57, was admitted to hospital on Oct 17, 1953, with a nine month history of dyspnœa on effort and more recently attacks of paroxysmal dyspnœa His own doctor had already given several injections of mersalyl without untoward effect There was no personal or family history of allergy

He had an enlarged heart with atherosclerotic aortic stenosis and auricular fibrillation Blood pressure 150/90 E C G showed left ventricular preponderance Urine normal

In hospital he was confined to bed and digitalised On Oct 18 1 ml of 'Neptal' was given intramuscularly without ill effect On Oct 20 he received mercaptomerin (2 ml subcutaneously) and this was repeated on alternate days until he had received 10 ml of the drug in five doses About twenty four hours after the first injection of mercaptomerin a generalised irritating erythematous rash developed This was not associated with fever and rapidly receded under treatment with promethazine ('Phenergan') (25 mg b d) It was thought that the rash probably indicated sensitivity to a barbiturate used to sedate him, but to determine the offending preparation *particular drugs were discontinued and then reintroduced* Butobarbitone ('Soneryl') (gr 3) caused no untoward reaction

On Nov 11 a test dose of 0 5 ml of mercaptomerin was injected subcutaneously Within a few minutes erythema developed around the injection site About an hour later the patient experienced tightness in the chest and epigastrium and breathing became laboured He rapidly became extremely shocked (pulse 45, blood pressure 70/30, heart sounds so soft as to be barely audible) He remained in this state for about an hour and then slowly improved so that within six hours he was relatively well again His condition was so suggestive of an acute coronary attack that two E C G s were taken The first, twenty minutes after the onset of the attack, showed increased T wave inversion in the left lateral chest leads A further tracing next day was substantially the same as that on admission and showed no evidence of myocardial infarction His further stay in hospital was uneventful There was no rise of temperature after any of the injections of diuretic

Case 3 —Mr B H M, aged 47, was admitted to hospital on Sept 27, 1954, with increasing dyspnœa on exertion and angina of effort for one year Ankle swelling had been noticed more recently There was no personal or family history of allergy

There were signs of congestive failure and the heart was moderately enlarged Pulse irregular due to auricular fibrillation Blood pressure 120/60 The lungs showed signs of emphysema and congestion

Measures to relieve heart failure included salt restriction, *digoxin, and mercaptomerin, which was given subcutaneously* in a freshly prepared solution Three injections, each of 2 ml, were given in all and after each the diuresis was satisfactory Thirty six hours after each dose the temperature rose (fig 2) and the febrile response increased with each injection The first two reactions were small and there were no other symptoms, but the third was accompanied by malaise and chills Mercaptomerin was therefore discontinued, and during his remaining stay in hospital he was afebrile Serum chemistry and urine were normal throughout No other cause for febrile episodes was discovered

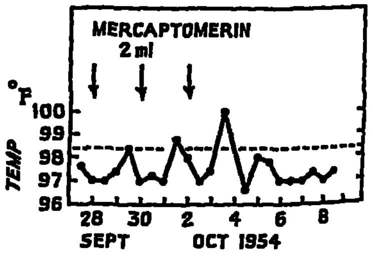

Fig 2—Pyrexia after mercaptomerin in a man of 47 with congestive failure

Case 4 —Mr S V B, aged 47, was admitted to hospital on *Dec 7, 1953, with a three week history of angina of effort,* dyspnœa on exertion, and increasing ankle swelling There was no previous history of allergy

He had early congestive failure with distended neck veins, orthopnœa, ankle œdema, and hepatomegaly The heart was moderately enlarged Pulse regular Blood pressure 105/65 Blood count and urine were normal Chest radiograph showed lungs much striated, as in bronchitis, with a small amount of pleural elevation at the left base

Treatment included salt restriction and mercaptomerin The solution was freshly prepared and given subcutaneously Five doses were given altogether at intervals of two days, the first was 0 5 ml and the other four 2 ml each After the third injection the temperature rose, and this fever persisted for five weeks, the highest reading was 102°F On the day

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PSYCHOTIC MOTHERS

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NOWADAYS much emphasis is placed on the child's need, if he is to develop normally, for close relationship with an affectionate mother The work of child-guidance clinics is directed to this end, and now an effort is being made at infant welfare clinics to help mothers solve problems within themselves or their children, so that mother and baby can get on together as well as possible from the earliest days of the child's life But some women cannot benefit from such help—namely, those with postpartum psychosis

In such cases the acute psychotic episodes end fairly rapidly, but the patients tend to relapse, and the illness usually lasts for some months The consequent separation of mother from child in the child's first year of life may impair its ability to form good relationships later on

Zilboorg (1931) and Deutsch (1947) remark that postpartum psychosis is not a specific entity, but a breakdown into schizophrenic or depressive or other illness according to the patient's predisposition Nevertheless all cases have one feature in common—hostility to the baby The patient's inability to bear this hostility causes her personality to break up and earlier infantile conflicts to be brought to life so that she becomes psychotic

The old fashioned remedy in such cases was to separate mother and child, and this often proved efficacious The child was tended by a nurse or a relative, and the mother, relieved of the unbearable hostility, was more likely to recover Today suitable mother substitutes are rare Moreover, the mother who has been admitted to an observation ward or a mental hospital for treatment, though she usually recovers in hospital, commonly relapses when she is again required to care for her baby

This difficulty has been overcome in a small series of cases by admitting the baby along with its mother The husband's cooperation was sought, and the methods and aims of the treatment explained to him While the nurses undertook the physical care of the child, the mother was encouraged to do as much for the child as she felt able, and she was enabled to discuss her sentiments about this with a psychotherapist, who tried to gain the mother's confidence

Under this arrangement psychotherapy proceeded surprisingly quickly, probably because after childbirth primitive drives are strong, and thought processes which at other times are unconscious are more readily accessible Thus the patient would consider and discuss fairly readily her past relationships and attitudes to herself and others, and would accept interpretations which at another time would have been strongly resisted, and make good use of these interpretations to resolve her difficulties Once this stage was reached, the patient gradually withdrew her interest from the psychotherapeutic sessions and transferred it to her baby

Thus the mother got to know the baby at her own pace, and had the daily reassurance that, despite all her own strange mixed feelings towards her infant, it still survived with the detached physical attention given by the nurses As her fear of her own negative feelings to the child lessened she gained more confidence to undertake its physical care, but she was not detached, for she felt that she could give her baby more than anybody else She could then become, as Dr D W Winnicott has put it, "an ordinary devoted mother"

Of the following four cases, the first two illustrate the tendency to relapse when full care of the baby is undertaken before the patient is ready for this, and the last two show how such relapses can be avoided

Case-records

Case 1 was a pretty, intelligent young woman, married to a man much older than herself on whom she could rely for security Being the youngest of a large family she had been pampered and treated as the delicate one She had always suffered from many minor ailments, including palpitations for which no organic cause could be found After three years of marriage the patient became pregnant She was well throughout pregnancy but towards the end was worried as to whether she would be able to care for the baby adequately

She was not noticed to be abnormal during the puerperium, but she felt very inadequate when she got home With much support from relatives she managed until the baby was 5 months old, when she became more tense and strained, then expressed delusional ideas, believing without reason that a film had been made about her and that other people were wearing her clothes and impersonating her She became withdrawn, and had to be admitted to an observation ward

Over the next two weeks the patient gradually became more in touch with reality When she was able to talk about her illness she admitted having felt depressed and inadequate since the birth of her child, she said that this was because her relatives had done too much for her, and she was over confident that she would remain well She was perplexed about her state of mind immediately before her admission to hospital, and could give no clear account of it She insisted on going home and taking full responsibility for her baby

When seen at the outpatient clinic the following week she was again withdrawn. She sat staring in front of her, she was disorientated in time and spoke off the point, saying such things as "are you going to bury me, is my baby dead?" Yet again she made a rapid superficial recovery in the observation ward, but in view of the previous failure to maintain improvement she was persuaded to enter a mental hospital as a voluntary patient

There she was given a course of deep insulin therapy with electroconvulsion therapy (E C T) in sopor towards the end of the course Schizophrenia with hysterical features was diagnosed at the mental hospital where the prognosis was regarded as not very favourable She left against advice after three and a half months

On returning home she once more tried to look after her child, this time succeeding for several weeks until she became as seriously disturbed as before, so that it was necessary for her to be admitted to the observation ward yet again This time, with the agreement of the superintendent of the mental hospital in which the patient had recently been, she was admitted to the neurosis ward of the general hospital with her baby also in hospital, and was treated by psychotherapy and gradually undertook the care of her baby She made a good recovery, and was discharged home after three months She has remained well and has cared for her child in the subsequent two years

Case 2 was the youngest of several children The mother died when the patient was 3 years old, so she was brought up by her father and an older sister She was considered a fairly normal child but did not mix well with children of her own age When she first became engaged to be married, and again just before her marriage, she had a "nervous breakdown" for which she received treatment at home, and she recovered She was strongly attached to her father Her husband was an immature young man who could lend the patient little emotional support They both wanted the baby

While in hospital when the child was 5 days old, the patient suddenly made a suicidal attempt She tried to throw herself out of a window, but was forcibly restrained by a nurse She was deeply depressed, and she was also deluded, believing that her husband had deserted her (whereas he was visiting her regularly), and that she was to be sent to prison for all the wrong that she had done On account of persistent suicidal intention, she had to go to a mental hospital under certificate

A course of E C T led to a good recovery, and she was discharged home to look after her baby, but two weeks later she was admitted to an observation ward again She made a rapid superficial recovery On her discharge the baby was put with foster parents and the patient got a job, where she seemed quite

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OBSERVATIONS ON RATS RECEIVING δ-AMINOLÆVULIC ACID OR PORPHOBILINOGEN WITH AND WITHOUT EXPOSURE TO ULTRAVIOLET RADIATION

Treatment (dose of drug 30 mg per kg of body-weight)	Symptoms	Ultraviolet fluorescence		Skin histology	Urine (24 hours)
		Skin (frozen sections)	Intestines		
δ Aminolævulic acid and ultraviolet irradiation	Irritability hyperæmia of skin	+ + + In stratum corneum	+ + +	Subepidermal blisters infiltration (fig 1)	
δ-Aminolævulic acid without irradiation	Nil	+ + In stratum corneum	+ +	Normal (fig 2)	Coproporphyrin 1 6 µg protoporphyrin 0 16 µg uroporphyrin 0 24 µg porphobilinogen ? trace
Porphobilinogen and ultraviolet irradiation	Nil	+ In stratum corneum	+ +	Normal (figs 3 and 4) one selected area shows collagen damage and infiltration (fig 4)	Corproporphyrin 0 48 µg protoporphyrin 0 10 µg uroporphyrin 17 2 µg porphobilinogen + +
Ultraviolet irradiation only	Nil	? Trace	+	Normal (fig 5)	

porphyria The important observation has, however, been made, in a self-experiment by Dr Scott, that its ingestion *is followed by transitory hypersensitivity to* sunlight (Berlin et al 1954a and b, Scott 1955)

Granick and Vanden Schrieck (1955) injected δ aminolævulic acid 130 mg per kg body weight into a white rat intraperitoneally and observed no symptoms of distress The rat's urine next day contained a little zinc porphyrin complex, but the contents of the stomach and duodenum, and the femoral bone marrow fluoresced strongly in ultraviolet rays

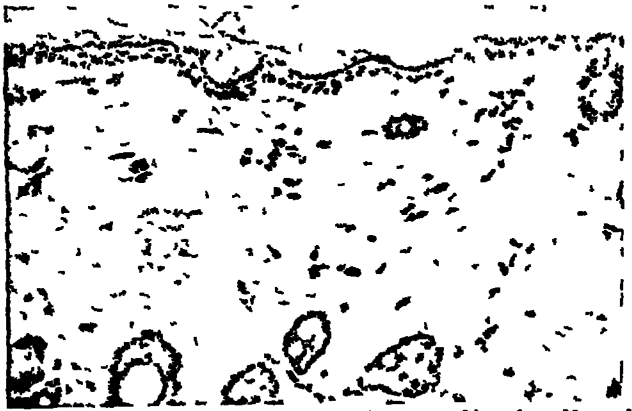

Fig 2—Skin of rat receiving δ-aminolævulic acid only Normal histology (Hæmatoxylin and eosin ×160)

Investigation

We have compared the effects of subcutaneously administered δ aminolævulic acid and porphobilinogen on albino rats with and without exposure to the radiation from a small carbon arc The animals were shaved on the back and sides, and 10 minutes after an injection (30 mg per kg body-weight) were exposed, with shaved *but uninjected controls for 15 minutes at 12 inches* distance There was no overheating under these conditions

The control rat and the rat injected with porphobilinogen showed neither irritability nor hyperæmia, but the rat injected with δ aminolævulic acid and irradiated showed definite signs of irritability, such as scratching, biting, and shaking itself—movements which continued for some time after removal to the cage—and its skin was hyperæmic The rat given the same dose of δ aminolævulic acid but not exposed to ultraviolet rays appeared perfectly normal

All the rats were killed after 24 hours, and portions of their *skins were fixed, sectioned, and stained or* examined immediately (frozen sections) by ultraviolet fluorescence microscopy The thorax and abdomen were also opened in each rat for macroscopic examination under ultraviolet rays The findings are listed in the accompanying table, and the histological changes in the skin are recorded in figs 1–5

Discussion

A considerable amount of porphyrin is formed from both δ aminolævulic acid and porphobilinogen, the greater part being eliminated via the bile into the intestine (Granick and Vanden Schrieck 1955, Scott 1955) The comparatively large quantity of uroporphyrin in the urine of the rat given porphobilinogen may have been derived non enzymically (Cookson and Rimington 1954) from porphobilinogen, which was also present in the urine Only the combined treatment with δ aminolævulic acid and irradiation caused photosensitivity, and fluorescence due to porphyrin was more intense in this rat than in the one not exposed to the arc-light The difference in fluorescence was greatest in

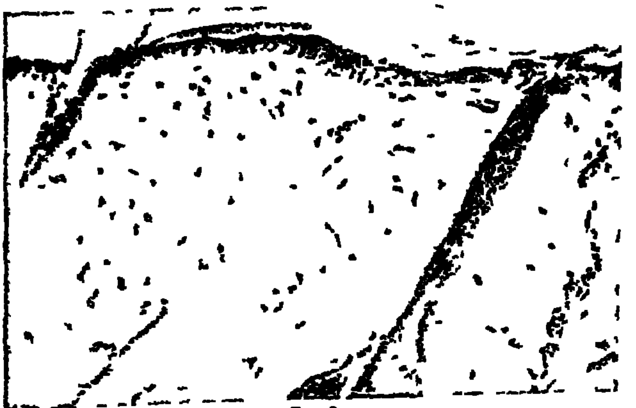

Fig 3

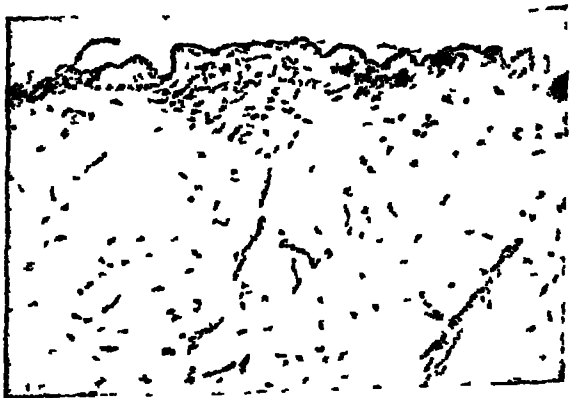

Fig 4

Figs 3 and 4—Skin of rat receiving porphobilinogen and ultraviolet radiation Histology generally normal (fig 3), but occasional affected areas (fig 4) with minor collagen damage and some infiltration (Hæmatoxylin and eosin ×160)

there was no abnormality of sensation Chvostek s and Trousseau s signs were negative The temperature was 99 8°F, the heart-rate 100 per min, and the blood pressure (which had never been measured before) 130/95 mm Hg She had diarrhœa and was incontinent of urine The diarrhœa continued in hospital for only four days, during the last two of which chloramphenicol was given No pathogenic organisms were cultured from the stool

Investigations

In the serum the level of potassium was 1 7, of sodium 147, of chloride 104, and of bicarbonate 29 m eq per litre The electrocardiogram showed evidence of potassium deficiency

Treatment and Progress

Potassium acetate was given by mouth, about 90 m eq being administered in the first sixteen hours Since there was no increase in muscle power or in potassium level the rate of administration was increased to about 250 m eq per twenty-four hours Muscle power then improved but was not normal until four days later On the sixth day, when the potassium level in the serum was 6 5 m eq per litre, the potassium was discontinued by this time she was taking food

On the third day she complained of pins and needles in the fingers and toes, and was found to have latent tetany, this continued for almost forty eight hours

The urine contained a trace of protein and was nearly neutral (pH 6 7–7 1), the highest specific gravity after eighteen hours' water deprivation and injection of 5 ml of 'Pitressin' was only 1 010 The centrifuged deposit contained a few white blood cells, but cultures were sterile The blood-urea was 82 mg per 100 ml on admission, and 72 mg per 100 ml two weeks later Seven months later it was 40 mg per 100 ml

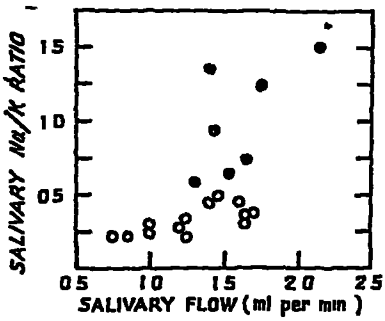

Fig 1—Salivary sodium/potassium ratios plotted against rate of salivary flow Open circles represent preoperative samples black circles postoperative samples

Renal conservation of potassium was defective During an eleven-day period when the level of potassium in serum varied between 1 7 and 2 1 m eq per litre, the mean daily output of potassium in the urine was over 70 m eq During a five-day period in which the patient was given ammonium chloride (115 m eq per day) the urine pH fell to 5 1, and the urinary content of titratable acid minus bicarbonate rose from −9 to +23 m eq per day, and of ammonium from 36 to 119 m eq per day

The patient remained well from the fifth day in hospital She was discharged after a stay of six weeks After discharge she took 80 m eq of potassium chloride daily, and said that she felt better than she had for some years, but the thirst continued

When the dehydration and electrolyte depletion had been corrected her blood pressure had risen, and it varied between 160/90 and 230/120 mm Hg During the twelve months between discharge and her second admission she continued to be hypertensive, the highest recorded pressure being 220/150 mm Hg

Second Admission

In April 1955, the patient was readmitted for further study as a possible case of Conn's syndrome Her blood pressure was 225/140 mm Hg with 20 mm of pulsus alternans, triple rhythm was heard, and radiography showed enlargement of the heart, the fundi were normal Although the blood pressure fell slightly during her stay in hospital (fig 5) it continued to be high, and when after a short time at home she was readmitted on June 8 for operation, it was 205/130 mm Hg

To show whether the patient had a tumour secreting salt retaining hormone, three main lines of investigation were followed

Salivary sodium and potassium levels—Conn (1955a) suggested that a low ratio of sodium to potassium in saliva and sweat indicated increased activity of salt retaining hormone, it was largely this finding that led him to postulate such increased activity as the cause of the electrolyte abnormality in his patient, since it showed that the abnormality of excretion was not confined to the kidney In our patient this ratio was found to be low (fig 1)

TABLE I—CORTISOL AND ALDOSTERONE LEVELS IN BLOOD AND URINE

Date (1955)	Specimen	Cortisol in whole blood or 24 hr urine (µg per 100 ml)	Aldosterone in whole blood or 24 hr urine (µg per 100 ml)
Jan 20	Blood	2 7	<0 1
May 4	Blood	4 2	<0 1
March 8–9	Urine	40	8
May 4–5	Urine	35	11
May 5–12	Urine	21	28
June 10		Operation	
Sept 25–26	Urine	8 7	1 1

Assays of *aldosterone in the blood and in the urine* were made by Mrs S A Simpson and Dr J F Tait at the Middlesex Hospital Medical School, who reported as follows "The blood was extracted at neutral pH Cortisol (hydrocortisone) and aldosterone were fractionated and estimated as described in detail previously (Simpson and Tait 1955) The urine was continuously extracted at pH 1 with chloroform for 24 hours at room temperature and the resulting free cortisol and aldosterone purified by column chromatography The aldosterone was measured by bio assay at this stage Aldosterone diacetate and cortisol monoacetate were also prepared from this fraction and, after purification, estimated by the soda fluorescence method (Bush 1952) A detailed description of the methods will be submitted for publication elsewhere

" The aldosterone and cortisol were analysed in a 200 ml sample of blood collected at 9 30 A M on Jan 20, 1955, and May 4, a 24 hour specimen of urine on March 8–9 and May 4–5, and in a 7 day bulked collection of urine between May 5 and 12 The results, together with those in a postoperative specimen of urine taken on Sept 25–26, are shown in table I The values for aldosterone using the bio assay procedure showed good agreement with those found by the physico chemical method within the limits of experimental error

" The mean value for cortisol in peripheral blood collected at 9 30 A M from normal males determined by the method used in the present investigation has been found to be 2 7 µg per 100 ml whole blood, with a range of 0 5–4 7 µg for eleven individual determinations a pooled specimen from twenty volunteers gave a value of 2 5 µg per 100 ml The mean value for aldosterone from the same subjects was 0 08 µg per 100 ml The mean value of the amount of cortisol in urine collected from six male patients not suffering from any obvious endocrine disease has been found to be 43 µg per 24 hours, with a range of 23–57, and that of aldosterone in the same urine 12 µg per 24 hours with a range of 8–16 Thus only the pooled urine

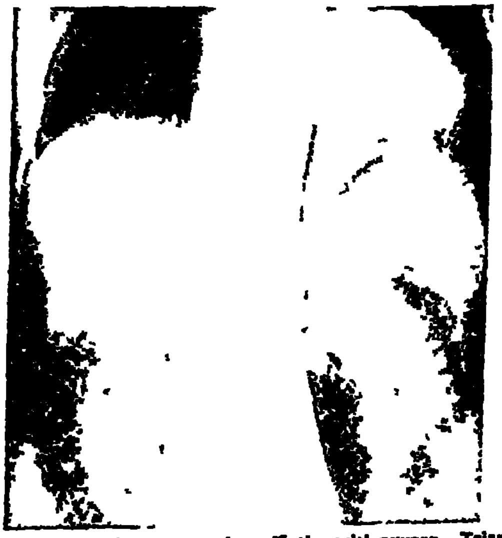

Fig 2—Tomogram after presacral insufflation with oxygen Triangular shadow above each kidney is cast by adrenal Round tumour is seen at apex of right adrenal

successful stand against his illegal dismissal from a government post

He graduated from Yale in 1908 and took his M D at Columbia College of Physicians and Surgeons in 1913 While holding an appointment at the Presbyterian Hospital in New York he served as instructor in clinical medicine at the college In 1917, with a research fellowship, he moved to the Russell Sage Institute of Pathology In 1921 he went to Yale as an associate professor of medicine, and he was elected to his chair in 1927

As the senior professor of medicine at Yale he took an important part in the movement for development of the public-health services, and he was a consultant to the United States Public Health Service on Federal grants for medical research Another of his advisory appointments was that of consultant to the Surgeon-General of the United States Army It was against his dismissal from this appointment on grounds of disloyalty that he successfully appealed in the Supreme Court last June

Of his scientific work one of his English colleagues writes

In his preface to the first, and alas only, volume of the second edition of what is known formally as *Quantitative Clinical Chemistry*, but familiarly as *Peters and Van Slyke*, Dr Peters remarked " When the task of writing the book was first undertaken, clinical chemistry was adolescent " The book was published in 1931, and ever since has been the standard reference in its subject In the progress of clinical chemistry from adolescence to maturity, no one has contributed more than Peters himself, and in the year of his death further notable contributions appeared from him and from his school He was perhaps specially concerned with water and electrolyte metabolism, his book on *Body Water* (1935) is a classic, and he has since reviewed this explosively expanding subject in *Physiological Reviews* and in successive editions of *Duncan's Diseases of Metabolism* Even before 1920 he and his group had published many important original papers on œdema, renal disease, and lipide metabolism His was perhaps specially notable for the equal stress which he laid on the clinical and chemical work in his unit, his young men were trained both to look after their patients and to carry out their own chemical estimations, and neither duty could be scamped or delegated Even when official duties and advisory work claimed much of his time, they could not submerge his originality

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Mr Percy G Phelps, of the firm of Down Bros and Mayer & Phelps, surgical instrument manufacturers, died on Jan 2 at the age of 80 He retired from the firm in 1952

Appointments

AINSLEY, N J, M D Belf, M R C P I asst pathologist, Bradford area
CLARK, A N G, M D Leeds asst geriatrician, Leeds A and B groups
CONNOLLY, MARGARET R L R C P E, F F A R C S, D A part time consultant anæsthetist under Liverpool R H B
KEARNEY, J M, M B Belf asst M O, British Transport Commission, London Midland Region
LEE, W R M B Lond., D OBST asst M O, British Transport Commission London Midland Region
LINDSAY, G G, M B Glasg, D.P H. depute M O H and port M O, Greenock
PATTERSON J L, M.B Glasg, D.P H deputy M O.H and principal school M.O, Lincoln C B
STRACH E H M D Prague M CH ORTH Lpool F R C S part-time consultant orthopædic surgeon, St Helens area
VULLIAMY D G M D Camb M R C P D C H consultant pædiatrician W Dorset and S Somerset hospitals

South-Western Regional Hospital Board

CIANTAR JOAN M.B Wales registrar in pathology, Bath group of hospitals
MANTLE J A, M B Birm. F R C S consultant orthopædic surgeon, W Cornwall clinical area
PIGGOT, JAMES M.B Belf F R C.S E registrar, Princess Elizabeth Orthopædic Hospital Exeter
WARNER JAMES M B Birm registrar in psychiatry Bristol mental hospitals

London County Council

LOWRY AUDREY M. M.R C S, D C H M O
MAGNER VALERIE C M.B N U I D C H M O
ROBINSON, SHEILA M, M B Camb M O
VAKIL, MARY A O, M B Belf M O

Notes and News

TEACHING HOSPITAL IN THE WEST INDIES

THE Secretary of State for the Colonies has appointed a committee with the following terms of reference

> " To inquire into the financial needs and methods of financing of the University College of the West Indies Teaching Hospital to make proposals for its essential capital and recurrent requirements in relation to the financial resources available and to assess the proportion of the cost arising from the teaching functions of the hospital "

The chairman of the committee is Dr R S Aitken, vice-chancellor of the University of Birmingham, and the other members are Dr E R Boland, dean of Guy's Hospital Medical School, Dr J W P Harkness, medical adviser, Development and Welfare Organisation, West Indies, and Mr G A Phalp, secretary of the United Birmingham Hospitals' Board

WELLCOME TRUST

GRANTS made lately by the Wellcome trustees include £25,000 to the Medical Research Council towards the cost of an investigation of trachoma to be carried out in Jordan and London under Sir Stewart Duke Elder The trustees have also allocated up to £33,000 for the purchase of three electron microscopes for indefinite loan to the Medical Research Council (for use initially in the department of biophysics at University College, London), to the physiological laboratory, University of Cambridge, and to the department of human anatomy, University of Oxford

PROGNOSIS IN ESSENTIAL HYPERTENSION

THE prognosis when essential hypertension is discovered in patients under 46 has been studied by Storm Mathisen in the University Clinic, Oslo[1] Hypertension (defined as a systolic blood-pressure of 160 mm Hg or more, and a diastolic blood-pressure of 95 mm Hg or more) was found for the first time in 290 patients (111 men and 179 women) who were in hospital with other illnesses, the mean age of the men was 37 and of the women 38 When these patients were recalled for examination ten years later (in 1950–51) 46 men (42%) and 52 women (29%) had died, the great majority from their hypertension Their average survival after the discovery of their hypertension was five years It was noteworthy, however, that the 97 cases in which the diastolic pressure sometimes fell below 95 mm Hg had a mortality of 8%, which compares very favourably with the 43% mortality of those whose diastolic pressure was not observed to fall below that level For the whole group of 290 patients, the death rate in men was more than eleven times, and in women more than seven times, greater than for the general population, but the death rate for patients with a diastolic pressure which sometimes fell below 95 was of the same order as for the general population.

Among the causes of death coronary thrombosis was uncommon, and though Storm Mathisen admits that this may be explained partly by the patients being young, he thinks that there would have been more such deaths if, in fact essential hypertension predisposes to coronary thrombosis

JOURNAL OF ANALYTICAL PSYCHOLOGY

THE first issue of this journal,[2] published on behalf of the Society of Analytical Psychology in London, is dedicated to Prof C G Jung and forms part of a specially bound volume presented to him by the society on the occasion of his 80th birthday A preface by Dr Michael Fordham, the editor, explains that the journal has been launched in order to afford an outlet for work by the growing body of analytical psychologists in this country, and not only to increase the influence of analytical psychology The editor is assisted by four distinguished British analysts and has secured the collaboration abroad of several eminent analytical psychologists The quality of this first issue augurs well for the journal's future development

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[1] Prognosen ved Essensiell Hypertensjon By HAAKON STORM MATHISEN Oslo 1954 Pp 124

[2] Published by Tavistock Publications Ltd, 2 Beaumont Street, London W 1, to which orders and inquiries should be addressed Subscriptions 21*s* per volume (at present two issues) 12*s* 6*d* per issue

TABLE II—RENAL CLEARANCES (EACH THE MEAN OF THREE PERIODS)

Date	Inulin (ml per min)	*p* amino hippurate (ml per min)	Filtration fraction	Potassium/inulin ratio
Before operation				
June 11, 1954	41 5	220	0 20	1 16
May 16, 1955	49 2	267	0 184	
After operation				
July 12, 1955	29 0	156	0 19	0 4

Hg There was a gap in the preoperative observations because she spent some days at home During the operation there were no large variations in blood-pressure, although it rose slightly while the adrenal was being handled Two days later the pressure was 160/90 mm Hg, and it fell further as time passed (fig 5) More recently higher readings have been obtained, the pressure at her latest follow up visit, on Oct 20, was 156/110 mm Hg A radiograph of the chest thirty one days after operation showed a reduction in the size of the heart and aortic knuckle the transverse diameter of the heart shadow twenty-two days before operation was 145 mm, and thirty one days after operation 130 mm

Heat elimination from the hand, at complete release of vaso constrictor tone achieved by warming, was measured in the right hand on two separate occasions before operation by a modification of the method described by Stewart (1911) The determination was repeated in the same hand under the same conditions after operation The heat elimination was normal preoperatively, and did not fall significantly despite the fall in blood pressure

The *renal clearances of inulin and* p *aminohippurate* were measured on two occasions before operation and again thirty two days afterwards (table II) The first two readings, which agree well, show subnormal function The postoperative determinations show much deterioration, which is reflected also in the serum urea level, which was 68 mg per 100 ml at this time, and which remained at about this level three months after operation The lowering of the clearances is approximately proportional to the lowering of the blood-pressure

The preoperative *clearance of potassium* exceeded that of inulin, although the concentration of potassium in the serum was only 1 9 m eq per litre From this finding, and because of the continued suppression of hydrogen ion excretion, tubular hypersecretion of potassium was presumed to be occurring After operation the ratio of the potassium clearance to the inulin clearance fell to 0 4 and the urine became acid (random pH 5 6)

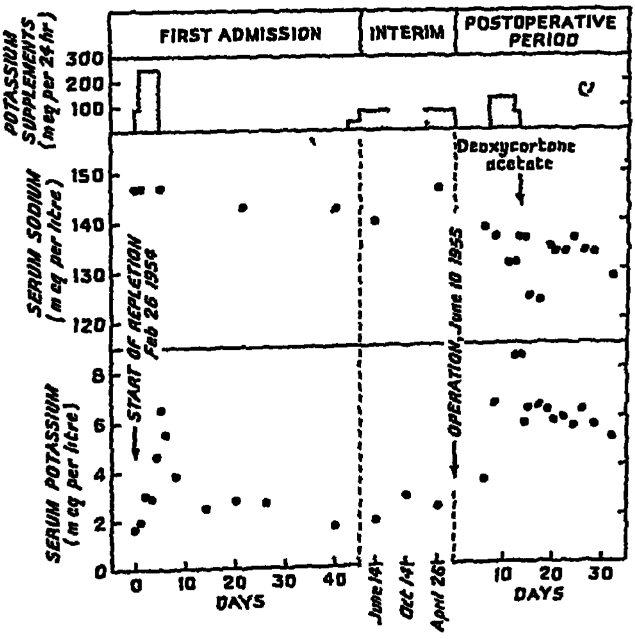

Fig 6—Levels of sodium and potassium in serum throughout period of treatment

The *salivary sodium/potassium ratio* rose greatly after operation (fig 1) To show that the difference is not due to an increase in salivary flow (Garrod et al 1955) the ratios have been plotted against rates of flow

The levels of *sodium and potassium in serum* during the whole period of treatment are shown in fig 6 Four of the seven preoperative sodium values are unusually high (147 m eq per litre) The fourteen values since operation were between 124 and 139 m eq per litre The preoperative potassium concentration, initially low, rose rapidly to a high level (6 5 m eq per litre) on a potassium supplement of 250 m eq per day On a normal diet without supplement it fell to the previous level after thirty five days, and was maintained between 1 9 and 2 9 m eq per litre on a supplement of 80 m eq daily After operation the level rose to 6 5, and, when potassium was added to the diet, to 8 5 m eq per litre At this point 5 mg of deoxycortone acetate was given The level has since remained between 6 5 and 5 2 m eq per litre without supplement

The *serum chloride* level was normal throughout, except on the fifteenth postoperative day when it fell to 94 m eq per litre in keeping with the low sodium level at that time The serum level of *total carbon dioxide* was usually normal, but one value of 32 m mol per litre was observed, and on another occasion the pH of a sample of arterial blood was 7 47

TABLE III—RESULTS OF ISOTOPE DILUTION

Date	Body wt (kg)	Exchangeable Na		Exchangeable K		Remarks
		m eq	m eq per kg	*m eq*	m eq per kg	
March 10, 1954	45 4	2150	47 4	1785	39 3	After repletion
April 7, 1954	44 6	2409	54 0	1441	32 3	After further depletion
June 15, 1954	50 0	2065	41 3	1608	32 2	On supplement
May 18, 1955	55 9			1655	29 6	On supplement
May 20, 1955	55 9	2600	46 5			
June 10, 1955						Operation
July 6 1955	55 0			2088	38 0	
July 8, 1955	55 0	1893	34 4			

The amount of *electrolyte in the tissues* was determined by three methods isotope dilution, analysis of muscle, and measurement of the electrolyte balance The total exchangeable sodium and potassium were determined, usually simultaneously, by a modification of the method of James et al (1954) The results (table III) are expressed both absolutely and in relation to body weight Increases in body sodium were accompanied by decreases in body potassium, and vice versa The first determination, made after the initial repletion with large amounts of potassium, gave values which were within normal limits, although, because of variations in the total mass of muscle and fat, these limits are wide and difficult to define Thereafter, until operation, the content of potassium was low, the content of sodium on April 7, 1954, when the patient had been without a potassium supplement for some weeks, was above normal After operation the most obvious change was a fall in the sodium content of 707 m eq from the last preoperative figure, the potassium content having increased by 433 m eq in the same time These changes are consistent with the hypothesis that the tumour was exerting a salt retaining, potassium losing effect

Also consistent with this hypothesis are the results (table IV) of analysis of the specimen of muscle removed at operation Normal values (Mokotoff et al 1952) are given for comparison

Balance measurements were made during two phases of the patient's illness first, from the time of admission until eighteen days later (during the first six days of this period large doses of potassium were given), and second, during the thirty days immediately after removal of the tumour In the first period there was a net gain of potassium of 767 m eq during the six days for which it was administered, when the supplement was stopped about 200 m eq was lost before approximate equilibrium was established Sodium was lost in excess of chloride during the phase of potassium loading later both sodium and chloride were retained On the assumption that chloride did not enter or leave cells intracellular sodium decreased by 500 m eq while intracellular potassium increased by 639 m eq over the eighteen day period Potassium entered the cells rapidly, but sodium was discharged

ORTHODOXY AND HETERODOXY II*

Sir HENEAGE OGILVIE
K B E , M A , M Ch Oxfd, F R C S ,
Hon F R C S C , Hon F R A C S , Hon F A C S
CONSULTING SURGEON TO GUY'S HOSPITAL

A QUARTER of a century ago I was invited to Chichester to read a paper on Orthodoxy and Heterodoxy in Surgery This was the first time that I had been asked to speak to a medical society It was the first time I had attempted to tackle an essay type of subject, and in this sense the invitation was a decisive event in my career Now I come again after twenty-five years to the same city to speak to the same society on the same subject My talk must therefore fall into two sections first, a re examination of my previous views on orthodoxy in the light of greater experience, and secondly a review of the verdict of history on the orthodoxies and heterodoxies of those far off days

Virtues of Orthodoxy

I pointed out then that a fundamental problem in all institutions is how to combine security with progress, tradition with discovery Security without progress means stagnation and decay, progress without security leads to anarchy and ruin

Orthodoxy means the holding of right or accepted views in matters of public interest The personal affairs of an individual are his own concern, but in matters affecting the many, a general standard of orthodoxy is necessary, indeed inevitable, from which standard any departures are judged Orthodoxy is the sifted and codified view of the majority When we say that a thing is orthodox, we mean that it is the belief of the majority, but not necessarily that we agree with it

Orthodoxy therefore represents the wisdom and learning of the past, and it provides the security of that wisdom An orthodox novelist, scientist, or doctor can be trusted to have as much learning as the last generation of his craft That may seem a small commendation, but it is in fact one of fundamental importance, because where there is no body of orthodoxy there is no assurance to the public that the specialist in any branch of learning knows anything at all A man may set himself up as a surgeon, a preacher, an engineer, or an architect without knowing as much of these arts as an African witch-doctor

This is the value, in surgery, of orthodoxy, and of the machinery of examinations, degrees, and corporations that upholds it It ensures that the surgeon does, at any rate, know something of his job The public has no assurance other than the label provided by the degree—a degree granted by a committee of the orthodox for a knowledge of orthodox practice—that they are entrusting their lives to someone who is not an ignoramus Without such a guarantee the sick man is indeed in a quandary One friend tells him to go to So and so, another to some one else, and he has no better reason than their opinion to guide him in his choice He has no better reason, for nothing better exists He has no expert knowledge himself to enable him to judge between the claims of rival hucksters, and, in the absence of orthodoxy, he would not even know where to acquire that knowledge He is likely to be swindled by teachers as ignorant as himself This is no fanciful picture This was the lot of the sick man throughout the world not many years ago It is the lot of the sick in many parts of the world today It is the lot even in this country of people who, when they are sick, spurn orthodoxy because they know better

Orthodoxy then is the essential basis of civilisation, and the real difficulty is to prevent orthodoxy passing into stagnation, to devise machinery for discarding theories that have ceased to accord with modern views, and practices that have ceased to have value, in short, for ensuring that the heterodox is heard, tested, and, if approved admitted to the body of the orthodox

Authority and Inquiry

The more ancient and stable is a civilisation, the more securely does orthodoxy become enthroned, because the more certainly does authority pass into the hands of the elderly The elderly, who have experienced life's troubles and sifted life's problems, and arrived in the end at an explanation that satisfies them and a modus operandi that works, are usually sure that their conclusions are the right ones, and that any new ideas presented to them are a revival in different guise of the doubts and questionings that disturbed them when they were young The teachings of medicine have always tended to be authoritative The word of Galen was law for more than a thousand years, and any attempt even to question his pronouncements was looked on as dangerous ignorance The Renaissance brought a new spirit of inquiry, but resistance to the new remained Darwin's teachings, humbly though they were propounded, were opposed not merely by the Church but by most scientists Lister's views on the causation of sepsis were scoffed at and his treatment was opposed by the majority of surgeons, and only at Guy's were they received immediately and enthusiastically Like many revolutionaries, Lister in turn became a pillar of the new orthodoxy he had created, and an opponent of the aseptic surgery that his followers were shaping

When I spoke in 1930, I was speaking, though I [illegible] not know it, in terms of a phase of the world's [illegible] that was even then passing away I spoke of "[illegible] tongue tied by authority, and folly doctor-li[illegible] con trolling skill," and of the need to fight for freedom [illegible] per rule of authority received its death blow in the first w[illegible] war, and was even then passing away, at any rates [illegible] countries outside the Iron Curtain Now we ha[illegible] reverse outlook In place of "look before you [illegible] have the maxim "try anything once" In pla[illegible] man of learning we worship the revolutionary We [illegible] displaced the Apollo Belvedere from our art galleries, a[illegible] put in his place a wire puzzle dedicated to the Unknown Political Prisoner

The spirit of inquiry is admirable if it is really inquiry and not uncritical novelty worship It is right that we should examine and consider every new thing that is presented to us, but not necessarily right that we should adopt it Most new things turn out in the end to be wrong When presented with a new project for acceptance, we should first ask "Is it reasonable?" Then, "Is it really new? Has it, or anything like it, been tried before? If so, has it failed, and why? Was the failure due to some inherent defect, or to some circumstances that can now be remedied? If it is reasonable but yet untried, can it be tried without risk? If there is a risk, how can that risk be eliminated or minimised? Are we justified in a full scale trial, or should we first try a pilot experiment? Can the experiment be done first on ourselves?"

Experimentation with the lives of others is as tempting to the rash surgeon as experimentation with the property of others is to the rash politician In each case success means personal credit, failure means a loss to someone else The worst examples of rash enterprise are seen in politics, for the politician must fire off all his rockets before the next election and he seldom has the time for careful consideration or for pilot experiments There has been in surgery no example of foolish enterprise and blindfold experiment comparable to the Ground Nut Scheme in East Africa The idea was magnificent, but

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* Read before the Chichester and District Hospitals Clinical Society on Oct 12, 1955

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pressure, are presumably due to a fall in perfusion pressure, the vascular resistance of the kidney remaining unchanged. The clearances behave similarly during reduction of the blood-pressure by various drugs (Freis et al 1953). Thorn et al (1952) found such changes after sustained falls in the blood pressure of hypertensives brought about by total adrenalectomy; the reduction in glomerular-filtration rate and renal blood-flow was greatest in those patients whose blood-pressures were lowered the most.

It is now well known that chronic potassium depletion can lead to a characteristic nephropathy, in which vacuolation and degeneration of tubular epithelium are associated with impaired capacity for urinary concentration and acidification, and with lowered glomerular-filtration rate and *p* aminohippurate clearance (Schwartz and Relman 1953, Relman and Schwartz 1955). All these features were present in some degree in our patient, although the impairment of acidification was slight (cf Clarke et al 1955). The results of nephron dissection show that the structural changes were almost confined to the proximal tubule. In some of Schwartz and Relman's cases slow recovery followed repair of the potassium deficit.

Summary

A patient with recurrent paralysis due to excessive urinary loss of potassium, and with hypertension, is described.

Alkalosis was slight or (more often) absent. Urinary concentrating power was lost, but the capacity for urinary acidification was only slightly impaired.

A tumour of the right adrenal gland was demonstrated radiographically, and its removal reversed the electrolyte abnormality and lowered the blood-pressure.

Urinary excretion of aldosterone was normal or only slightly increased, but fell after operation. Blood-aldosterone levels were within normal limits.

Renal biopsy showed vacuolation of the tubular epithelium almost entirely confined to the proximal tubule, with minimal changes in the distal tubule.

Isotope dilution and muscle analysis showed that the patient's tissues contained more sodium and less potassium than normal; operation ultimately reversed these changes, but balance data showed that sodium retention occurred for a short time after operation.

Renal clearances of inulin and *p* aminohippurate, initially low, were further reduced after operation, approximately in proportion to the reduction of blood pressure.

We are much indebted to those colleagues named in the text, and to Dr O Garrod, who have been concerned in the investigation or treatment of this patient, and who have allowed us to quote their findings. We also acknowledge gratefully the help of Dr Paul Fourman and the technical assistance of Mr Emlyn Morgan. One of us (M G T) held a Cardiff Royal Infirmary research fellowship in medicine.

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PLASMA FIBRINOLYTIC ACTIVITY IN CIRRHOSIS OF THE LIVER

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A PROTEOLYTIC enzyme is present in normal blood in the form of an inactive precursor, plasminogen, which is associated with the globulin fraction. An inhibitor, antiplasmin, is present in excess in the albumin fraction. Plasmin activity can be produced by streptokinase, which activates plasminogen; by chloroform, which destroys antiplasmin; and by techniques such as fractionation of the plasma which separates the plasmin-antiplasmin complex (Macfarlane and Biggs 1948). Plasmin not only produces fibrinolysis but also digests plasma-proteins (including fibrinogen), casein, and gelatin.

Goodpasture (1914) first reported spontaneous fibrinolysis in cirrhosis of the liver: the clotted plasma obtained from 3 cases liquefied when incubated at 37°C for sixteen hours. He added a 4th case, but in this the plasma was obtained after death. In contrast he found that the blood clots of healthy controls remained unlysed for many days.

Since then spontaneous fibrinolysis has been found in various diseases. It has been observed in patients who have undergone surgical operations (Macfarlane 1937), and according to Ratnoff (1952) Fantl and Simon described its occurrence during electric shock therapy. It has been induced in healthy people by the injection of adrenaline and by severe exercise (Biggs et al 1947).

It has been assumed in the past that spontaneous or induced fibrinolytic activity in the plasma was due to plasmin, but according to Biggs and Macfarlane (1953) Fantl and Simon showed that the fibrinolysin found in the blood of rats subjected to electrical convulsions had no effect on fibrinogen. Bidwell and Macfarlane (1951) noted similarly that the fibrinolysin found in the blood of man after severe exercise had no effect on fibrinogen. They also showed that this fibrinolytic activity was not influenced by the serum inhibitor of plasmin. Biggs and Macfarlane (1953) considered that either the naturally activated factor was not plasmin or, if it was, its action was considerably modified.

Uncontrollable hæmorrhage from multiple sites associated with extreme fibrinolytic activity of the plasma after splenectomy in a patient with cirrhosis of the liver directed our attention to this problem. We report here our observations on the incidence and intensity of spontaneous fibrinolytic activity of the plasma in cirrhosis of the liver and the influence of surgical trauma thereon.

Material and Methods

Observations were made on 30 consecutive cases of cirrhosis of the liver, and on 12 consecutive cases of

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Results

Chlorpromazine 1 mg per kg body-weight intravenously abolished "spontaneous" tetanus (i e no intended afferent stimuli applied) and reflex tetanus for 77 min (mean of 7 experiments) The minimum time was 27 min, and the maximum 120 min During this time the animal did not respond with muscle spasm to the standard afferent stimulus, which before the drug was given produced a pronounced increase in spasm (fig 1) If no afferent stimulus was applied the tetanus was abolished for periods up to twice as long Larger doses of chlorpromazine abolished reflex tetanus for up to 4 hours

The animals were quiescent after chlorpromazine 1 mg per kg body-weight, but normal rabbits given this dose would hop about if encouraged Respiration was unaffected

Control injections of saline did not reduce the tetanus

Promethazine also abolished tetanus, but only in high dosage (4 mg per kg body-weight) and for a shorter time (less than 1 hour)

With these results in mind it was felt justifiable to attempt to control human tetanus convulsions with chlorpromazine alone, for spontaneous respiration and retained consciousness might be of very great advantage, whereas unconsciousness, with or without neuromuscular block, prolonged for many days and possibly even weeks, could not but influence the patient unfavourably

Case-report

A boy, aged $2^1/_2$ years, crushed the tip of a finger in a door on Aug 25, 1955, and was taken to hospital No tetanus antitoxin was given He was later transferred to the plastic unit at Mount Vernon Hospital, where he underwent a repair operation on the same day

On Sept 6 his mother noticed that he could not open his mouth, and on Sept 9 he was readmitted to Mount Vernon Hospital with generalised tetanus convulsions He had continuous trismus and frequent series of opisthotonic spasms, although if undisturbed he would sleep fretfully for periods of 10 minutes without spasm After about 5 hours observation in this state he was given 15 mg (approximately 1 mg per kg body-weight) chlorpromazine intravenously, and within 10 minutes had fallen into a sound sleep with his mouth relaxed for the first time for 3 days 30 minutes later his wet sheets were changed without provoking a spasm, and only one severe spasm occurred in the next 3 hours It was decided to continue with chlorpromazine alone and to increase the dose if necessary An intravenous drip was maintained, and into this, every 2–5 hours, doses of chlorpromazine were given according to the severity of the convulsions

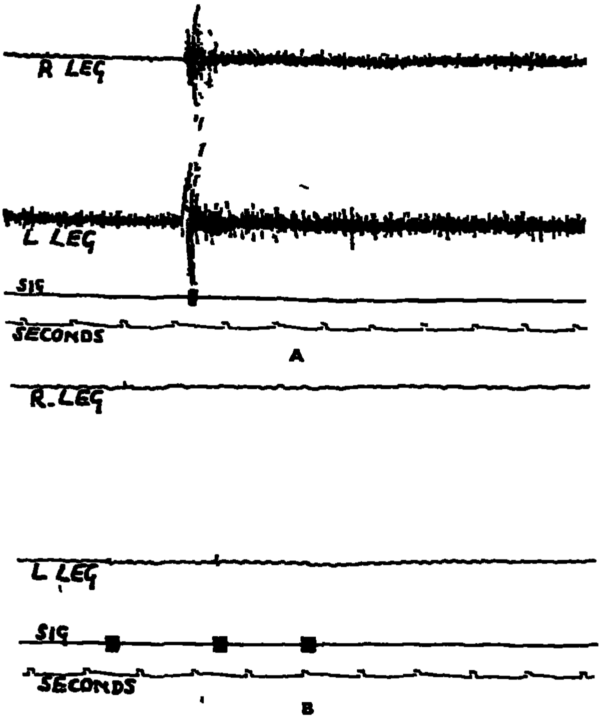

Fig 1—Electromyographs from gastrocnemius region of each hindleg of rabbit after injection of tetanus toxin into left gastrocnemius A severe resting tetanus on left and minimal tetanus on right, with subsequent gross tetanus in both legs, after application of standard afferent stimulus at signal, B, after chlorpromazine 1 *mg* per kg intravenously there is no resting tetanus and three standard afferent stimuli have no effect.

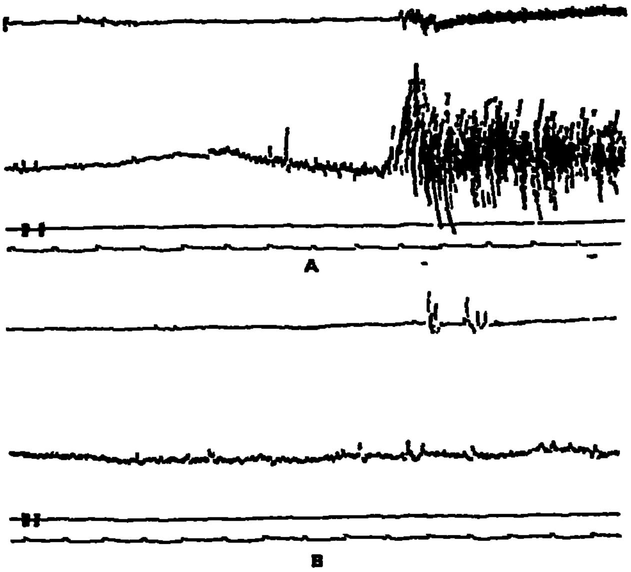

Fig 2—Electromyographs from case of tetanus (surface electrodes) Tracings from above down represent electrical activity of anterior tibial muscles, electrical activity of calf muscles signal, seconds. A, at the signal an oxygen tube was passed up the nose resulting in vigorous spasm of both groups of muscles B, after chlorpromazine the same manœuvre produced no response

The records are not accurately quantitative There is considerable electrode artefact in all tracings, as care was taken to disturb the patient as little as possible in placing the electrodes

The aim was to control the convulsions at a level at which they did not exhaust the child unduly, rather than to achieve complete relaxation (fig 2) That chlorpromazine was effective against the convulsions was demonstrated by their regular cessation or mitigation 20–30 minutes after a dose and their regular recrudescence some time later On three occasions the tetanus became completely out of control, and prolonged and almost continuous severe spasms occurred for 4–6 hours On each occasion it was suspected that the intravenous infusion was not flowing freely, the limb having become grossly œdematous, and on each occasion control was rapidly re-established by an injection of chlorpromazine directly into a fresh vein It was noticed that these occasions each followed a reduction of dosage during the previous night and that a larger dose was required to re-establish control than was needed to maintain control once this was achieved The maximum single dose of chlorpromazine was 40 mg These three occasions also coincided with some extra stimulation—e g, a lawnmower working outside the window, or extensive mouth toilet Apart from these occasions the degree of control varied, but opisthotonic spasms occurred no more than three or four times in a day and minor spasms lasting less than 15 seconds ten to fifteen times a day These spasms usually occurred at nursing times when vigorous afferent stimuli were unavoidable, or 2–4 hours after a dose of chlorpromazine More than half the nursing care, which was applied 30 minutes after a dose, was carried out without provoking severe spasms

At no time was consciousness lost as a result of administering the drug The child was always easily rousable from sleep Respiration was unaffected Phenobarbitone was given to control restlessness as the chlorpromazine was withdrawn Chlorpromazine was given for 16 days, the total daily dose

TABLE II—INFLUENCE OF SPLENECTOMY ON FIBRINOLYTIC ACTIVITY OF PLASMA IN 6 CASES OF CIRRHOSIS OF LIVER
(Operation specimen obtained fifteen minutes after removal of spleen)

Case no	Sample	Fibrin (mg per 100 ml) after incubation for ½–24 hr —			
		½	6	12	24
3	Initial	289	0		
	Operation	0*			
	4 hours	189	24	0	
	24 hours	259	208	181	165
	1 month	455	0		
4	Initial	166	0		
	Operation	160	0†		
	24 hours	498	498	461	423
	1 month	197	0		
9	Initial	251	109	0	
	Operation	294	0†		
	24 hours	267	182	192	188
	1 month	288	128	0	
21	Initial	181	128	80	0
	Operation	246	0†		
	4 hours	181	139	112	0
	24 hours	259	117	‡	69
29	Initial	272	232	214	200
	Operation	230	58	42	0
	4 hours	203	192	‡	‡
	24 hours	460	433	411	411
30	Initial	342	288	280	259
	Operation	85	0†		
	4 hours	133	128	128	128
	24 hours	353	321	307	280

* Test done on undiluted plasma A firm clot formed on the addition of thrombin
† Fibrinolysis complete in less than three hours
‡ Not done

6 of the patients with cirrhosis showing low spontaneous fibrinolytic activity (cases 24 and 26–30) were each given 1 ml of 1/1000 adrenaline hydrochloride subcutaneously The fibrinolytic activity of the plasma from specimens of blood obtained ten, twenty, forty, sixty, ninety, and a hundred and twenty minutes after the injection was estimated In all 6 cases the fibrinolytic activity was intensified, reaching its maximum within twenty minutes The findings at this time are set out in table III In case 26 multiple petechiæ developed in the skin during the test

Fig 2 contrasts the average findings twenty minutes after the injection of adrenaline in these 6 cases with those in 6 healthy controls From this figure it will be seen that, even when the existence of spontaneous fibrinolysis is allowed for, the response of the patients with cirrhosis was significantly greater The duration of this action of adrenaline was much longer in the patients with cirrhosis than in the healthy controls Fig 3 contrasts the duration of effect in the control showing the most active fibrinolytic response to adrenaline with that of case 26, which is representative of the cirrhotic group

TABLE III—EFFECT OF SUBCUTANEOUS 1/1000 ADRENALINE HYDROCHLORIDE ON FIBRINOLYTIC ACTIVITY OF PLASMA IN 6 CASES OF CIRRHOSIS OF LIVER WITH LIMITED SPONTANEOUS FIBRINOLYTIC ACTIVITY

Case no	Time	Fibrin (mg per 100 ml) after incubation for ½–24 hr			
		½	6	12	24
24	B	273	193	†	182
	A	256	0*		
26	B	307	203	193	171
	A	295	0*		
27	B	187	139	†	128
	A	133	64	0	
28	B	241	128	126	123
	A	272	85	0	
29	B	272	232	214	200
	A	250	[illegible]	0	
30	B	342	288	280	259
	A	272	0*		

B = Before adrenaline
A = 20 minutes after adrenaline
* Fibrinolysis complete in less than three hours
† = Not done

Cases 2 and 17 were given daily for five days 10 mg of corticotrophin by slow intravenous drip The results are set out in table IV It will be seen that in both cases there was significant reduction in fibrinolytic activity by the fifth day Six days later it had returned to its previous level Case 31 (see table IV) was first seen on the seventh day of treatment with corticotrophin 120 mg intramuscularly daily, when portal-vein thrombosis had developed The fibrinolytic activity of the plasma was negligible, but four weeks later fibrinolysis was complete in less than six hours

Discussion

No influence on fibrinogen was observed in the plasmas showing spontaneous fibrinolytic activity or when this latter was increased by adrenaline or during operation One of us (H C K) has made further observations which show that the fibrinolysin does not act on prothrombin, gelatin, or casein and is unaffected by the serum inhibitor of plasmin It must be concluded that the fibrinolysin found in cirrhosis of the liver is not plasmin It is present in the plasma in active form and is apparently similar to the cadaveric fibrinolysin described by Mole (1948)

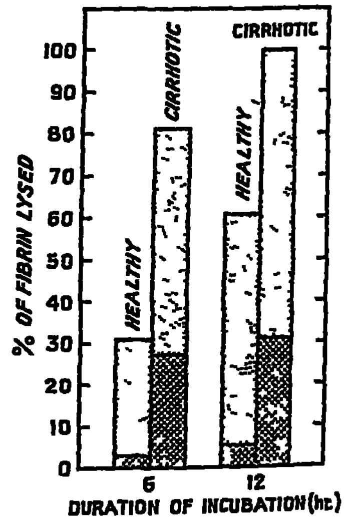

Fig 2—Mean fibrinolytic activity of plasma before and after subcutaneous injection of 1 ml of 1/1000 solution of adrenaline hydrochloride in 6 cases of cirrhosis of liver and in 6 healthy controls *hatched*, before adrenaline *stippled*, increase after adrenaline

Ratnoff (1949), who studied fibrinolysis in 28 cases of cirrhosis of the liver, reported that in 11 of them clotted plasma was lysed within twenty-four hours, and in 15 of the remaining 17 cases between twenty four and forty-eight hours Marrazza et al (1954) found that 5 of 23 cases of cirrhosis of the liver showed complete lysis in twenty-four hours, 15 in forty-eight hours, and the remaining 3 in seventy two hours Both Ratnoff (1949) and Marrazza et al (1954) used recalcified whole plasma, but, as shown by Macfarlane (1937), diluted plasma (used in the present cases) is more sensitive Therefore no comparison of the intensity of activity can be made between these three series It should be noted, however, that our experience is that the fibrin formed by the addition of thrombin is more resistant to fibrinolysis than is that formed by recalcification of citrated plasma

Marrazza et al (1954) concluded that there was a direct relationship between the intensity of the fibrinolytic activity and the severity of the liver lesion Ratnoff (1949) followed the clot lysis time in 6 of his patients as they improved In 2 of these, clinically milder cases than the others, the clot lysis time lengthened, but in the remaining 4 clinical improvement was unaccompanied by any change in the clot lysis time In the present series no relationship existed between the severity of the disease as adjudged clinically, by liver-

Summary

Chlorpromazine and promethazine abolish the muscle spasm of experimental tetanus in rabbits

These drugs probably act by depressing spinal cord interneurones or brain-stem reticular formation

Severe tetanus convulsions in a child were controlled by means of large doses of chlorpromazine alone

We thank Mr R L G Dawson, of the plastic surgery unit, Mount Vernon Hospital, for the opportunity to treat the case reported here One of us (D R L) is grateful to Prof G Payling Wright for helpful discussions The tetanus toxin was given by the Wellcome Research Laboratories We are grateful to the resident medical and the nursing staff of Mount Vernon Hospital, especially Sister K H Joiner, for their coöperation

ADDENDUM

Since this paper was completed Cole and Robertson (1955) have confirmed the effect of chlorpromazine in clinical tetanus when combined with phenobarbitone or chloral hydrate

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SYSTEMIC REACTIONS TO A MERCURIAL DIURETIC (MERCAPTOMERIN)

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The great value of certain organic compounds of mercury in the treatment of œdema, especially that of heart-failure, is well established and many preparations are now in everyday use The occasional occurrence of side effects, some of them serious, is generally recognised and in particular their effect in causing or aggravating kidney damage Conditions listed in *The Extra Pharmacopœia* (*Martindale*) (1952) as contra-indications to mercurial diuretics are acute nephritis and severe renal damage

Toxic Reactions

We have classified the toxic reactions to these drugs into five main groups

(1) Inflammation at the site of injection.

(2) Reactions attributable to the diuresis These are related to disturbance of electrolyte balance, chiefly chloride depletion and dehydration Pre existing renal impairment predisposes to these upsets. Diuresis may cause concentration of nitrogenous waste products and uremia (Barker 1937) Other manifestations are weakness, muscle cramps, and mental changes, with confusion, restlessness, excitement, coma, and death Acute retention of urine may develop

(3) Reactions caused by the mercury in the drug The most important are renal damage, principally tubular, and gastro intestinal lesions The effects are albuminuria, hæmaturia, the passage of casts, anuria, stomatitis, excessive salivation, and hæmorrhagic colitis A variety of skin lesions have also been described.

(4) Cardio-toxic effects, which include ventricular fibrillation and ventricular asystole Although these are usually ascribed to the mercury ion, animal experiments suggest that different organic preparations of mercury produce different cardiac upsets (Chapman and Shaffer 1947) Further, these effects on the heart have been observed most commonly in animals given large doses *Some of the rare sudden deaths* after intravenous injection of a mercurial in heart-failure in humans are attributed to an effect on the myocardium (Volini et al 1945)

(5) Other sudden deaths after intravenous injection have been regarded as anaphylactoid reactions Other allergic reactions described include fever, erythematous and urticarial skin lesions, bronchial spasm, and pulmonary œdema

Acute attacks of gout, toxic psychosis, digitalis poisoning, spontaneous tetany, cerebral thrombosis, and the precipitation of grand mal in known epileptics have been listed among the toxic reactions Of these, acute gout has been regarded as allergic, the others have been thought to be related to electrolyte disturbances or to dehydration after a large diuresis Marrow depression with neutropenia *and* agranulocytosis has been described

In 1942 Degraff and Nadler reported that all deaths from mercurial diuretics up to that time were associated with intravenous injection We have now traced 3 deaths after administration by other routes 1 followed an intraperitoneal injection (Molnar 1935), another was due to tubular necrosis with renal failure after prolonged dosage, mostly intramuscular (Waife and Pratt 1946), and in the 3rd case severe allergy developed after intramuscular injection (Wallner and Herman 1950)

Mercaptomerin

The need for a safe and effective mercurial diuretic that is easily administered is one which manufacturing chemists have endeavoured to satisfy In mercaptomerin sodium ('Thiomerin' Sodium) a relatively recently introduced organic mercurial, *the makers claims of low* toxicity, satisfactory and often prolonged diuresis (Batterman et al 1949, Herrmann et al 1949, Wmik and Benedict 1949, Stewart et al 1950), and little or no locally irritant effects when given subcutaneously would appear well founded if one excepts some of the earlier batches of drug

The studies of Lehman (1947) in experimental animals suggest that mercaptomerin is very much less toxic than certain theophyllinated mercurials as judged by changes in the Q R S of the electrocardiogram Herrmann and his associates (1949), who noted the effect on the E C G.s of patients treated with intravenous mercaptomerin reported no significant changes in conduction or rhythm The results of intradermal testing in humans (Ruskin et al 1950), of subcutaneous and intramuscular injections in mice (Lehman et al 1949), and prolonged use subcutaneously in routine clinical practice show so little evidence of reaction at the injection site that the preparation has been hailed as the mercurial diuretic of choice for home use by the patient or his relatives (Billman et al 1950, Engelberg and Simmons 1950) These claims have not been accepted universally

Observations on dogs made by Handley and his colleagues (1949) using the intravenous route suggest that, weight for weight in terms of mercurial content mercaptomerin is more toxic than meralluride ('Mercuhydrin') After injection mercaptomerin appears to dissociate somewhat slowly and both the therapeutic effect and infrequency of toxic reactions are believed to be related to that *slow dissociation.* Diuresis is less brisk but more prolonged *than with other mercurial* diuretics Lehman et al (1949) suggest that if sufficient time *for dissociation of the compound* is allowed mercaptomerin develops toxicity similar to that of other organic mercurials

Our purpose is to draw attention to reactions which occurred in 4 patients who received mercaptomerin by subcutaneous injection In 1 the development of hæmorrhagic colitis was ascribed to metallic mercury, while in 3 the reactions appear to have been allergic

Case-records

Case I —Mrs G D, aged 70, was admitted to hospital on Nov 12, 1952, because of increasing exertional dyspnœa for

Ratnoff (1949) found that the clot lysis time was three days or longer in 13 patients with infective hepatitis, 2 of whom were in hepatic coma, and in 6 patients with obstructive jaundice. By the same technique in 28 of 29 cases of cirrhosis he found that it was two days or less. The relative inactivity of the plasma in infective hepatitis has been confirmed by Marrazza et al. (1954).

The relative inactivity of the plasma in primary carcinoma is of interest, as are also the high levels of fibrinogen observed. Since each of the livers was cirrhotic, it seems reasonable to suggest that the development of the carcinoma had led to the disappearance of fibrinolytic activity from the plasma. Although the series is too small to warrant inclusion, evidence is accumulating which indicates that spontaneous fibrinolysis is inhibited in cirrhotic patients during intercurrent pyrexial illness and after gastro-intestinal bleeding.

Summary

A study of the fibrinolytic activity in the plasma of 30 cases of cirrhosis of the liver by the quantitative technique described by Biggs and MacFarlane (1953) is reported.

Fibrinolysis was complete in less than six hours in 7 cases, between six and twelve hours in 9, and between twelve and twenty-four hours in 5. In the remaining 9 cases there was a loss of 25–67% of the initial levels. The average reduction in fibrin content after incubation for twenty-four hours was 83%.

These findings are contrasted with those obtained in 12 cases of primary carcinoma arising in cirrhotic livers and in 20 healthy controls. In the former the average reduction in fibrin after incubation for twenty-four hours was 12%, and in the latter 13%.

No relationship was observed between the severity of the cirrhosis and the intensity of the fibrinolysis.

Splenectomy in 6 patients with cirrhosis caused immediate intensification of the fibrinolytic activity—an influence which passed off within four hours. It is in this period that there is risk of hæmorrhage associated with fibrinolysis. Within twenty-four hours of operation spontaneous fibrinolytic activity ceased.

The subcutaneous injection of adrenaline in 6 cases of cirrhosis led to increased fibrinolytic activity, which was on the average of greater intensity and of longer duration than that in healthy controls.

Corticotrophin administered to 2 of the cases showing active fibrinolysis led to a significant reduction in the fibrinolytic activity on the fifth day. It is concluded that suprarenal cortical activity depresses the spontaneous fibrinolytic activity of the plasma, and may play a part in the development of thrombosis of the portal vein observed postoperatively or during corticotrophin therapy in cirrhosis of the liver. The findings in 1 case of cirrhosis of the liver in which portal-vein thrombosis developed during the administration of corticotrophin are reported. At the time when the thrombosis developed, fibrinolytic activity was absent but a month later it was intense.

The fibrinolysin had no influence on fibrinogen, and it is concluded that it is not plasmin but is similar to cadaveric fibrinolysin described by Mole (1948).

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Preliminary Communication

THE INHIBITION OF CLOT LYSIS BY CORTICOTROPHIN

In the course of observations on spontaneous fibrinolytic activity of the plasma in cirrhosis of the liver Kwaan et al.[1] have found that this activity ceased within twenty-four hours after splenectomy and remained absent for seven to twenty-one days before returning to pre-operative levels. They consider that suprarenal cortical activity in the countershock phase may be responsible for the disappearance of fibrinolytic activity and may play a part in the development of postoperative portal-vein thrombosis.

Eisenmenger et al.[2] reported 3 cases of cirrhosis of the liver in which portal-vein thrombosis developed during treatment with corticotrophin. Kwaan et al. observed one patient with cirrhosis of the liver who was first seen on the seventh day of treatment with intramuscular corticotrophin 120 mg. daily, when portal-vein thrombosis had developed. The fibrinolytic activity of the plasma was then negligible, but four weeks later it was intense. Kwaan et al. also reported a significant reduction in spontaneous fibrinolytic activity in 2 cases of cirrhosis of the liver on the fifth day of administration of corticotrophin.

These facts led us to investigate the influence of stimulation of the suprarenal cortex on the lysis of clots produced experimentally.

Methods

In each of 40 adult rabbits thrombosis of the marginal vein of one ear was produced by a minor modification of the technique reported by Grossi et al.[3] A length of the vein was isolated between two bulldog clamps and the medial tributaries occluded by a clamp applied parallel to the marginal vein. A 25-gauge needle was inserted, the vein emptied of blood, and 0·05 ml. of a solution of thrombin 500 units per ml. injected. The vein was allowed to fill by releasing the upper clamp, which was then reapplied. In all the rabbits a firm clot formed, and after fifteen minutes the clamps were removed.

For two days before production of the thrombosis and throughout the period of observation 26 of the rabbits were given intramuscular corticotrophin 10 units per kg. of body-weight daily, divided into 3 doses. The remaining 14 rabbits served as controls. The segments of the veins were examined at short intervals by transillumination and the lengths of clots measured. At the conclusion of the observations all were subjected to microscopy.

Result

In each of the control rabbits the clot disappeared and free flow through the vein was established in from twelve to thirty-nine hours (average twenty hours). Before it disappeared the clot became progressively shorter and free in the vein; thereafter it rapidly disappeared. A biopsy specimen of the vein was taken forty-eight hours after the production of thrombosis, and on histological examination there was no evidence of thrombus. In every case the vein appeared normal.

In 25 of the 26 rabbits treated with corticotrophin the thrombi persisted until the experiment was terminated by the removal of thrombosed segments for histological examination, which in 12 of them was carried out on the sixth day, and in the remaining 13 on the eighth day, after the production of thrombosis. In the exception, forty-eight hours after production the clot had shortened of the fifth and last injection a bloody diarrhœa began and persisted for four weeks, gradually abating No infective cause could be found Sigmoidoscopy on two occasions revealed a granular bleeding rectal mucosa with a few shallow ulcers The urine was normal throughout He was not given dimercaprol (BAL) or other specific treatment for heavy metal poisoning At the time of his discharge on Jan 25, 1954, he was free from all bowel symptoms

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[1] Kwaan, H. C., McFadzean, A. J. S., Cook, J. *Lancet*, Jan. 21, 1956, p. 132.

[2] Eisenmenger, W. J., Slater, R. J., Bongiovanni, A. M. *Amer. J. Med.* 1952, 13, 27.

[3] Grossi, C. E., Clifton, E. E., Cannamela, D. A. *Blood*, 1954, 9, 310.

Discussion

The reactions in these 4 patients were of two types in the first 3 they appear to have been allergic, while in case 4 the hæmorrhagic colitis is most easily explained by excretion of metallic mercury through the wall of the gut —a well-recognised sequel of poisoning with inorganic mercury. The discussion which follows deals mainly with the allergic reactions

Most published reports on mercaptomerin and the makers' original claims suggest not only a low incidence of reactions at the site of injection but also virtual absence of general systemic toxic reactions Herrmann et al (1949), however, reported 2 patients who had mild systemic reactions—chills, fever, and diarrhœa Gold et al (1952) also reported mild systemic reactions (muscle pain and fever) The systemic toxic reaction was severe in 3 of our patients and mild in 1 (case 3) In cases 1 and 2 the reactions were characterised by severe prostration and circulatory collapse, and in cases 1 and 3 by fever We can find no published account of so severe a reaction as those observed in cases 1 and 2 though reactions more or less similar both in type and severity have been reported with other organic mercurial diuretics given by various routes—e g, Snell and Rowntree (1928) (intravenous 'Merbaphen'), Gelfand (1949) and Harris (1953) (intramuscular mercuhydrin), and Andrews (1931) (*intravenous* 'Salyrgan')

In their time relationship to the giving of the injection and in the prominence of cyanosis and circulatory collapse, the reactions in our patients are very similar to those described following the use of other mercurials Certain characteristics of these reactions suggest an allergic mechanism Harris (1953) points out that they rarely follow the initial dose of the drug Their severity increases with each successive dose and is unrelated to the size of the dose The arguments in favour of an allergic basis are well stated by Gelfand (1949) who, in a patient treated with mercuhydrin, also demonstrated skin sensitivity to serum from another patient treated with mercuhydrin It appears that the effect of the first few doses is to sensitise the patient and that later doses induce an allergic response In most cases and initially this response is mild, fever, chills, and cutaneous eruptions being common manifestations The early reactions in our first 3 patients were of this order When, in such cases, the use of the same mercurial is continued, even in small doses, violent and dangerous reactions may follow (cases 1 and 2) In case 3 if treatment had been continued more severe reactions would probably have occurred Here it may be mentioned that cases 1 and 2 were under the care of different members of the staff and that their assessments of the illness which followed the use of the drug were almost identical In each case those concerned suspected an acute coronary attack and anticipated a fatal result

In case 1 the reaction after the last injection was unusually long and severe Improvement appeared to follow cortisone and we should use that drug again in similar circumstances In seeking safeguards against such reactions, the absence of any past history or family history of allergy in our patients is important Harris (1953) states that preliminary skin-testing is rarely helpful in detecting latent allergy

It is interesting that hypersensitivity to one organic mercurial may not imply hypersensitivity to other members of the group (Fox et al 1942) Conversely, lack of allergic response to one compound is no guarantee that other compounds would be safe (case 2)

The variations in the organic moiety from preparation to preparation could reasonably explain variations in the incidence of allergic reactions Gold et al (1952), who endorse the view that some patients have apparently allergic reactions to mercaptomerin, suggest that dissociation of the organic mercurial into its inorganic and organic moieties is necessary for both the therapeutic action and toxic effect

Our 4 cases were collected within a period of two years from a hospital with about 120 general medical beds and this suggests that systemic reactions to mercaptomerin may not be rare The drug was given as directed by the makers The 4 cases were under treatment when different consignments of drug were in use in the hospital Other patients treated with the same batches of mercaptomerin were not affected

It is apparent that mercaptomerin can cause a generalised systemic reaction Degraff and Nadler (1942), referring to all organic mercurial diuretics, asserted "that all of the commercially available drugs of this group have at some time or another been reported as producing alarming symptoms" Mercaptomerin does not appear to be the exception and reactions to that drug may be extremely severe The patient's history is unlikely to indicate a probable reaction On the other hand, unexplained fever, especially if repeated, after the injection of an organic mercurial is, in our opinion, an indication to stop giving that preparation and to use a different one Attempts to establish the guilt of the original compound are not without risk to life *

Summary

4 patients had systemic toxic reactions to subcutaneous injections of mercaptomerin ('Thiomerin') The reactions did not appear to differ from those induced by other organic mercurial diuretics given by other routes The mechanism of the reactions is discussed

We are grateful to Dr C G Parsons for permission to *publish cases 2, 3, and 4, to Mr J G Williamson for the* diagrams and to Miss J Buckingham for secretarial help

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* In the leaflet enclosed with each bottle the makers of 'Thiomerin' Sodium now include the following *note* "Discontinue injections if symptoms of hypersensitivity to mercury appear, as flushing of the face, fever, chills, gastrointestinal disturbances, cutaneous eruptions, pruritus or urticaria Some individuals may be sensitive to one mercurial yet tolerate another"

such deaths should be ascribed to gross mismanagement of anæsthesia He was disappointed that no mention had been made of any therapeutic measure He wondered whether after an anoxic incident ensuing cerebral œdema prolonged and increased the damage, and might hypothermia be indicated to mitigate the damage in this immediate postanoxic period?

Dr B G B LUCAS thought that more stress should be laid on the difference between cerebral anoxia and cerebral ischæmia In the latter not only was the oxygen cut off but in addition there was deprivation of substrate, in these cases the damage was more severe and recovery less likely He had found it difficult to obtain experimental evidence of cerebral damage due to anoxia alone, but ischæmic changes induced by centrifugation were easily demonstrable

Dr F FONSECA (Portugal) asked whether glutamic acid had been tried in cases of cerebral anoxia, and Dr LUCAS replied that he had had no success with it but thought that succinic acid had helped in 2 out of 3 cases of carbon-monoxide poisoning in which he had tried it

Dr D H P COLE drew attention to hyperpyrexia as an important clinical sign He said that he and Dr D E Argent had been treating cerebral anoxia by a dehydration regimen in accordance with the hypothesis put forward by Seldon that some of the cells were reversibly damaged by the anoxia, and that their survival was threatened by ensuing cerebral œdema caused by simultaneous anoxic damage to the cerebral capillaries He had seen beneficial results in cases of cerebral anoxia treated by intravenous 50% sucrose followed by a 10% dextran drip A lot of the terrible post-anoxic sequelæ might be avoided if this therapy were used more often

Dr WOOLF replied that in his view cerebral œdema had only a very small effect on the vitality of nerve cells but was, nevertheless, important as a cause of cerebral damage owing to its effect on nerve fibres and especially myelin sheaths

Professor MEYER, replying to the discussion, said that from the pathogenic point of view anoxia was a combination of direct action of oxygen want on the nerve cells, capillary stasis resulting in ischæmia, and increased permeability resulting in œdema All these factors must be considered in explaining the localisation of the lesions He cited a report by Landenberg that cerebral œdema might exercise particular pressure on certain arteries at the base of the brain or in the depth of sulci

Dr BEDFORD did not subscribe to the use of hypothermia in these cases, he found it difficult to envisage cerebral ischæmia occurring clinically without cerebral anoxia

Dr ALLISON said that the term "organic neurasthenia" was undesirable as it conveyed the impression of a functional origin He had been impressed by the clinical similarity between post-anoxic and some post-traumatic conditions and wondered whether œdema was perhaps a common factor

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New Inventions

AN IMPROVED METABOLIC BED

FOR quantitative analysis in the diagnosis and management of disease, accurate collection of urine and fæces over timed periods is commonly necessary Some form of metabolic bed must be used for infants or incontinent patients, and prevention of pressure sores may be difficult if collections are prolonged By means of a specially designed foam mattress on a wooden frame, collections have been made without difficulty from children for several consecutive days for detailed metabolic studies, particularly in phenylketonuria

The mattress (fig 1), made of foam-rubber, has a single central hole 6–8 in in diameter (the size depending upon the size of the patient), and a smaller hole 2 in in front of the main one carries the glass or plastic urinal required for collection in boys The mattress is encased in an impermeable rubber sheath to which the foam-rubber is firmly attached throughout This permits sterilisation and also prevents wrinkling of the mattress, which is one of the principal factors in the development of sores Washable rubber flanges protect the inner surfaces of the two holes, and through the larger hole fæcal collections are made without soiling the mattress The entire mattress can be scrubbed and can be sterilised by autoclaving, either with formalin or by steam sterilisation

The mattress is placed on a wooden frame (fig 2) which has a firm plywood base complete except for two holes corresponding to those in the mattress itself The under-part of the frame is hollow and a flap permits siting of receptacles beneath the holes in the mattress for collection of urine and fæces separately The frame and mattress are made to fit inside a standard child's cot The head of the frame can be raised, this eases nursing and prevents the child slipping off the mattress holes The child rests directly on the rubber skin of the mattress with draw-sheets above and below the holes and with the buttocks resting over the larger hole A cruciform binder, with armholes and with buttons down the back, secures the child in the required position and allows considerable freedom of movement of the arms and legs, only the pelvis being held above the mattress hole A second, similar, restrainer applied correctly —i e, with the buttons at the front—prevents the child from falling forward, but still allows freedom of

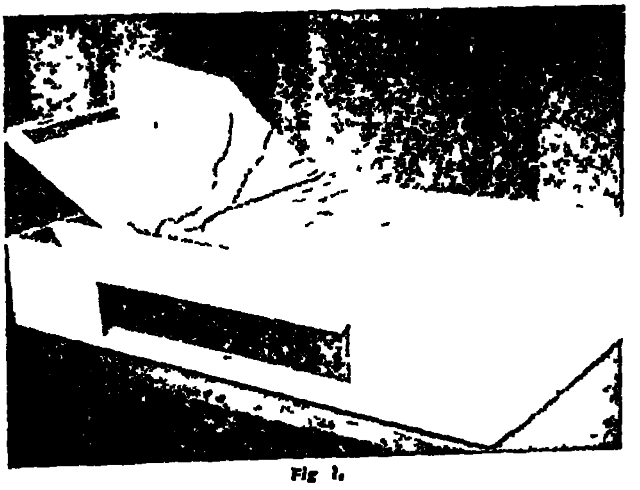

Fig 1.

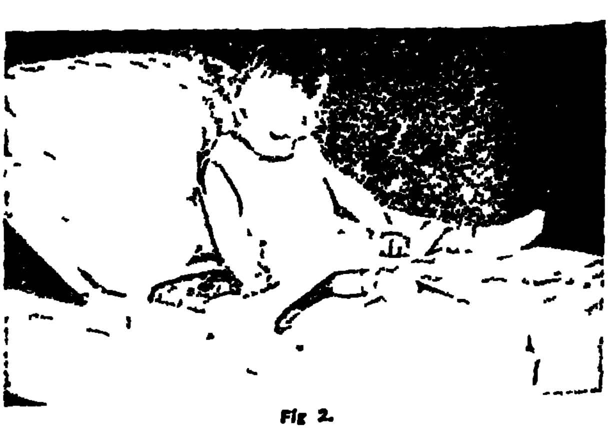

Fig 2.

normal and worked well After some weeks, since the patient seemed so settled, the baby was brought home and the patient looked after him Almost immediately she began to relapse, until she was again so depressed that she had to be admitted to an observation ward. Here once more she made a rapid superficial recovery

She was transferred to the neurosis ward, and was told that she could have the baby in hospital with her, but this she thought was no use since she felt that she would never again be a good wife or an adequate mother She wished to go out to work so as not to be a burden on her family She was allowed to go out to look for a job, but after a time she decided to try having the baby in hospital She became more depressed for a time, and was by now very drawn and haggard Psychotherapy was continued, and gradually the patient did more for the child became less depressed, and made a good recovery which has enabled her to look after her child for the subsequent two years.

Case 3 had been a quiet child, who mixed poorly and had difficulty in asserting herself She was thought to have been spoilt by her parents Her husband was perhaps rather obsessional, but was very reliable and helpful to the patient and was clearly fond of her The baby was wanted; the labour which was normal, was conducted in the patient s own home The patient found feeding the baby difficult, and despite much support and help she became gradually more withdrawn until, when the baby was a month old, she was very strange in manner, and told her husband that she had pneumonia (although really she was physically fit), that she felt that people were accusing her of neglecting the child, and that she was going to be stoned to death She was admitted to the observation ward, where she became well enough to be transferred after seventeen days to the neurosis ward Her husband encouraged her to stay, and brought the baby to her in hospital She was treated by psychotherapy, discussing her fears about the child, and her difficulty in caring for him, besides her past relationships, particularly with her parents She made a good recovery She has remained well and has cared for her child without interruption for two years

Case 4 was brought up in a Dr Barnardo s home from the age of four years, because her mother, who was pregnant at the time of her husband s death could manage to care for only the youngest and oldest of her nine children The mother visited the patient infrequently, so gradually they meant less to each other After leaving the home the patient did a domestic job until her marriage In the puerperium she became depressed, and so was transferred to the psychiatric unit, where she attempted suicide and continued to get more depressed She was transferred to a mental hospital under certificate

After two months in the mental hospital during which she had a course of E C T, she was discharged recovered and was referred back to the outpatient department This patient stayed at home with her husband while the baby remained in the nursery, where he had been while the patient was in hospital The matron of the nursery coöperated with treatment, allowing the patient to choose how much she did for the baby, and encouraging her to come to the nursery as often as she wished The patient attended the outpatient department for psychotherapy several times a week. At this time she discussed her relationship to her husband and child, whereas in her more disturbed state she had discussed her past relationships The patient gradually assumed charge of the baby, until she took him home and was fully responsible for him. She has not relapsed

Six patients have been successfully treated in this way and have not relapsed in the two years over which they have been followed up This series, though small suggests that in cases of postpartum psychosis the patient should be treated in a unit to which her baby is also admitted

This work was done in the psychiatric, maternity, and pædiatric departments of the West Middlesex Hospital.

I would like to thank Dr F P Haldane psychiatrist, West Middlesex Hospital for permission to publish this paper, and Miss H. B Schaler for assisting in the follow up

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δ-AMINOLÆVULIC ACID AND PORPHYRIA

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IN 1954 Goldberg et al showed that porphobilinogen has no pharmacological actions which can explain the symptoms of acute porphyria The immediate precursor of porphobilinogen is δ-aminolævulic acid (Dresel and Falk 1953, Gibson et al 1954 Granick 1954, Schmid and Shemin 1955) which can take the place of glycine and "active" succinate in the synthesis of porphyrin and hæm (Shemin and Russell 1953, Neuberger and Scott 1953) and is excreted in the urine by patients with acute porphyria (Granick and Vanden Schrieck 1955) We have therefore investigated some of the pharmacological properties of δ aminolævulic acid using two samples of the hydrochloride kindly placed at our disposal by Prof A Neuberger, F R S, and Dr J J Scott

During attacks of acute porphyria the patient may have hypertension and tachycardia In the cat, δ aminolævulic acid in doses of 100 μg per kg body-weight (in one test 0 5 mg per kg) did not alter heart-rate or blood-pressure There was neither potentiation nor inhibition of responses to adrenaline or to noradrenaline

Other symptoms of an attack of acute porphyria may be abdominal pain, constipation and distension of the large gut Isolated guineapig ileum gave no response to a dose of 100 μg in a 20 ml bath. In this dosage δ-aminolævulic acid had no effect on contractions produced by histamine, by acetylcholine, and by 5-hydroxytryptamine On isolated rat's colon the same dose had no effect and did not alter the responses produced by acetylcholine and by 5 hydroxytryptamine

The result of this preliminary investigation suggests that δ-aminolævulic acid does not possess any pharmacological properties that might explain the cardiovascular and the abdominal symptoms which are a constant and prominent feature of an attack of acute porphyria δ-Aminolævulic acid administered by mouth to man is rapidly excreted by the kidney (Berlin et al 1954a), as is porphobilinogen (Goldberg and Rimington 1954), and causes no symptoms resembling those of acute

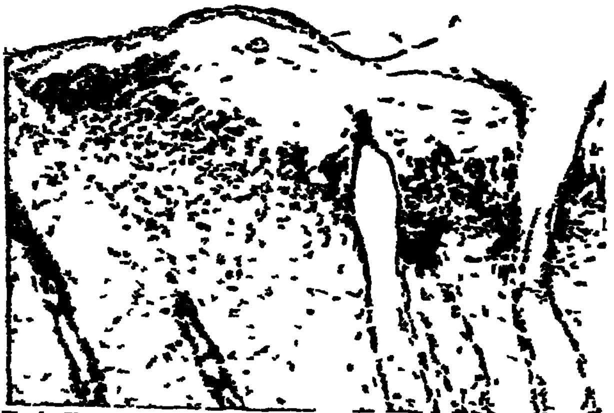

Fig 1—Skin of rat receiving δ-aminolævulic acid and ultraviolet irradiation Note early blister gross damage to collagen, and lymphocytic infiltration (Hæmatoxylin and eosin ×160)

Only the neurological section seems uneven there is, for example, no discussion of the common problem of cervical spondylosis and its effects upon the cord, and the article on acroparesthesia does not mention the good results achieved by decompression of the median nerve

A most valuable feature is the emphasis on the biochemical and physiological aspects of disease, and the account by Professor Loeb of the metabolic processes in diabetes is outstanding

Studies on the Cerebral Cortex

SANTIAGO RAMON Y CAJAL Translated by LISBETH M KRAFT London Lloyd Luke 1955 Pp 179 27*s* 6*d*

DURING 1901 and 1902 Cajal published a series of papers in the *Trabajos del Laboratorio de Investigaciones Biologicas de la Universidad de Madrid*, on the "limbic lobe," which Broca had described in 1878 Cajal's studies were undertaken to discover the relationship of this part of the brain to olfactory function They formed part of a more extensive paper on the origins and terminations of the olfactory, optic, and acoustic nerves in vertebrates which had already been presented to the Royal Academy of Medicine of Madrid Many will be grateful to Dr Kraft for her admirable and careful translation, and to Dr Paul D Maclean who encouraged her to undertake the work and so make another of Cajal's classical studies available to the English-speaking world for the first time in its original form' The publication is timely in view of the present great interest in the control of psychomotor epilepsy The drawings are well reproduced

Selection of Anesthesia

JOHN ADRIANI, M D, director, department of anesthesiology, Charity Hospital, professor of surgery, school of medicine, Tulane University, Louisiana Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 327 47*s* 6*d*

THIS book is best considered in relation to the circumstances of anæsthesia in the United States, where most anæsthetics are still administered by nurse-technicians Supervision may be by an anæsthetist, but is often by the surgeon, so that the selection of drugs and technique may have to be made by someone who has no special knowledge or training in the specialty For him and for physicians who are asked to advise on the fitness of patients for anæsthesia, Dr Adriani has collected a considerable amount of factual knowledge The pharmacological effects of drugs used in anæsthesia, and their relation to non-surgical conditions and to the operation, are set out so that the method best suited to the individual case can be chosen

Some may doubt whether this is the best way of selecting an anæsthetic, since practical experience is often a better guide to safety than a theoretical knowledge of drug action, though a combination of both is obviously ideal Nevertheless, as the doctor must in this case advise the technician, it is as well that he should have some understanding of the problems from the anæsthetic rather than the purely pharmacological or physiological point of view This he can obtain simply and accurately from Dr Adriani's book, but he must make some allowance for the differences in clinical practice on the two sides of the Atlantic

Textbook of Occupational Therapy

With chief reference to Psychological Medicine E N M O'SULLIVAN, M B, D P M, superindentent Killarney Mental Hospital London H K Lewis 1955 Pp 319 21*s*

THIS comprehensive book deals with every aspect of occupational therapy, with special reference to psychiatry It covers the history, objects, organisation, and craft analysis, and there is a description of the mental diseases likely to be met with by the therapists

Dr O Sullivan recognises that occupational therapy covers much more than merely crafts and he sees the importance of recreation pure and simple, as well as work in the utility sections He stresses the importance of constant contact with the doctor who should always prescribe and supervise

The establishment of 3 trained occupational therapists in a hospital of 1000 beds seems very modest, but when the establishment is increased, as Dr O'Sullivan suggests, by attaching nurses and special technicians skilled in certain handicrafts, patients will have the best of different disciplines His re educational scheme is well planned too well planned perhaps, since the complete regimentation that he describes on pp 115–118 might fail to be therapeutic

In contrast to most mental hospitals in this country, the segregation of the sexes in Dr O'Sullivan's hospital appears to be rigid, and apart from entertainments a special occupational therapist is allocated to each sex

This book is a valuable addition to the medical and nursing libraries of the mental hospital

Atlas de chirurgie thyroidienne

JACQUES FRANCILLON, chirurgien des Hôpitaux de Lyon, CLAUDE GABRIELLE, Interne des Hôpitaux de Lyon Paris Expansion Scientifique Française 1955 Pp 180 Fr 3000

BY means of copious and clear illustrations with an explanatory text opposite each, the authors deal fully with the surgery of the thyroid They describe in detail several operation techniques, emphasising the many difficulties and suggesting methods of surmounting them Unfortunately the choice of techniques is left to the reader, who is given no lead as to which the authors think best

Different methods of incision are described, but the writers apparently prefer the old fashioned "U" incision, since this is used in all the illustrations of technique

A chapter is devoted to dislocation of the thyroid, and includes a minute description of its blood supply and all possible methods of hæmostatic control The normal and abnormal anatomy of the recurrent laryngeal nerves and of the parathyroids are fully described

Another chapter reviews the many techniques employed for the resection of the thyroid lobes, with and without exteriorisation And the final chapter describes in minute detail different techniques in suturing and drainage

A wide survey has been made into the literature and techniques of thyroid surgery which should prove extremely interesting to surgeons experienced in this specialty

The Practitioner's Handbook to the Social Services

ALFRED H HAYNES, F W I Bristol John Wright 1955 Pp 124 9*s* 6*d*

WRITTEN by a practising social welfare officer, the book gives a good account of the details of the Welfare State in this country Even those in general practice, who are in daily contact with social as well as medical problems, and who are most familiar with the machinery of the National Health Service, will be surprised at the extent of the social organisation here described The practitioner will find the answers to problems of social administration into which he had some insight but lacked full knowledge

In its fourteen chapters the book includes the work of executive councils, regional hospital boards, and local health authorities, and accounts of National Insurance, National Assistance, Education Housing Legal Aid, and other services to the community Mr Haynes's experience has enabled him to interpret the many Acts of Parliament and other official documents in a readable way

The book will be useful to the visitors to this country who require a short but comprehensive account of our social services, and to the new entrant to general practice

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Whitaker's Almanack 1956 (London Whitaker Pp 1190 17*s* 6*d*)—This year's issue includes as features additional to its well known repertory (1) the Ministry of Labour's Index of Retail Prices, showing the level for each month from June, 1947, to August, 1955, and detailed figures for the latter month, (2) two tables showing the distribution of gross and net incomes, (3) a table showing personal expenditure and (4) a comparison of the expenditure of Local Authorities and that of the Central Government The principal ships of the Royal Navy at last stage a come back and the national and the local Nature reserves are described the epidermis, suggesting an intensification by irradiation of the transformation into porphyrin Pimenta de Mello (1951) found the urinary coproporphyrin of lead-poisoned rabbits to be much increased by exposure of the animals to ultraviolet rays, and Gillman et al (1945) observed an increased amount of porphyrin in biopsy specimens of human liver from pellagrins after body irradiation

A factor which may play a dominant rôle in determining the distribution of porphyrin after injection of either δ aminolævulic acid or porphobilinogen is the relative ease with which these two precursors may enter cells Fowl erythrocytes permit the ready entry of δ aminolævulic acid but are much less permeable to porphobilinogen (Falk et al 1956) Should these permeability differences extend to other cells, one could imagine the rapid entry into the epidermis (and tissues generally) of δ aminolævulic acid from the body-fluids and its transformation there into uroporphyrin, enhanced perhaps by light, the brilliant fluorescence of the exposed epidermis and its injury under irradiation would therefore be understandable

More detailed work is obviously necessary to substantiate this hypothetical explanation of the present findings, but a further analysis of the problem, together with assays of excreted δ aminolævulic acid and porphobilinogen by patients with porphyria having cutaneous and abdominal symptoms respectively, should help us to understand the chemical-pathological differences between these types At any rate it seems to be acceptable, from the experiments here recorded, that δ aminolævulic acid alone cannot be held directly responsible for the abdominal or cardiovascular disturbances seen in the typical attack of acute porphyria

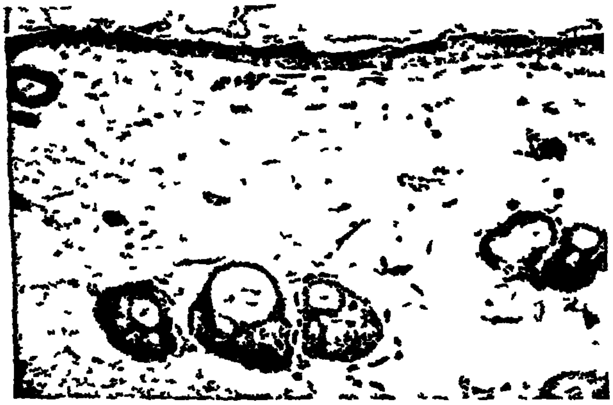

Fig 5—Normal control (Hæmatoxylin and eosin ×160)

Frozen sections were prepared by Mrs J Hardy and photomicrographs by Mr A Bligh Dr R Moulton assisted in the pharmacological preparations, and Miss B Tooth with the urine analyses

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CONN'S SYNDROME WITH SEVERE HYPERTENSION

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WE describe here a patient in whom an excessive loss of potassium in the urine was associated with the presence of a benign adrenocortical tumour, and was abolished by its removal When this patient first came under our care, Conn's (1955a) account of primary aldosteronism had not been published, and we were content to attribute the loss of potassium to a primary renal lesion The patient was not acidotic, however, and her urine could be acidified, so her case was comparable to that of Earle et al (1951), and contrasted with the more usual "potassium-losing nephritis" in which failure of hydrogen ion excretion accompanies the inability to conserve potassium

When Conn (1955a) described his patient in whom a salt-retaining hormone was secreted in excessive amounts by an adrenocortical tumour, and suggested that other cases of supposed potassium-losing nephritis had a similar cause (Conn 1954), we reinvestigated our patient (who had meanwhile been kept well with a supplement of potassium) and found a tumour of the right adrenal gland This patient differs from the small number already recorded (Conn 1955b) in several respects, among which was her severe hypertension The satisfactory fall in blood-pressure which followed operation supports Conn's suggestion that other such cases should be sought among hypertensives

Case-report

A housewife, aged 43, was admitted to hospital in February, 1954, because of weakness of the limbs and neck and diarrhœa For nine days she had had up to six watery motions daily, without mucus or blood At 2 A M on the sixth day she was awakened by nausea, on trying to get up to vomit she found that she could not move her limbs or raise her head off the pillow For about three years she had had attacks, each lasting about a week, in which her arms felt stiff and useless, she was unable to perform actions requiring sustained muscular contraction, such as holding a knife to cut bread Her husband noticed that during these attacks her head would loll forward, and that when she walked her feet would slap on the floor About the time that these attacks began she noticed excessive thirst, worse during the attacks, but present also during the intervals between them This was accompanied by nocturia, at first infrequent but becoming more severe, so that she had regularly had to pass urine three or four times a night She had never noticed any abnormality of the urine, nor had she had any symptoms suggesting a urinary infection No member of her family had had any kind of paralysis

Examination

The weakness was patchy and asymmetrical The patient could not lift her head off the bed, abduct either arm, or extend either elbow, flexion of the left elbow, grip of the right hand, and flexion of the hips and knees were also weak Other movements were strong The tendon reflexes were brisk, and place primarily within the cells, which may help to explain the absence of œdema despite considerable sodium retention. A striking feature in the patient described by Dr **Chalmers** and his colleagues was the degree of hypertension, which fell from 220/140 mm. Hg to 160/90 after removal of the tumour. It remains to be seen how far the renal disturbances are permanent: some are directly attributable to potassium depletion and hence are potentially reversible, others may be related to nephrosclerosis.

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In the early stages of aldosteronism the correct diagnosis may be suggested by a combination of hypertension and hypokalæmia, which may be suspected from the electrocardiogram. It is important to determine what rôle, if any, aldosterone has in the genesis of essential hypertension: already it has been claimed that the excretion of the hormone is increased in this disease.[27] A puzzling feature of Conn's syndrome is the absence of œdema. Professor **Mach** and his associates have described a woman with recurring attacks of œdema and sodium retention who excreted increased amounts of aldosterone but did not have hypokalæmia or polyuria.[22] They suggest that the clinical picture may be determined by the amount of aldosterone secreted, since small doses of deoxycortone cause salt and water retention whereas, in dogs, large doses induce a polyuria and hypokalæmia.

Contraception

> "*Control by men and women over the numbers of their children is one of the first conditions of their own and the community's welfare, and in our view mechanical and chemical means of contraception have to be accepted as part of the modern means, however imperfect, by which it can be exercised.*"—Royal Commission on Population.[28]

Contraception now plays an important, and many would say a beneficial, part in our daily lives. Apart from those who object on religious grounds, there are probably few married couples who do not at some time employ it. But it is not true, as many unmarried people assume, that there exists "contraceptive information" which makes it possible to avoid or space pregnancies without difficulty, and without prejudice to coital enjoyment. Contraception by the best available methods, occlusive or spermicidal, is a nuisance and often an anxiety. It can be practised with fair success, so far as avoidance of pregnancy is concerned, by educated people with good sanitary facilities, using it upon premeditated occasions, but for the ill-equipped or unintelligent it is quite inadequate. This view is well restated by Dr G. I. M. **Swyer**[29] in the January issue of *Family Planning*, which celebrates the twenty-fifth anniversary of the Family Planning Association. Reviewing the work on contraceptives now in progress, **Swyer** says that research on less clumsy and more reliable techniques for controlling fertility has had a recent impetus from fears about the world's food-supply; and it is reasonable and right to expect contraception to contribute to the solution of this problem. But the tone of some "neo-Malthusian" comment merits the rebuke directed by **James Parkinson** to **Malthus**, that "if the population exceeded the means of support, the fault lay not in Nature, but in the ability of politicians to discover some latent defect in the laws respecting the division and appropriation of property." A more liberal justification for contraceptive research lies in the part which a simple and reliable method could play in extending human freedom of choice and deepening human relationships. The biologist who gives time to this problem need have no doubt that he is meeting a universal human need and wish.

An ideal contraceptive should, in the words of **Parkes**,[30] "be effective over a known period of time, simple enough to be generally available and easily usable by any people intelligent enough to know the possible consequences of coitus, and whether they do or do not wish to conceive. Ideally, it should involve only occasional dosage by mouth. It should certainly not depend on local action contemporaneous with coitus. It should have no other effects than the prevention of conception"—or, of course, prejudice subsequent fertility when discontinued. In seeking biological means of achieving this, attention has been devoted to two groups of substances: (1) antihyaluronidases, which interfere with the penetration of the ovum by sperms, and (2) two materials which have been regarded as hormone antagonists—namely, extract of gromwell (lithospermum), which appears to antagonise the pituitary gonadotrophins, and *m*-xylohydroquinone. This second substance was identified by **Sanyal**[31] as the ingredient of oil of peas which reduced the fecundity of rats on a pea-meal diet, and it seems to antagonise vitamin E and to inhibit the actions of œstrogen and progesterone on the endometrium. Synthetic *m*-xylohydroquinone has had fairly extensive field trials in India,[32] [33] capsules being administered to women monthly at about the time of ovulation; and it certainly appears to reduce fertility. But recent papers by **Sanyal** and his co-workers provide a striking example of the problems which arise in such work. With contraceptives, though toxicity tests in animals can and must be undertaken, clinical trial on human patients, on a large scale, is the only final means of estimating efficacy and judging untoward effects on health, subsequent fertility, and any pregnancies which may occur in spite of the drug. In these respects *m*-xylohydroquinone satisfied its investigators—on the basis of some blood, urine, and pulse-rate investigations during the experiment, undertaken, it seems, to meet criticism from America that toxicity had not been fully excluded; and in view of the fact that it had been previously given to over 800 private patients without complaint, **Sanyal, Banerjee,** and **Sen**[33] conclude that "all these definitely prove that *m*-xylohydroquinone is not at all toxic to the human system." They now propose to investigate its exact mode of action. As the substance concerned is said to be a hormone antagonist affecting both œstrogen and progesterone, one must hope that their confidence is justified, for the tests so far reported would prove the harmlessness of, say, benzpyrene. In present circumstances women in Asia might well be prepared to accept some degree sample of the present patient (May 5–12) showed an abnormally high aldosterone content as far as can be ascertained with the limited data so far available. The extract from this specimen was also extensively fractionated by partition column chromatography, and no biological activity as detected by the Na K method (Simpson and Tait 1952) was found in any fraction except those expected to contain aldosterone At the levels tested, aldosterone therefore accounted for at least 90% of the biological activity in this extract

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The results of the assay of the pooled specimen were not available until after operation, so the information obtained from this line of approach at that time was that an excess of aldosterone was not present in the blood or urine It nevertheless seemed necessary to try to demonstrate an adrenal tumour anatomically

Anatomical study —No adrenal tumour was palpable and plain radiography and intravenous pyelography showed no abnormality except poor concentration of the dye, the kidneys were of normal size After presacral insufflation with oxygen (Dr Bryan Williams) plain radiographs although they showed the renal and splenic outlines clearly, failed to reveal an adrenal tumour, but tomograms showed at the apex of the right adrenal a superimposed shadow, almost perfectly round and about 2 5 cm in diameter (fig 2)

Operation

On June 10 the right adrenal was exposed by Mr D B E Foster A friable yellow tumour of the size and position suggested radiographically was found and removed together with the whole of the right adrenal gland. Renal and muscle biopsies were also taken, *the kidney did not look abnormal*

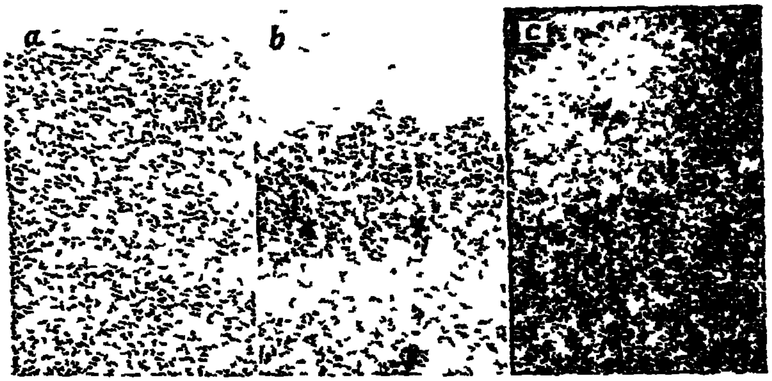

Fig 3—Non-tumorous part of right adrenal gland *a*, hæmatoxylin and eosin *b*, Sudan IV, *c* digitonin with polarised light. Composite photograph showing absence of sudanophilic and birefringent material from zona glomerulosa, and abundant sudanophilic material in zona fasciculata. (×65)

Pathological Reports

Dr H. J Whiteley reported as follows "The *adrenal tumour* was well encapsulated, the cut surface being a uniform golden-yellow Microscopically the tumour was a well differentiated cortical adenoma, showing areas of secretory activity The rest of the adrenal was small, the cortex being 0 4 mm thick (normal 1–1 5 mm) The cells of the zona glomerulosa were small, and contained scanty sudanophilic droplets and no birefringent material. The zona fasciculata was narrow, the cells containing abundant large sudanophilic droplets and some birefringent material. The zona reticularis contained a small amount of sudanophilic material (fig 3) These findings suggest that in the non tumourous portion of the right adrenal (*the left* was not examined) the zona glomerulosa was secreting, and that the zona fasciculata was atrophic and non secreting "

Section of the kidney (Dr A. G Heppleston) showed hypertensive nephrosclerosis with great thickening of the arteries, there was no fibrinoid necrosis Some vacuolation of the tubular epithelium was seen, in order to discover how this vacuolation was distributed in the tubule the biopsy specimen was investigated by the technique of *nephron dissection* by Dr E M Darmady and Miss F Stranack, who reported as *follows* "microdissection of a portion of biopsy material was carried out by the technique previously described (Oliver 1939 Darmady and Stranack 1954) On superficial examination the total number of nephrons appeared to be normal, and interstitial fibrosis was slight or absent On tracing the nephron the outline of the glomerulus was found to be normal (By this technique accurate assessment of the glomerular structure cannot be made) The proximal tubule, however, was abnormal, in that its epithelium was unusually translucent and the tubule was distorted with areas in which the cells were large and vacuolated and the epithelium heaped up (fig 4*a*) When the nephrons were traced lower minimal changes of a similar nature were found in some of the distal tubules, while others, in which the general outline and mucosal pattern were normal showed some increased vacuolation of the epithelium The collecting tubules were normal (fig 4*b*) The striking feature was the localised vacuolation and distortion of the proximal tubule, it is unusual to find changes in the proximal tubule alone without gross lesions lower in the nephron Precise localisation of the lesion may suggest that this is the site of control of acid base balance

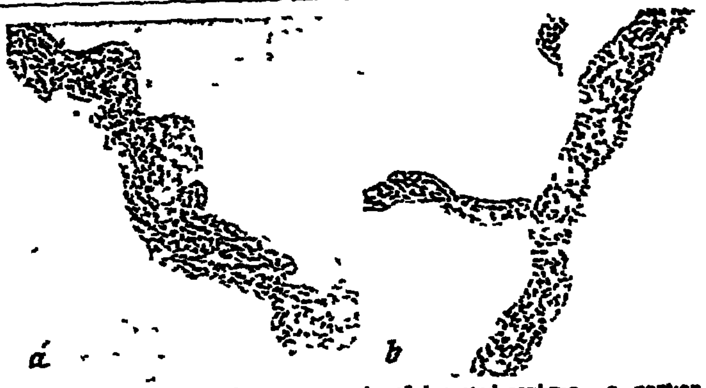

Fig 4—Phase contrast photomicrographs of dissected nephron *a* portion of proximal tubule showing distortion and vacuolation of epithelium (×95), *b*, portion of the distal tubule showing that the outline and arrangement of the tubule is normal some increased vacuolation of the epithelium is seen (×64)

Postoperative Progress

The operation itself was uneventful By the third day after operation moderate lumbar œdema had developed but this subsided over the next few days The only subjective change caused by the operation was the abolition of the thirst and polyuria The average urine volume during eleven days in April, 1955, was 2340 ml per day, and during thirty days after operation 1438 ml (The maximum specific gravity, however, was still only 1 012 ten weeks after operation)

The effect of operation on the *blood pressure* is shown in fig 5, which compares the levels during the admission before operation with those during convalescence During the patient's stay in hospital for investigation her blood pressure tended to fall and the pulsus alternans disappeared, but the blood-pressure two days before operation was 205/130 mm

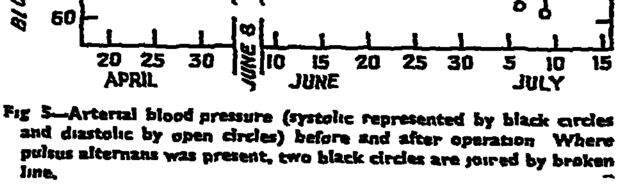

Fig 5—Arterial blood pressure (systolic represented by black circles and diastolic by open circles) before and after operation Where pulsus alternans was present, two black circles are joined by broken line.

broad-spectrum antibiotics in general, or the risk of blood dyscrasia, which is associated with chloramphenicol in particular. Postural drainage, bronchoscopic aspiration of pus, aerosol administration of drugs, and instillation of the appropriate antibiotic directly into the affected segment of lung are adjuvants to chemotherapy which have been advocated,[1 5 9–13] but Shoemaker et al consider them unnecessary. Surgery, they believe, should be confined to resection in cases in which there is recurrence after adequate medical treatment, in which bronchial drainage is impeded by organic obstruction, or in which carcinoma is suspected. These views are now probably widely accepted, although Waterman et al[5] have lately contended that the pendulum has swung too far away from surgery. They think that there is a restricted field in which external drainage is preferable to resection—in old, feeble patients, for example. They believe also that many physicians have an exaggerated idea of the decline in incidence of simple lung abscess, but whatever the exact fall, there seems little doubt that the condition is nowadays much less common in hospital practice than it was, probably because of the alacrity with which chemotherapy is given when there is evidence of respiratory infection. When a lung abscess is encountered it is, therefore, all the more important to bear in mind the possibility of an underlying bronchial carcinoma[8 14] or foreign body, and it is probably wise to carry out bronchoscopy in all cases irrespective of the initial response to treatment.

OBSTRUCTION OF THE SUPERIOR VENA CAVA

THE superior vena cava is most often occluded by external pressure from malignant tumours or aortic aneurysms, and when such lesions are present it is neither reasonable nor possible to try to relieve the obstruction by operation. But sometimes the obstruction may be the result of a more benign process, such as phlebitis, chronic fibrosing mediastinitis, or mediastinal tuberculous lymph-glands. Although many patients with an obstructed superior vena cava have no symptoms, the rise in venous pressure may cause persistent cyanosis, swelling and venous engorgement of the head and neck, and severe headaches and dyspnœa. For these patients operation may be indicated. Replacement of the great veins presents problems different from those of arterial grafting. The venous wall is thinner and more compressible, and the blood flows more slowly and at a low pressure. Consequently any disparity in length or diameter results in angulation or ridging of the graft, and this may lead to thrombosis, particularly at the suture line.

Deterling and Bhonslay[15] have replaced the superior vena cava in dogs by various materials. Aortic homografts, they found, were easy to handle and suture into place, although within a few weeks of insertion the graft shrank to an elliptical cross section with internal furrows and corrugations. They say the functional results were reasonable even though the diameter of the graft was eventually reduced by 40%. Venous autografts worked very well at first, but all of them were completely occluded by thrombosis within a month. Synthetic materials were even more disappointing and none of those tried, including 'Ivalon' sponge, 'Dacron' taffeta fabric, and woven seamless nylon, functioned satisfactorily. In the patient they treated, who had complete caval and azygos obstruction by tuberculous glands, the thrombosed segment was resected and replaced by an aortic homograft. This has worked well for eighteen months and the patient's symptoms have been completely relieved. This is the 9th case so far reported in which a superior-vena-caval obstruction has been treated by grafting. In 6 of these the venous autograft either thrombosed after operation or was described as a "partial" success. After the other 3 operations, in which aortic homografts were used, 1 patient died four months later, at which time the graft was patent, and 1 graft was a failure; the 3rd is the case described by Deterling and Bhonslay. They rightly conclude that this generally unsatisfactory picture underlines the need for further investigation into large vein replacement.

CUTANEOUS LYMPHATICS

THE part played by lymphatics in vascular diseases of the legs continues to interest clinical investigators. Butcher and Hoover[1] have studied the abnormalities of cutaneous lymphatics associated with stasis ulcer, lymphœdema, and cutaneous autografts. Their method was essentially that of Hudack and McMaster[2], sky blue dye (in aqueous 4% solution) was injected through a 30 gauge needle into the most superficial layer of the dermis. The spread of the dye locally can be recorded photographically, and massage and movement of the foot or leg drives the dye proximally to the collecting lymphatics and glands. Butcher and Hoover found that the patterns of superficial dermal lymphatics in the extremities of normal individuals showed little variation in length, diameter, or number of channels and that the pattern was more difficult to demonstrate in thin skin. Similar forms of lymphatic spread were seen in the skin around uncomplicated varicose veins; in the presence of cutaneous pigmentation the lymphatics were dilated and the dye diffused more rapidly through these walls. After a stasis ulcer had developed the lymphatic network in the surrounding skin failed to fill, although Kinmonth[3] demonstrated patent lymphatics in the deep tissues underlying stasis ulcers. It is hard to decide whether the lymphatics are obliterated immediately before the ulcer forms or whether the obliteration follows infection and sclerosis secondary to the ulcer.

Superficial lymphatics were also observed by the dye method in 22 partial-thickness skin-grafts in the leg. The channels in the donor skin persisted in a dilated form for three to six months after the grafting, but with longer intervals the calibre of the lymphatics seemed to return to normal in the skin which remained pliable and normal in texture and colour. In contrast, lymphatic channels could not be identified in the scaly, weeping, and pigmented grafts. Many connections between the lymphatics in the satisfactory grafts and those of the skin around became obvious two to four months after grafting. These findings suggest, according to Butcher and Hoover, that the establishment of lymphatic channels between the donor and host skin is of considerable importance and where this fails successful resurfacing cannot take place. The corollary to this is that excision of an ulcer prior to grafting must be wide enough to include all tissues in which lymphatics have been obliterated.

Lymphatics could not be demonstrated by Butcher and Hoover in the involved skin of patients suffering from lymphœdema præcox—in striking contrast to the findings of Kinmonth and Taylor[4] that a network of abnormally dilated lymphatics could be consistently outlined after intradermal injection of patent blue V. Kinmonth and Taylor exposed the distended channels and injected X-ray contrast media, which displayed the

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TABLE IV—RESULTS OF ANALYSIS OF MUSCLE REMOVED AT OPERATION (M.EQ PER KG OF FAT FREE DRY MUSCLE)

—	Potassium	Sodium	Chloride
Present case	386	215	87
Normal*	435–481	114–119	66–71

* Mokotoff et al 1952

relatively slowly at first There was a remarkable coincidence between the calculated increase of intracellular sodium plus potassium and the clinical manifestation of tetany (fig 7) (cf Fourman 1954)

During the postoperative period the balance measurements show an apparent gain, over thirty days, of 260 m eq of sodium, 764 m eq of chloride, and 610 m eq of potassium These figures are surprising in view of the results of isotope dilution (table III), which showed a loss of 707 m eq of sodium The gain of 433 m eq of potassium found by this method agrees well enough with that found by the balance method The postoperative isotope determination coincided with the end of the balance period, but the preoperative determination was made three weeks before operation, so exact concordance is not to be expected A more important probable cause of the discrepancy is the occurrence of unmeasured losses of sodium in sweat during the balance measurement, which was made during unusually hot weather These losses may be large enough to account for the different results obtained by the two techniques Wilson et al (1954) compared the results of balance measurements with those of two isotope measurements In the case of sodium, in all instances where the discrepancies were large the balance method showed the greater gain, discrepancies up to 259 m eq per week were observed, and were attributed to unmeasured extrarenal loss of sodium The daily errors added together for the whole period of thirty days make the cumulative balance figures untrustworthy, but the balance study provides reliable information about electrolyte gains and losses over short periods In particular it shows that there was not a sudden large loss of sodium after removal of the tumour, during the first five days after operation balance showed an apparent gain of 221 m eq of sodium While this gain may have been overestimated because of extrarenal loss, the existence of sodium retention is corroborated by the appearance of œdema at this time

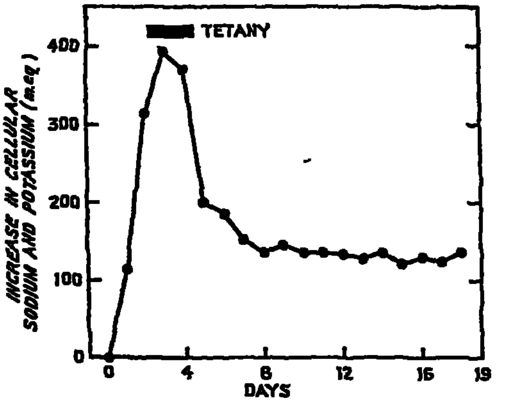

Fig 7—Calculated increase in cellular sodium plus potassium correlated with appearance of tetany

Discussion

Our patient resembles in many respects that of Conn (1955a and b) Both presented with potassium depletion due to excessive renal loss which was abolished by removal of an adrenocortical tumour Both had hypernatræmia, thirst, and polyuria, and these also were abolished Both had hypertension, but this was severe only in our patient In both the salivary sodium/potassium ratio was depressed, and this ratio increased after operation Conn's hypothesis that the syndrome is caused by excessive secretion of salt-retaining hormone was confirmed in his case by the presence of large amounts of this hormone in the urine and in the tumour itself

There are, however, several differences between Conn's patient and ours In the first place it has not been possible to demonstrate more than a small increase in the urinary excretion of aldosterone In the second place, our patient did not lose a large amount of sodium immediately after operation, on the contrary she became œdematous on the third day This difference may be accounted for in several ways Conn's patient received an infusion of hydrocortisone during and just after operation, which may have promoted a sodium diuresis In our patient the potassium supplement was discontinued at the time of operation, and we have demonstrated that this might lead to sodium retention Another possibility is that the fall in blood-pressure, much greater in our patient, might have reduced her glomerular-filtration rate enough to limit her capacity to excrete sodium At all events, in retaining sodium she was responding normally to an operation This response does not seem to depend on any increase in the secretion of adrenocortical hormone (Mason 1955)

We would also like to draw attention to the almost complete absence of alkalosis, in marked contrast to Conn's case Among other cases of proved or presumed primary aldosteronism, one had no alkalosis (Earle et al 1951), while others did (Evans and Milne 1954, Mader and Iseri 1954) Our patient had tetany only during repletion with large amounts of potassium, when there was evidence of an increase in intracellular cation

Before the tumour was removed it was uncertain whether the blood-pressure would fall subsequently. It seemed possible that the hypertension was caused either by renal damage or by a hormone secreted by the tumour On the latter hypothesis, the pressor effect might have been exerted either directly or through the disturbance in body content and distribution of electrolyte The satisfactory fall in blood-pressure which, in the event, followed operation has not enabled a firm choice to be made between these possibilities Removal of the tumour has lowered the output of aldosterone to a subnormal level, and converted a salt plethora at least transiently into a salt depletion, with low serum-sodium level and a low total exchangeable sodium (34 6 m eq per kg) Such changes might lower the blood-pressure in hypertension due to any cause, including renal damage On the other hand the serum-sodium level has since returned to normal, while the blood-pressure remains well below preoperative levels The observed facts would, however, be consistent with the hypothesis that the hypertension was due to a hormone secreted by the tumour

As between the possibilities that the hormone caused hypertension directly, or indirectly through electrolyte disturbance, we can only say that the blood-pressure fell, not immediately after removal of the tumour, but during several days Also, our observations on heat elimination from the hand did not resemble those reported in phæochromocytoma (Hamilton et al 1953), where the hypertension is undoubtedly caused directly by a circulating hormone If the hypertension was caused through electrolyte disturbance the hormone responsible was probably aldosterone itself, since this steroid accounted for 95% of the biological activity in the mineralocorticoid assay While suggesting that aldosterone caused the hypertension by producing a salt plethora, we feel obliged to mention that there is, as yet, *no direct evidence* that this hormone will produce hypertension in the same manner as deoxycortone acetate and other corticoids (Gaunt 1955)

A disturbing consequence of the fall in blood-pressure has been the reduction in renal plasma-flow and glomerular-filtration rate, resulting in nitrogen retention † These reductions, being proportional to the fall in blood-significantly high proportion of young women with secondary amenorrhœa could be classified as obese

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† Because of the fall in renal clearances after operation interpretation of the urinary steroid values is *difficult*, but compared with the last values obtained before operation urinary excretion of cortisol has been reduced by a factor of 2 5, whereas the corresponding factor for aldosterone is 25

There is no good reason to believe that fertility commonly suffers when a woman gains weight *after* childbirth In a study of parous obese women, Odell and Mengert[13] recorded an average parity of 4 5 (which they thought high) among their patients at the time of interview, and Sheldon[8] found no evidence of menstrual upset (or of infertility) among a group of women complaining of obesity following pregnancy Certainly many women who become very fat after pregnancy have unimpaired fertility, but this is not true for all It is impossible to progress further without recognising different clinical groups of obesity "Simple obesity"[14] is certainly not always simple, although it may not fall into the category of any of the grosser endocrinopathies Sheldon[8] found two distinct groups amongst his patients, one of which appeared to be the pre diabetic group, and there may well be other clinical subgroups If hypothalamic disturbance (which can be of psychogenic origin) causes obesity by promoting excessive appetite, then it is reasonable to suppose that a secondary pituitary upset may cause gonadal failure in these women Thus, it is probable that, with advancing knowledge, more and more cases of "simple obesity" will fall into the category of true endocrinopathies, and Widdowson's views on reproduction and over-nutrition may be confirmed

PLAIN RADIOGRAPHY OF THE INTESTINE

WITHIN twelve hours of the birth of a normal infant air has become dispersed through the entire length of the gut,[15] and thereafter in health it is never entirely absent Some gas is nearly always found in the fundus of the normal stomach, in the colon, and in little collections in the small bowel Because of its low radio-opacity it forms an excellent natural contrast medium In intestinal obstruction, straight radiographs of the abdomen can give valuable information about the site and sometimes the nature of the obstruction The bowel below the level of the obstruction soon becomes empty of gas, while the loops above become distended with gas and fluid In lower ileal obstruction, distended loops of small bowel form a step ladder pattern across the abdomen, and the colon is collapsed and empty of gas When the obstruction lies in the colon, it may be hard to distinguish distended colon from distended small bowel, but generally the lateral position and deep haustra of the colon can be separated from the thinner and more frequent folds of the ileum or the still more feathery pattern of the jejunum The higher the obstruction, the less the radiological signs, especially if vomiting keeps the bowel empty

X ray examination cannot exclude strangulation of the gut, but Frimann-Dahl[16] has pointed out that in a strangulated loop only sanguineous fluid collects, and the loop may be visible as a rounded tumour like mass set amongst gas filled gut Should the volvulus be incomplete, gas can enter the loop and give the "coffee bean" sign of Rigler The gas shadows sometimes serve to show the nature of an obstruction due to internal herniation distended crescentic loops of bowel in the right hand side of the abdomen point to herniation into the lesser sac Gallstone ileus produces the triad of gas in the biliary tree, small-bowel distension and the faintly calcified shadow of a large stone in the terminal ileum In paralytic ileus both large and small gut are dilated, and X ray examination is helpful here in excluding obstruction of the small bowel so that conservative treatment can be pursued with greater confidence The progress of intubation and decompression can then be followed on serial films In peritonitis, exudate may separate the loops of gut and the properitoneal fat lines disappear Localised abscesses—e g, from an appendix—may be outlined by gas filled bowel In ascites the gut floats on top of the fluid when the patient is erect, and the density of the lower abdomen is much increased by large effusion When the gut has perforated, it may take some time for air to percolate upwards and become visible below the diaphragm in films taken with the patient upright, and in all patients a supine lateral film will show gas between liver and anterior abdominal wall

Straight radiography of the abdomen is particularly valuable in children, in whom the gas shadows are often more pronounced In the newborn it may give valuable clues to the malrotations and atresias[17], and the length of the stenosis in imperforated anus can be estimated Signs of small bowel obstruction in an otherwise normal abdomen may point to meconium ileus, and the faint intraperitoneal calcifications of meconium peritonitis may be detected In an "acute abdomen" the cautious administration of lipiodol to a child (or barium to an adult) is not now regarded with the same disquiet as it used to be, and this move will often provide valuable additional information

DEATHS DURING ANÆSTHESIA

THE report of the Ministry of Health for 1954 records[18] that the number of deaths during anæsthesia in England and Wales has declined year by year since 1938 In 1953 there were 562 deaths, 284 of them in men and 278 in women, or about 1 per 1000 of all deaths in the population These figures cannot be accurately related to the total number of anæsthetics given in the same year, for which there are no recorded statistics but in 1954 the Ministry made a pilot survey which showed that about 8 million anæsthetics were administered during that year in the hospitals of England Though the over-all figure for deaths is declining, for patients over the age of 65 there is an upward trend This is perhaps not surprising, particularly in view of the fact that more major operations are being carried out on older people It is, moreover, in accordance with the findings of Beecher and Todd,[19] who recently investigated the mortality due to anæsthesia in ten teaching hospitals in the United States Wisely, no attempt has been made to correlate particular agents or techniques with mortality (indeed, it would not be fair to do so with the data available) but it is interesting to note that thiopentone alone was mentioned on the death certificates in 314 anæsthetic deaths in the period 1949–53

The Ministry's report gives grounds for satisfaction and it reflects how successfully anæsthetists have advanced their specialty in the post war years Nevertheless, some may ask whether these figures really do tell the true story Sudden death due to anæsthesia rarely gives rise to specific post mortem findings, and, as the report points out, the only person who really knows the cause of an anæsthetic death is the anæsthetist who gave the anæsthetic Useful results are likely only from a well planned investigation, such as that organised by the Association of Anæsthetists of Great Britain and Ireland with detailed and first hand accounts of the actual occurrence

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Prof ARTHUR FELIX, D SC, F R S, director of the International Enteric Reference Laboratory in London and long a member of the staff of the Lister Institute, died on Jan 14 at the age of 68

Mr WILSON HEY, consulting surgeon to Manchester Royal Infirmary, died on Jan 15 at the age of 73 primary carcinoma arising in cirrhotic livers, in patients admitted to the university medical unit, Queen Mary Hospital In each case the diagnosis was established by aspiration biopsy The healthy controls were medical undergraduates

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[13] Odell L D Mengert W F J Amer med Ass 1945 128 87
[14] Richardson J S Postgrad med J 1952 28 618
[15] Paine J R Nessa C B Surgery 1942 11 281 Wasch M G Marck A J Pediat 1948 32 479
[16] Frimann Dahl J Brit J Radiol 1955 28 541

[17] Hajdu N Ibid, p 590
[18] Report of the Ministry of Health for 1954 Part II p 1[illegible]
[19] Beecher H K Todd D P Ann Surg 1954 140 2

Fibrinolytic activity was determined by the quantitative technique described by Biggs and Macfarlane (1953) The initial level of fibrin was taken as that estimated thirty minutes after the addition of thrombin, and the duration of incubation was arbitrarily selected as six, twelve, and twenty-four hours To ascertain whether the fibrinolysin also destroyed fibrinogen, duplicate sets of tubes were set up containing the same quantities of citrated plasma and buffered saline solution, but the thrombin was added after incubation for six, twelve, and twenty four hours, and thirty minutes later the fibrin contents were estimated To determine whether clotting was necessary to activate the fibrinolysin, washed fine fibrin webs, formed on roughened glass rods, were immersed in specimens of undiluted plasma showing active fibrinolysis These webs were formed by adding thrombin to a 1/25 dilution of normal plasma in veronal-acetate buffered saline solution of pH 7 4

Results

The fibrinolytic activity of the plasma in the 30 cases of cirrhosis is set out in table I From this it will be seen that fibrinolysis was complete in 7 cases in less than six hours, in 9 between six and twelve hours, and in 5 between twelve and twenty four hours In the remaining 9 at the end of twenty four hours a variable but reduced quantity of fibrin remained, representing a loss of 24–67% of the initial amount (average 41%) The average reductions in fibrin content in these 30 cases are set out graphically in fig 1 in which they are contrasted with those of 20 healthy controls In the controls the reduction in the fibrin content after incubation for twenty four hours was 0–32% (average 13%)

No relationship could be demonstrated between the intensity of the fibrinolysis and the severity of the disease assessed clinically either by tests of liver function or by the appearances on aspiration biopsy Indeed, cases 26 and 27 with limited fibrinolytic activity were adjudged among the most seriously ill There was no correlation with the presence or absence of ascites or with the plasma albumin and plasma globulin levels All the patients had gross splenomegaly with pancytopenic hypersplenism

TABLE I—SPONTANEOUS FIBRINOLYTIC ACTIVITY OF PLASMA IN 30 CASES OF CIRRHOSIS OF LIVER

Case no	Duration of incubation (hr)						
	½	6		12		24	
	Fibrin (mg per 100 ml)	Fibrin		Fibrin		Fibrin	
		mg per 100 ml	% lysed	mg per 100 ml	% lysed	mg per 100 ml	% lysed
1	112	0	100				
2	139	0	100				
3	289	0	100				
4	166	0	100				
5	455	0	100				
6	320	0	100				
7	264	0	100				
8	182	70	61	0	100		
9	251	109	57	0	100		
10	321	45	86	0	100		
11	182	90	51	0	100		
12	578	216	63	0	100		
13	214	16	93	0	100		
14	385	70	82	0	100		
15	278	90	67	0	100		
16	321	114	65	0	100		
17	209	109	48	32	85	0	100
18	353	288	19	69	81	0	100
19	312	171	45	70	78	0	100
20	281	134	52	70	75	0	100
21	181	128	29	80	56	0	100
22	123	86	30	70	43	43	65
23	671	353	39	316	55	187	67
24	273	193	29	*		182	33
25	363	*		307	15	273	25
26	307	203	34	193	37	171	44
27	187	130	26	*		128	32
28	251	128	49	128	49	123	51
29	272	232	15	214	21	200	26
30	342	288	16	280	18	259	24

* Not done

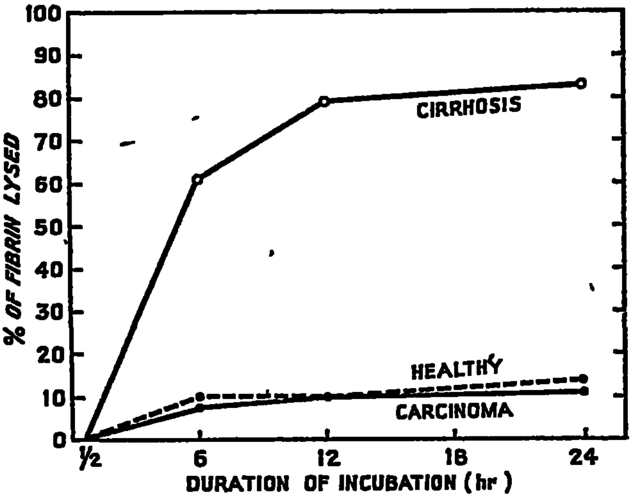

Fig 1—Average fibrinolytic activity of plasma in 30 cases of cirrhosis of liver, 12 cases of primary carcinoma of liver, and 20 healthy controls

The disappearance of ascites with treatment exerted no influence on the intensity of the fibrinolysis, nor did clinical improvement in the patients' condition Repeated observations in 10 cases for from one to three months showed decreased fibrinolytic activity in 3, the clinical condition in 1 had deteriorated, whereas in the remaining 2 there was little change

The incubation, even for twenty four hours, of unclotted plasma from each case did not reduce the fibrinogen content Fine fibrin webs, prepared as described above, lysed when immersed in specimens of undiluted plasma showing active fibrinolysis

The average reductions in fibrin content in the 12 cases of primary carcinoma, each of which arose in a cirrhotic liver, are set out in fig 1 After incubation for twenty-four hours the reduction in fibrin content was 0–30% (average 12%) The initial levels of fibrin were 272–722 mg per 100 ml (average 466 mg per 100 ml)

6 patients with cirrhosis (cases 3, 4, 9, 21, 29, and 30) had undergone splenectomy under general anæsthesia to correct the associated pancytopenia, and fibrinolytic activity was determined at intervals during and after the operation The results are set out in table II Specimens of blood taken fifteen minutes after removal of the spleen in each case showed an intensification of fibrinolytic activity This increase was well marked except in case 29

In case 3 no clot formed on the addition of thrombin to diluted plasma, so the fibrinolytic activity was estimated on undiluted plasma, and lysis was complete in all the tubes when first inspected after thirty minutes In this case whole blood clotted in fifteen minutes but was fluid again within thirty seconds

Cases 3, 21, 29, and 30 were investigated four hours after splenectomy, when the fibrinolytic activity was found to have reverted to the preoperative level in each case

In the 4 patients showing active fibrinolysis preoperatively (cases 3, 4, 9, and 21), the plasma twenty-four hours after splenectomy showed well marked reduction in activity Though not recorded here this reduction was found to persist for seven to twenty one days 3 of these patients (cases 3, 4, and 9) were reinvestigated a month after operation, when the fibrinolysis was found to have returned to its preoperative intensity and biological studies affect their attitude to it , and of giving an exemplary study to its patients in the application of science and logic to an ethical problem Most of my comment here will deal with the committee's views on homosexuality—in part because modern knowledge has added remarkably little to our attitude towards prostitution, and because (judging from the past) no law or recommendation is likely to have any significant effect upon any but the most obviously professional form , but chiefly because it is society's attitude towards homosexuality which calls most urgently for revision today

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It seems to me that a distinguished committee has worked hard, has tried to set a moral and social example, and has made a number of humane and sensible suggestions, and simultaneously, by the language of some passages of its report, has thrown away an opportunity which will not soon recur It has dissipated any chance of serious ethical discussion in a series of pontifications Doctors, the Departmental Committee may conclude, are no different from the rest, though they express their prejudices in longer words This is a disappointing conclusion, even if it might have been expected it is instructive, however, because the striking discrepancy of tone between the scientific and the exhortatory passages of the report suggests that even on an expert committee there has been a distribution of function exactly like that in society as a whole The report reads as a dialogue between a sensible psychiatrist of conservative opinions, and an *alter ego* of a very different kind The scientific have said their say, but the final document gives a strong impression that it has been written in its rhetorical passages by a single person of definite and restrictive opinions

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The psychiatric members of the committee, who have done their job well, would probably agree that public reaction to homosexuality has a close affinity with the psychology of anti Semitism, and with the pursuit of heretics who menace the tribal magic Such thinking is possibly the result of people's overreaction against components in their own make-up and it could well be argued that the presence of individuals overreacting in this way in the various organs of society, especially Parliament and the courts, is more harmful in the long run than that of conscious and practising exponents of the hated behaviour whose existence the committee has earned notoriety by stressing For homosexuality this stream of disturbed opinion has created a characteristic terminology, based on typically adrenergic words such as 'unnatural vices" "moral fibre" which is sapped, and "unmentionable" practices which are indulged in

Quite the worst feature of the B M A 's evidence is that it has bodily taken over this diction The conspiratorial atmosphere is maintained by repetition of words like "insidious," corruption,' perverted' "indulgence" (We even encounter the expression ' homosexuals and their sympathisers,' which brings to mind the disclaimer in press correspondence denying that the writer is a Communist or a Communist sympathiser Some such equivalent phrase may soon be required in medical articles) The *general tendency* of this diction is to reverse the sense of the scientific evidence, and to counter any emotional disinflation of the subject That a predominantly psychiatric and scientific committee should let itself be reported in such language is frightening

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The committee might, perhaps, properly reply that whatever they had said they would have failed to satisfy all shades of extremist opinion, and that if persons who are neither psychiatrists nor engaged in research on human behaviour feel that the report's recommendations are misguided, they should send their views to the Departmental Committee This is fair enough, perhaps yet a report which is made in the presence of such an opportunity as this, and which welcomes with both hands the chance to combine science and ethics, does invite public comment Moreover it is not the recommendations of the B M A special committee which are disappointing most of them are, as I have said, humane and sensible , and they probably do in fact represent a modal average of medical opinion in this country The disappointing feature of the report is far less its matter than its manner Its failure is almost wholly one of attitude, and much of it lies in the presentation—often the verbal presentation—of what the committee has to say

As a contribution to healing it incurs three charges first, it is couched in language which throws away the fundamental point of difference between the medico scientific approach to unpopular sexual behaviour and that of society, or the Sunday Press Secondly, its discussion of scientific data is skeletal, the bones being apparently chosen to avoid dangerous thoughts, but clothed in a great deal of moral adipose tissue And thirdly, it offers no single comment on either of the two aspects of homosexual conduct which medicine is almost alone qualified to discuss—the reality of the moral and physical ill effects on individuals and society which might justify prohibiting it, and the psychosocial origins of the attitude which society adopts toward it I do not think these are unfair criticisms at least they provide as good a peg as any upon which to hang a discussion of the responsibility of medicine for giving insight to public opinion

Neither is the committee much happier in its encounters with biology, although the scientific sections are gratifyingly written, from the standpoint of diction and attitude, "in another hand" It provides no adequate review of the literature, and the bibliography contains six references, though other work is quoted in the text Its brush with genetic determinism is important, for the 'essential" homosexual real or imaginary is a potentially important intruder in legislation Beside his popularity with predominantly homosexual individuals, who share the general comfort which we derive from "organic" explanations of our peculiarities he could very easily acquire a legal status according immunity to himself and continued punishment to others who cannot prove their activities to be 'essential rather than merely experimental

There is one scientific omission moreover, which cannot be overlooked "Homosexual" behaviour is presumably the display, between individuals of the same sex of an imitation of reproductive mating behaviour, which may or may not end in some kind of sham copulation It occurs under ordinary conditions of observation almost universally among immature and segregated, and not uncommonly in adult unsegregated males of most if not all mammalian species as well as in other bisexual organisms Similar behaviour has been described between human males in every culture of which we have record, without any obvious psychotic

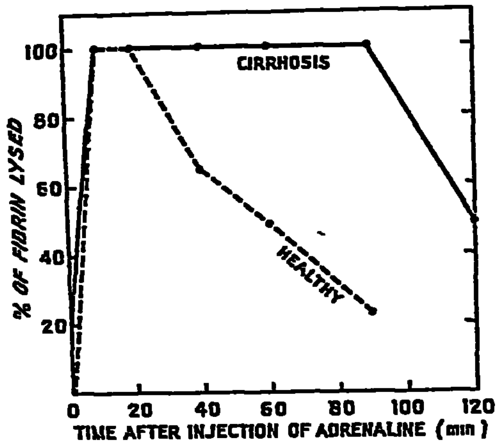

Fig 3—Duration of effect of subcutaneous injection of 1 ml of 1/1000 solution of adrenaline hydrochloride in representative case of cirrhosis of liver and in most intense and prolonged response observed in 6 controls, after 12 hours incubation

function tests or by the appearances on liver biopsy. Further evidence that no relationship exists between over-all impairment of liver function and the occurrence of fibrinolysis is afforded by the findings in the cases of primary carcinoma in a cirrhotic liver, since in all these cases liver function was grossly disturbed. Ascitic fluid in cirrhosis of the liver is fibrinolytic, but there was no correlation between plasma activity and the presence of ascites. The resolution of ascites with treatment produced no influence on fibrinolysis, nor did clinical improvement in the patient's condition.

The production of fibrinolysis by operation on patients with apparently normal livers is variable. Macfarlane (1937) recorded an incidence of 70% and Imperati (1937) 50%. Each of the 6 patients with cirrhosis subjected to splenectomy showed intensification of the pre-existing fibrinolytic activity. Further the intensity of the fibrinolysis resulting, even allowing for the existence of a preoperative level, was significantly greater than any observed by us after various operations, including splenectomy, on patients with normal livers. In view of the variability of the effect of operation on patients with normal livers we do not consider any such controls satisfactory. This difficulty does not arise with the response to the subcutaneous injection of adrenaline, since Biggs et al. (1947) have shown that this invariably induces fibrinolytic activity in healthy people. The response of the patients with cirrhosis to the subcutaneous injection of adrenaline, even when the presence of spontaneous fibrinolytic activity is allowed for, was not only of significantly greater intensity than that of the healthy controls but also of significantly longer duration. It may well be that further experience with the adrenaline test will show that the results thereof mirror the effects of operation and will permit the detection of those cases of cirrhosis in which fibrinolysis may become of such intensity as to play a part in the production of the hæmorrhage referred to above. The development of multiple petechiæ in case 26 after the injection of adrenaline supports this view.

TABLE IV—INFLUENCE OF CORTICOTROPHIN ON SPONTANEOUS FIBRINOLYTIC ACTIVITY OF PLASMA IN 3 CASES OF CIRRHOSIS OF LIVER

Case no	Sample	Fibrin (mg per 100 ml) after incubation for ½–24 hr			
		½	6	12	24
2	Initial	139	0		
	Fifth day of corticotrophin 10 mg i.v. daily	203	†	203	186
	Six days later	176	0		
17	Initial	209	109	32	0
	Fifth day of corticotrophin 10 mg i.v. daily	229	251	241	180
	Six days later	228	82	0	
31	Seventh day of corticotrophin 120 mg i.m. daily*	256	232	224	212
	A month later	181	0		

* = Day of development of portal vein thrombosis
† = Not done

The intensification of fibrinolytic activity, which is one of the immediate results of operation, appears to pass off in four hours and it is within this period that there is risk of hæmorrhage of the type previously referred to. Within twenty-four hours the spontaneously occurring fibrinolytic activity present preoperatively is inhibited and this inhibition persists for from seven to twenty-one days. It seems that the initial shock phase is associated with increased fibrinolytic activity and the succeeding countershock phase with its abolition. The view that suprarenal cortical activity inhibits spontaneously occurring fibrinolysis is supported by the observations on the 3 patients given corticotrophin. In both cases 2 and 17 there was a significant reduction in fibrinolytic activity on the fifth day of treatment with corticotrophin. Six days after the corticotrophin had been stopped the fibrinolytic activity had returned to the pre-treatment level. Case 31 was first seen on the seventh day of treatment with corticotrophin 120 mg intramuscularly daily, when evidence of portal-vein thrombosis had developed. The fibrinolytic activity of the plasma then was negligible but four weeks later it was intense. Further support is obtained from the observations by Kwaan and McFadzean (1956), who have shown that the administration of corticotrophin will prevent the lysis of clots produced experimentally in the marginal vein of the ear of the rabbit—a lysis which presumably results from release of fibrinolysin. Truelove (1952) found that corticotrophin did not prevent the development of fibrinolysis after either exercise or adrenaline in volunteers, and we have confirmed his findings with adrenaline. His conclusion, however, that adrenocortical activity had no direct relationship to the phenomenon of fibrinolysis cannot apply to spontaneous fibrinolysis in cirrhosis of the liver.

Macfarlane and Biggs (1948) considered that the most obvious function of fibrinolysis was the proteolysis of pathological fibrin deposits, and Mole (1948) suggested that it might be the physiological means whereby fibrin deposits are prevented from forming on the vascular endothelium in health, especially if its source was, as he believed, the endothelium. Portal-vein thrombosis remains a hazard of splenectomy in cirrhosis of the liver and of the administration of corticotrophin in this disease. Eisenmenger et al. (1952) reported its occurrence in 3 patients so treated. In each there is inhibition of spontaneous fibrinolysis and this may play a part in the development of such thrombosis.

The adverse effect of intense fibrinolysis on hæmostasis is manifest, yet it seems that such activity alone may not cause hæmorrhage. For example, in case 3 the clot formed spontaneously from whole blood obtained fifteen minutes after removal of the spleen lysed in thirty seconds and the clot formed by the addition of thrombin to undiluted citrated plasma lysed in less than thirty minutes; yet clinically there was no bleeding. Again, in case 26, after the injection of adrenaline multiple petechial hæmorrhages appeared in the skin, yet equally intense fibrinolysis was provoked by adrenaline in other cases without the development of such hæmorrhages.

The mechanism of production of spontaneous fibrinolytic activity in cirrhosis of the liver remains obscure. Cirrhosis appears to be the only primary hepatic disease in which spontaneous fibrinolysis has so far been reported and biological studies affect their attitude to it, and of giving an exemplary study to its patients in the application of science and logic to an ethical problem Most of my comment here will deal with the committee's views on homosexuality—in part because modern knowledge has added remarkably little to our attitude towards prostitution, and because (judging from the past) no law or recommendation is likely to have any significant effect upon any but the most obviously professional form, but chiefly because it is society's attitude towards homosexuality which calls most urgently for revision today

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Discussion

As was pointed out by Jaques [4] experimental venous thrombosis is difficult to produce in healthy animals The method here reported may have an application in this field

It appears reasonable to suggest that the clots in the veins of the control rabbits stimulated the production of fibrinolysin with consequent lysis of the clots and that corticotrophin inhibited this production This view supports the hypothesis advanced by Kwaan et al [1] that suprarenal cortical activity was responsible for the postoperative disappearance of spontaneously occurring fibrinolysin from the plasma of patients with cirrhosis of the liver They consider that the disappearance of fibrinolytic activity is a possible factor in the development of portal-vein thrombosis in cirrhosis of the liver after splenectomy or during corticotrophin therapy

The inhibition of fibrinolysis may play a part in the genesis not only of postoperative venous thrombosis but also of atherosclerosis, because Duguid [5] whose observations have been confirmed by Harrison,[6] Geiringer [7] and Crawford and Levene [8] holds that the initial phase of development of atherosclerosis is the occurrence of mural thrombi Persistence of such thrombi leads to thickening of the intima and subsequent fatty change produces the typical appearance of this lesion The inhibition of fibrinolysis by suprarenal cortical activity may be a factor in determining the persistence of mural thrombi, and the observations reported here have a value in the experimental investigation of atherosclerosis

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[4] Jaques L B *In* Flynn J E Blood Clotting and Allied Problems New York, 1951 , p 42

[5] Duguid J B *J Path Bact* 1946 58 207 1948 60, 57.

[6] Harrison C V *Ibid* 1948 60 289

[7] Geiringer E *Ibid* 1951, 63 201

[8] Crawford, T Levene C I *Ibid* 1952 64 523

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ROYAL SOCIETY OF MEDICINE

Clinical Consequences of Cerebral Anoxia

THE neurological section met on Jan 5, under the presidency of Dr REDVERS IRONSIDE

Dr R S ALLISON (Belfast) referred to hypoxic reactions occurring in medical practice, the chief causes of which were cerebral circulatory failure, dehydration, barbiturate poisoning, and electrolytic imbalance He described an instance of a patient with chronic duodenal ulcer who had been vomiting and taking alkaline powder regularly, and whose confused mental state was related to a fall in cerebral oxygen saturation He emphasised that hypoxic effects in all patients were often mistaken for hysteria When the severity of anoxia was unknown and the patient was still unconscious when seen, it was difficult to forecast the prospects of survival ; but repeated epileptiform fits and sweating were ominous signs, and, if the patient survived, irreversible damage to the nervous system might result in a partial decerebrate state

The principal neurological sequelæ after severe anoxia were hemiplegia, parkinsonism, dysphasia, and visual agnosia Multiple defects in intellectual function were also found in all cases, and constructional apraxia was especially common This might persist after full consciousness had been regained, and interfere with performance if the patient was allowed to return too soon to work

Dr P D BEDFORD (Oxford) drew attention to further clinical states Transient effects of cerebral anoxia included sleep disturbances, nightmares, and somnambulism, and these also occurred in heart-failure, toxæmia and pyrexia some other transient disorders were nocturnal confusion, periodic breathing, organic cerebral reactions, and organic neurasthenia He thought that many of these disturbances were produced in old people by histotoxic drugs which also depressed the respiratory centre and he recommended cautious dosage and preferably replacement by paraldehyde Permanent clinical effects included organic neurasthenia, with symptoms such as lack of concentration and dementia as seen after asphyxial episodes, operations under general anæsthesia or in shock from massive hæmorrhage or coronary occlusion Localised cerebral damage due to focal cerebral infarcts occurred in cor pulmonale Dr Bedford wondered whether personal susceptibility or idiosyncrasy explained why many patients were unaffected by a period of anoxia

Prof A MEYER reported on brains he and his collaborators had examined in 6 cases of cerebral anoxia due to ether and nitrous oxide Cardiac or respiratory arrest had occurred in all cases, varying from 1 to 25 minutes The commonest lesions were necrosis of the third layer of the cerebral cortex, Purkinje cells, striate body, and globus pallidus The reticular zone of the substantia nigra, the corpus subthalamicum, and the dentate nucleus were less commonly affected Surprisingly severe necrosis of the thalamus was observed in 3 cases and it had also been encountered in cases of carbon-monoxide poisoning, hypoglycæmia, and death from hanging

Professor Meyer thought that it should be often possible to differentiate between senile and anoxic changes Selective vulnerability was a complex problem and depended on several factors which might vary between different types of anoxia as well as between individual cases

Dr A L WOOLF was interested to hear Professor Meyer cite epilepsy as a cause of cerebral anoxia He referred to a child with severe epilepsy twenty-four hours after head injury in whom the convulsions were followed by deepening unconsciousness and death in four days The changes in the brain were similar to those described by Professor Meyer in his other cases of anoxia

Dr CECIL GRAY (Liverpool) expressed disapproval at ether and nitrous oxide being nominated as the cause of death in many of the cases mentioned by the speakers ,

Special Articles

TOO MUCH BARBITURATE?

EILEEN M BROOKE
M Sc Lond.
STATISTICIAN, GENERAL REGISTER OFFICE, LONDON

DEATHS in England and Wales due to poisoning by barbituric acid and its derivatives have increased considerably in recent years, until in 1954 they numbered 575 From 1939 to 1945 the annual variation in the number of deaths was small and suicides were not greatly in excess of accidental deaths, the yearly average being

Suicides	Males	16	Accidental deaths	Males	12
	Females	*27*		*Females*	*19*

From 1946 onwards there has been a signal increase in all four groups, shown in table I and fig 1

The average numbers of male and female suicides by barbiturates during 1952–54 were respectively 9 0 and 7 3 times the average for 1939–45, the corresponding figures for accidental deaths were 5 7 and 5 0

During the sixteen years since 1939, the crude suicide-rates for both males and females, when all methods of committing suicide are considered, have tended to oscillate rather than to show a definite upward or downward trend (table II)

The rates for barbituric acid poisoning, however, after remaining fairly uniform up to 1945, have since shown a somewhat rapid upward trend While male total suicide-rates have been consistently in excess of female, the female rates for barbiturate poisoning have been higher than the male from 1943 onwards It seems that a preference has been shown lately for using barbiturates as suicidal agents, rather than some other lethal means

On the assumption that different agents would be used in the same proportions in subsequent years as in 1945, the numbers of suicides expected to be due to each agent have been calculated for 1947, 1950, and 1953, and these "expected" numbers, compared with the actual numbers, are shown in table III

Whereas the number of suicides due to barbiturates might have been expected, on the 1945 basis, to increase by 1954 from 20 to 28 for males and from 35 to 46 for females, the actual increases were from 20 to 161 and from 35 to 230 respectively In 1947 the numbers who used other analgesic and soporific drugs exceeded the expected number, but in 1950 and 1954 the actual numbers were considerably less than anticipated Gas poisoning was also used more frequently in the later years than expected, whereas the numbers of deaths due to the more violent methods—hanging, drowning, shooting, and the use of cutting instruments—were all less It appears, therefore, either that the tendency is for the more active and violent methods of suicide to be abandoned in favour of the more passive methods of barbiturate or gas poisoning, or that an actual reduction has occurred in the suicide rates from more violent methods, but has not been accompanied by a decrease in the rates for barbiturate or gas poisoning Table IV shows the variation in suicide-rates between 1944 and 1954 according to the means used

The medical officer of health for Hampstead, Dr Geffen,[1] commenting on the suicide rates in his Metropolitan borough, made some apposite remarks Investigating the high suicide rate of 1950, he found that, of 86 suicides during 1950–53, 23 used barbiturates He suggests that "some steps should be taken to prevent the ease with which the public can obtain dangerous medicines in lethal quantities" He does not think that "the person who has made up his mind to commit suicide will *sooner or later do so*" *but that* "*it is likely* that the presence of a fatal drug, or an easy means of terminating his life, may cause him to take a fatal step at a time when temporarily his mind is unbalanced"

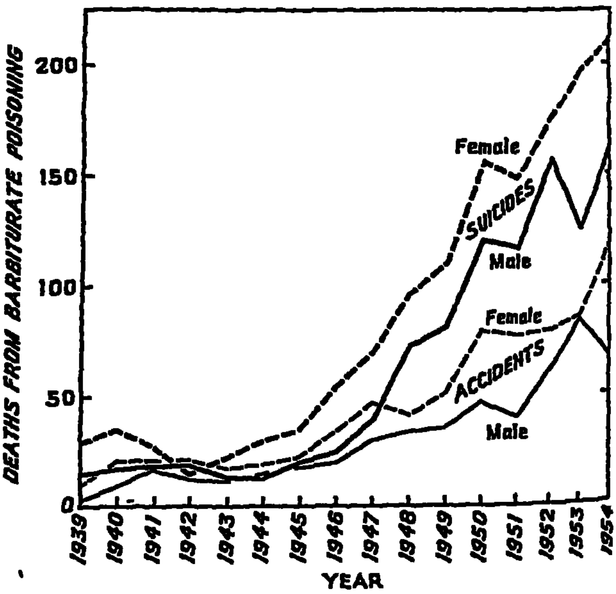

Fig 1—Number of suicides and accidental deaths from barbituric acid poisoning, 1939 to 1954

Dr Geffen also alludes to "fashions in suicides" which may be influenced by publishing accounts of the methods used Coal gas is usually readily available, and, while barbiturates are not freely sold to the public, it will be seen below that they are frequently prescribed under the National Health Service The increase in the suicide rates by these two methods, when rates in which other

TABLE I—NUMBERS OF DEATHS FROM POISONING BY BARBITURIC ACID AND ITS DERIVATIVES, 1939–54*

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Suicides	M	14	17	18	19	13	13	20	24	39	73	81	122	100	157	124	161
	F	29	35	27	11	22	30	35	54	70	96	110	156	148	176	197	230
Accidents	M	3	9	17	13	12	15	18	20	30	34	36	47	40	61	84	77
	F	10	21	21	21	17	19	22	31	47	41	51	80	77	79	85	117

* Data from the Registrar General's Statistical Review 1954, Part I Tables (Medical)

TABLE II—CRUDE SUICIDE-RATES PER MILLION LIVING FOR (1) ALL AGENTS, (2) BARBITURIC ACID POISONING, 1939–54

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All agents	M	168	159	135	121	134	125	126	144	137	145	147	136	135	132	112	119
	F	78	75	62	62	63	65	66	75	76	79	75	70	72	68	76	71
Barbituric acid	M	0 71	0 93	1 04	1 13	0 80	0 80	1 22	1 28	1 99	3 58	3 91	5 76	4 75	7 44	[illegible]	7 56
	F	1 35	1 62	1 2[illegible]	0 63	1 02	1 39	1 61	2 16	3 16	4 20	4 85	6 55	6 [illegible]0	7 70	8 [illegible]0	10 [illegible]

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1 Geffen D H Report on the Health of the Metropolitan Borough of Hampstead, 1954

movement in the sitting position The natural springiness of the sponge-rubber permits considerable movement and prevents local pressure effects, in fact the "bouncing" effect of the sponge-rubber has given considerable enjoyment to the younger patients and encouraged movements It has not therefore been found necessary to fix the arms, but with more active children the legs have to be lightly secured to the sides of the frame in the manner shown, in order to prevent them from turning over completely on the mattress

Collections have been made for up to three consecutive days, longer periods are not advised because of the risk of pressure-sores around the buttocks due to the lip of the larger hole Usually intermittent twenty-four-hour collections are made (e g, in the study of phenylketonuria) once or twice weekly for balance studies, and shorter timed collections can be made for other diagnostic purposes

It is a pleasure to acknowledge the help and advice of Mr R L Dunn, research and development department, Dunlop Rubber Company, Ltd., Liverpool, by whose 'Dunlopillo' division the mattresses were made I am also grateful to Dr F L Ker, medical superintendent, Little Bromwich Hospital, for permission to describe the binder, to Sister C W Harris for nursing the patients, and to Dr R F Fletcher for the photographs The plastic urinal is manufactured by the Laboratory Glass Blower Company, Valley Works, Lane End Road, Sands, High Wycombe, Bucks

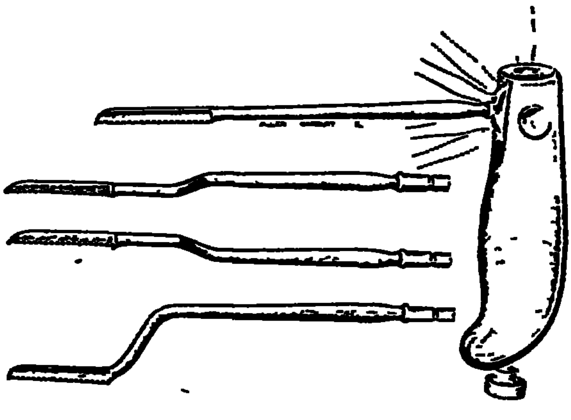
Metabolic Research Unit
Little Bromwich Hospital,
Birmingham

J D BLAINEY
M D Lond, M R C P

COMBINED NASAL SAW

ONE of the difficulties encountered in the use of the conventional type of nasal saw is that the angle of the blade in relation to the handle does not always offer the correct working position Another difficulty has been that the size and shape of the handle in most of the existing patterns do not always fit with ease to the hand

Messrs Allen & Hanburys Ltd have made, at my suggestion, a combined saw consisting of a special handle and four rapidly interchangeable blades The handle is designed to fit comfortably to the hand and contains a blade socket on a rotating mount which can be locked at any desired lateral angle over a wide range In addition the socket is so arranged that the blade can be used in an "in-line" position with the handle



The set of blades comprises two fine nasal saws cranked right and left, a broad saw with a double row of teeth on a straight shaft, and a Ragnell-type jaw saw

The virtue of this combined saw lies in the handle, which is not only comfortable to hold but also allows the angle of the blade to be easily adjusted to ensure the best working position for the surgeon, with corresponding freedom from fatigue

Stoke Mandeville Hospital
Aylesbury, Bucks

J P. REIDY
F.R C S

Reviews of Books

Professional Negligence

J P EDDY, Q C London Stevens 1955 Pp 146 13s 6d

IN the lectures on which this book is based, Mr Eddy first discusses the general principles of the law of negligence and then deals separately with the different professions The subject is not an easy one, but Mr Eddy has a very readable style and, with few exceptions, he has avoided difficult legal language

In the chapter on doctors, Mr Eddy discusses the standard of care required of medical men, the duty of the doctor to warn the patient of danger which may arise from a particular course of treatment, the legal implications of the confidential relationship between doctor and patient, and the liability of hospitals He ascribes the growth in the number of actions against hospital authorities to four causes—the changed status of the hospitals, the payment of hospital staffs the legal aid system, and the decision of the Court of Appeal in *Cassidy v Ministry of Health* (1951)

Many pages are devoted to a résumé of the more important decisions on the liability of hospitals, including some even more recent than that in the Cassidy case In earlier cases the courts began with the doctor or nurse, if it were shown that he or she had been negligent, then the court would consider whether that person could be regarded as a servant for whose negligence the hospital was liable In Cassidy's case, the Court of Appeal approached the matter rather differently The decision supports the proposition that the hospital itself is under a duty of care to those in its charge, of course, the hospital must act through doctors and nurses, but the hospital cannot escape liability on that ground This approach had indeed been adumbrated by the Court of Appeal in the earlier case of *Gold v Essex County Council*—which is also discussed by Mr Eddy—but it was not the basis of the decision in that case

Logically pursued, this new approach might make it irrelevant to consider the status of the doctor involved in the case, so that the hospital would be liable equally for the negligence of consultants and men under contracts of service The three members of the Court of Appeal were not required to decide that point in the Cassidy case because all the doctors involved were under contracts of service Lord Justice Denning made it plain, however, that he at least was willing so to decide In any event, his judgment makes it clear that the reason why employers were liable for the negligence of servants is "not because they could control the way in which the work was done—they often had not sufficient knowledge to do so—but because they had employed the staff and had chosen them for the task and had in their hands the ultimate sanction for good conduct, the power of dismissal"

All this is implicit in the copious extracts quoted by Mr Eddy, but his own summing up of the Cassidy decision is somewhat guarded and he does not speculate on the possible implications of the decision for the profession Caution on this difficult subject is perhaps the prudent course, however, and many readers will certainly be indebted to Mr Eddy for his clear summary of the cases

A Text Book of Medicine

9th ed Editors RUSSELL L CECIL, M.D, SC.D, professor of clinical medicine emeritus, Cornell University, New York, ROBERT F LOEB, M D, LL D, Bard professor of medicine, Columbia University, New York Philadelphia and London W B Saunders 1955 Pp 1786 £5 5s

FOR twenty-five years this celebrated textbook has enjoyed an enviable reputation on both sides of the Atlantic Despite the great number of authors (there are over 170 contributors) the standard is almost uniformly high and the information up to date If the reader wants to look up the use of 'Versenate' in lead-poisoning, or the therapeutic uses of cobalt, or the indications for surgery in heart-disease, or the present position of pulmonary function tests, the information is there, supported by useful references

Special Articles

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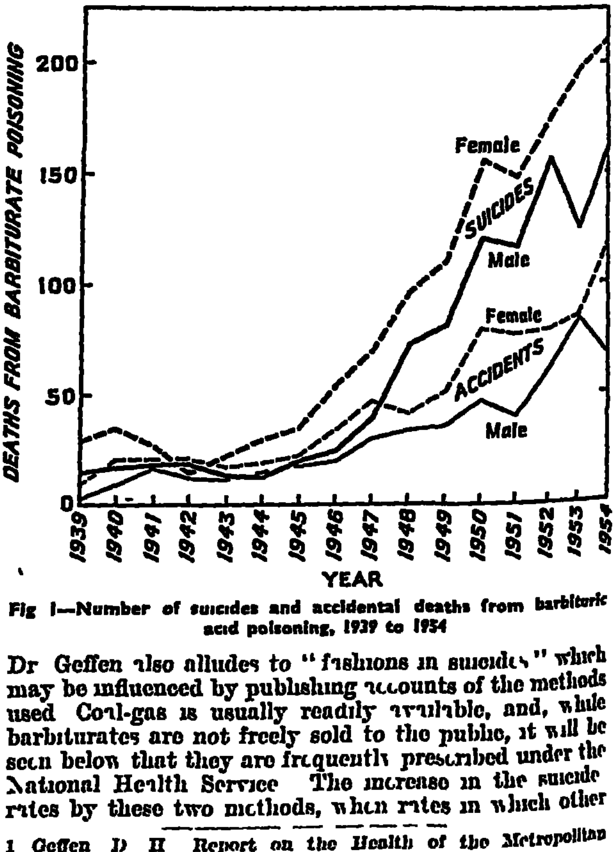

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[1] Geffen D H Report on the Health of the Metropolitan Borough of Hampstead 1954

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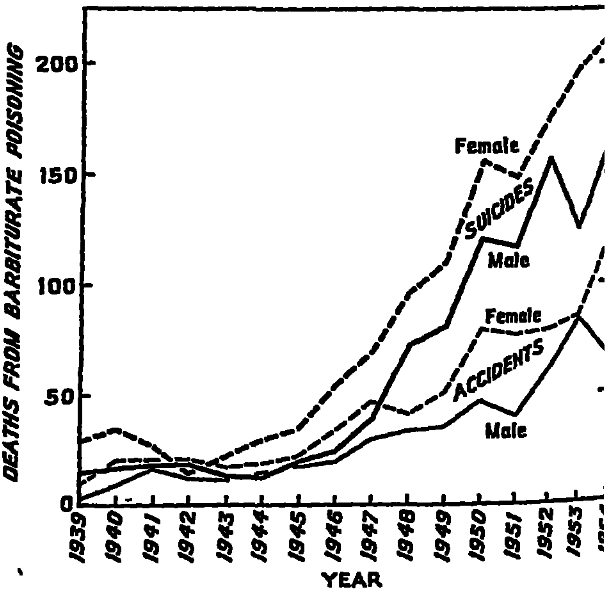

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	F	1·35	1·62	1·2[illegible]	0·65	1·02	1·39	1·81	2·46	3·16	4·29	4·[illegible]	6·[illegible]	6·[illegible]	7·70	8·70	10·01

of risk if it freed them from the burden of child-bearing—often itself fatal But most medical workers would hold that where calculated risks are taken they should in fact be calculated, and the calculation should include that of the patients

Conducted with better facilities, the studies of lithospermum extract are rather less alarming, and with this preparation the risks of clinical trial would not exceed those of any other new and active biological agent Should it prove to be an antigonadotrophin inhibiting ovulation, its use (as **Swyer** points out) might have to be periodically discontinued to prevent derangement of ovarian function, but it is apparently not fully effective in this respect Phosphorylated hesperidin (rehibin), which inhibits the seminal hyaluronidase, offers what seems a less hazardous approach, though its efficacy by mouth has not been proven Local action on the sperms, either before or after they leave the male, seems greatly preferable to alteration of the female endocrine balance (Some of the methods that have been proposed, such as the use of œstrogens to induce tubal spasm which will imprison the ovum, seem to offer almost unlimited possibilities of mischief, and **Zuckerman**'s[34] account of the recent Tokyo conference mentions a chemical which has already produced abnormal fœtuses in a clinical trial) Among the more familiar expedients to which **Swyer** refers, improved occlusive tampons suitable for use under tropical conditions offer at least a partial protection, and work on these is going on Immunological methods of inducing "hostility" to sperms of a given father have so far progressed little, and would probably fall in the category of "luxury" contraceptives It is the poor man (or woman) under bad conditions who most needs and desires an advance in biological methods of controlling fertility We should work more systematically to provide it for him Both in quantity and quality, existing research leaves a lot to be desired,[35] and the "disreputability" of contraception still anachronistically limits the number of first-rate workers

Attention should be drawn, however, to an aspect of this research—or rather of public reaction to it—which is seldom mentioned The people of some Asian and African countries, though they want contraceptive facilities as a right, have reservations which in their position we might share Any suggestion that "the West" was trying to produce a substance with which foodstuffs could be doctored and the fertility of Eastern peoples reduced might release a reaction far more powerful than the Indian Mutiny precipitated by the use of pig grease on cartridges Such suspicions have been voiced, they have all the psychological attributes of an ideal rumour, and unguarded remarks about the beneficial effects of radiation in lowering the population of the world (in countries other than that of the speaker) may lend colour to them For such reasons the spirit in which biologists and doctors approach this problem, and their motives in working on it, may be as important to their ultimate success as is their technical proficiency If, as many believe, we are developing in contraception a human right and a human freedom, it will do no harm to say so fairly often

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[34] Zuckerman S *Nature, Lond* Jan 14 1956, p 58

[35] Pirie N W *Lancet*, 1952 i 54

Annotations

TREATMENT OF LUNG ABSCESS

There are few diseases in which more spectacular therapeutic progress has been made in recent years than in simple lung abscess As recently as 1936, Allen and Blackman[1] reported a mortality of 34% Treatment at that time consisted essentially in external drainage of the abscess, and complications such as empyema and brain abscess were frequent The advent of sulphonamides had no great influence on prognosis, but the technique of surgical drainage improved so much that by 1941 Neuhof and his colleagues[2] were able to record a mortality of only 4% for acute cases, though the mortality for subacute and chronic localised abscesses remained as high as 23% Penicillin produced an even greater change by reducing the number of cases in which surgery was required, and Shoemaker et al[3] now affirm that simple lung abscess should be regarded as a "medical" disease As for ætiology, they hold the generally accepted view that although some simple lung abscesses are caused by trauma or blood-borne infection, or develop from a specific bacterial pneumonia the great majority result from aspiration of infected material from the mouth or upper respiratory passages into the lungs The natural defences of the lower respiratory tract against intrusion from above are relaxed during sleep and other states of unconsciousness, and it is significant that in a considerable proportion of cases of lung abscess there is a previous history of gross dental sepsis, oropharyngeal operation, epilepsy, general anæsthesia, or a bout of drunkenness[3–6] Moreover, Brock et al[7] demonstrated that material introduced into the trachea gravitated into the dependent upper lobe when the subject was lying on his side, and into the dependent apex of the lower lobe when he was lying on his back, and as these are the commonest sites of abscess formation the inference is obvious

Shoemaker et al[3] analysed the results in 67 simple lung abscesses treated between 1950 and 1954 Surgical resection was used in 24—in some of the earlier cases because it was thought to be the best treatment and in others because carcinoma was suspected Confidence in the efficacy of chemotherapy grew with experience however, and it was eventually concluded that this was the treatment of choice, regardless of the duration of the abscess, so that in 1954 resection was performed in only 2 cases, in both because of possible malignancy Only 1 patient in the series failed to respond to adequate chemotherapy, and here the presence of a broncholith provided an explanation Penicillin was considered the best antibiotic, and it was used in all cases with sulphonamide added, unless for some reason the latter was contra-indicated Cavities closed in four to eight weeks, and residual radiographic opacities decreased in size over a period sometimes as long as six months

Gittens and Mihaly[4, 8] evaluated the efficacy of various antibiotics in lung abscess, but they were unable to decide that one was more successful than another Nevertheless, they too concluded that penicillin is the drug of choice because, apart from its small cost, prolonged administration does not entail certain dangers, such as fungal overgrowth in the lungs and disturbance of the intestinal bacterial flora which are associated with the newer

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[1] Allen C I, Blackman J F *J thorac Surg* 1936 6 156

[2] Neuhof H Touroff A S W Aufses A H *Ann Surg* 1941 113 209

[3] Shoemaker E H Yow E M, Byrd W C *Arch intern Med* 1955, 96 683

[4] Gittens, S A Mihaly J P *Amer J Surg* 1955, 89 986

[5] Waterman D H Domm, S E, Rogers W K *Ibid*, p 995

[6] Strang C Simpson, J A *Thorax* 1953, 8 11

[7] Brock R C Hodgkiss, F Jones, H O *Guy's Hosp Rep* 1942 91 131

[8] Gittens S A Mihaly, J P *Amer Rev Tuberc* 1954, 69, 5

Special Articles

TOO MUCH BARBITURATE?

EILEEN M BROOKE
M Sc Lond
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DEATHS in England and Wales due to poisoning by barbituric acid and its derivatives have increased considerably in recent years, until in 1954 they numbered 575 From 1939 to 1945 the annual variation in the number of deaths was small and suicides were not greatly in excess of accidental deaths, the yearly average being

Suicides			Accidental deaths		
	Males	16		Males	12
	Females	27		Females	19

From 1946 onwards there has been a signal increase in all four groups, shown in table I and fig 1

The average numbers of male and female suicides by barbiturates during 1952–54 were respectively 9·0 and 7·3 times the average for 1939–45, the corresponding figures for accidental deaths were 5·7 and 5·0

During the sixteen years since 1939, the crude suicide-rates for both males and females, when all methods of committing suicide are considered, have tended to oscillate rather than to show a definite upward or downward trend (table II)

The rates for barbituric acid poisoning, however, after remaining fairly uniform up to 1945, have since shown a somewhat rapid upward trend While male total suicide-rates have been consistently in excess of female, the female rates for barbiturate poisoning have been higher than the male from 1943 onwards It seems that a preference has been shown lately for using barbiturates as suicidal agents, rather than some other lethal means

On the assumption that different agents would be used in the same proportions in subsequent years as in 1945, the numbers of suicides expected to be due to each agent have been calculated for 1947, 1950, and 1953, and these "expected" numbers, compared with the actual numbers, are shown in table III

Whereas the number of suicides due to barbiturates might have been expected, on the 1945 basis, to increase by 1954 from 20 to 28 for males and from 35 to 46 for females, the actual increases were from 20 to 161 and from 35 to 230 respectively In 1947 the numbers who used other analgesic and soporific drugs exceeded the expected number, but in 1950 and 1954 the actual numbers were considerably less than anticipated Gas poisoning was also used more frequently in the later years than expected, whereas the numbers of deaths due to the more violent methods—hanging, drowning, shooting, and the use of cutting instruments—were all less It appears, therefore, either that the tendency is for the more active and violent methods of suicide to be abandoned in favour of the more passive method barbiturate or gas poisoning, or that an actual reduct has occurred in the suicide rates from more viol methods, but has not been accompanied by a decrea in the rates for barbiturate or gas poisoning Table shows the variation in suicide-rates between 1944 a 1954 according to the means used

The medical officer of health for Hampstead D Geffen[1] commenting on the suicide rates in his Metr politan borough, made some apposite remarks Invest gating the high suicide rate of 1950, he found that, 86 suicides during 1950–53, 23 used barbiturates H suggests that "some steps should be taken to preve the ease with which the public can obtain dangero medicines in lethal quantities" He does not think th "the person who has made up his mind to comm suicide will sooner or later do so" but that "it is like that the presence of a fatal drug, or an easy means terminating his life, may cause him to take a fatal ste at a time when temporarily his mind is unbalanced

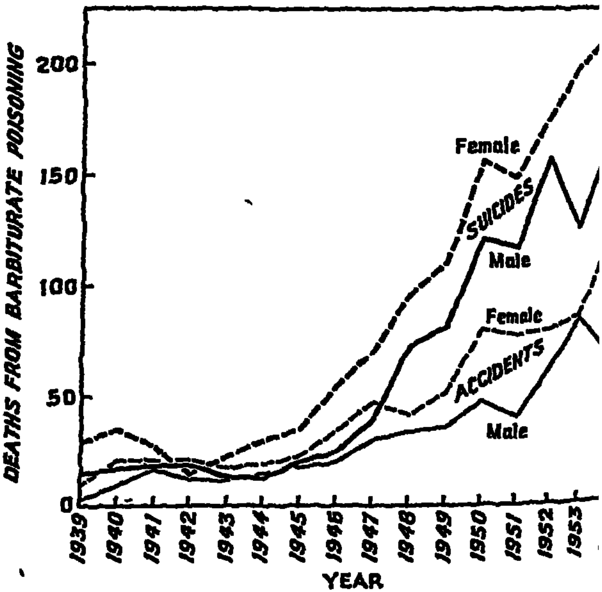

Fig 1—Number of suicides and accidental deaths from barbitur acid poisoning 1939 to 1954

Dr Geffen also alludes to "fashions in suicides" whic may be influenced by publishing accounts of the method used Coal gas is usually readily available, and, whil barbiturates are not freely sold to the public, it will b seen below that they are frequently prescribed under th National Health Service The increase in the suicid rates by these two methods, when rates in which othe

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—		1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1954
Suicides	M	14	17	16	19	13	17	20	24	39	71	81	122	100	157	124	161
	F	29	35	27	14	22	30	35	54	70	96	110	156	115	176	197	230
Accidents	M	3	9	17	13	12	15	18	20	30	31	36	47	40	61	81	[illegible]
	F	10	21	21	21	17	19	22	14	17	41	51	80	77	79	85	117

* Data from the Registrar-General's Statistical Review, 1954 Part I Tables (Medical)

TABLE II—CRUDE SUICIDE-RATES PER MILLION LIVING FOR (1) ALL AGENTS, (2) BARBITURIC ACID POISONING, 1939–54

—		1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1954
All agents	M	168	159	135	125	[illegible]	[illegible]	126	144	137	115	117	[illegible]	[illegible]	132	112	[illegible]
	F	78	75	[illegible]	62	63	58	66	[illegible]	76	79	[illegible]	70	[illegible]	64	76	61
Barbituric acid	M	0·71	0·93	1·04	1·13	0·80	0·80	1·22	1·25	1·99	3·58	3·91	[illegible]	4·75	7·44	[illegible]	[illegible]
	F	1·35	1·62	[illegible]	0·65	1·02	1·39	1·61	2·46	3·16	4·29	4·68	[illegible]	[illegible]	7·70	8·60	10·01

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[1] Geffen D H Report on the Health of the Metropolit Borough of Hampstead, 1954

extension of dilated and incompetent lymphatics up to the root of the limb It is possible that all patients with lymphœdema præcox have, before the advent of the cellulitis and lymphangitis to which they are so prone, a dilated and incompetent lymphatic system The subsequent infection, mainly by the streptococcus, obliterates the lymphatic channels and so prevents their demonstration by dye techniques This interpretation could well reconcile the different findings An alternative explanation is that both absence and incompetence of lymphatic channels cause tissue fluid to accumulate and either abnormality may be associated with the clinical picture recognised as lymphœdema præcox

It is becoming clear that the skin and deeper lymphatics are often involved in a variety of vascular diseases So far this has not greatly influenced treatment, but the knowledge is interesting in itself and may lead to therapeutic advances

ABRASION TREATMENT OF ACNE SCARS

THE pimples of acne vulgaris are bad enough as a temporary embarrassment, but the scarring that can follow is a much more serious and permanent disfigurement A great deal of this may be prevented by persistent treatment under experienced supervision, but many cases of acne are neglected because the complaint is almost physiological in adolescence and usually clears up spontaneously In the past, a number of different forms of treatment for acne scars have been suggested, each amounting to some means of superficial destruction of the skin Painting with liquid phenol, followed by "neutralisation" with alcohol, seemed to carry such a disproportionate risk of poisoning that it never became popular Abrasion with sterilised carpenters' sandpaper[1] began a new vogue which has largely been abandoned for fear of foreign-body reactions from implanted silica A refinement of the method is to use rotating abrasive discs or emery wheels A form of mechanical abrasion was suggested as long ago as 1905, when Kromayer[2] introduced small rotating burrs and cylindrical knives for this purpose A modern development has now become so popular in the United States that complete kits for "dermabrasion," as it is called, are widely available The special features of the method[3] include the use of an electric motor producing 12,000 r p m, a range of small wire brushes held with the axis of rotation at right angles to the surface of the skin, and refrigeration with ethyl chloride, which serves both as local anæsthesia and skin hardener Rapid evaporation of the ethyl chloride is maintained by a continuous stream of air 'Freon 114,' which is dichlorotetrafluoroethane, has recently been used[4] instead of ethyl chloride, because it is said to be non toxic, it is non-inflammable, and it is not an anæsthetic on inhalation

Some reports of the results of this treatment were very enthusiastic and were given wide publicity in America One report said that the results are so good that no patient should be refused treatment The American Medical Association's committee on cosmetics called for a report on the method, and this was prepared by Rattner and Rein[5] They state that a high degree of cosmetic repair can be obtained in some cases, but "the results of treatment are usually good rather than dramatic" and they are unpredictable in an individual case The commonest complaint—namely, "dilated pores"—cannot be improved, nor can very wide or deeply pitted scars be greatly modified Their own experience has led them to advise against this treatment in 40–60% of those applying for it Disastrous results have been rare Small horny inclusions or milia form a common but temporary complication Infections have not been troublesome, but in some cases erythema or pigmentation has persisted for some months after treatment Some slight scarring has been seen, but this has responded to further abrasion and no cases of keloidal scarring have been reported This absence of scarring is perhaps the most surprising feature of the method One paper[6] insists that it is possible "to plane down almost to subcutaneous fat and still have noncicatricial healing"

There are only a few places in this country where this treatment is being tried, and it is unlikely that it will ever become a routine matter in our dermatological out patient departments It seems to be a method of value for selected cases of scarring from old acne, chickenpox, or other causes Less enthusiasm is likely for some of its suggested uses, such as the treatment of pigmented lesions and keratoses where histological control is desirable The treatment may be most sought after by patients for whom anything short of miraculous restoration would be inadequate, and who are perhaps rather obsessional about their appearance Indeed, it is in the selection of cases that Rattner and Rein urge most caution It has long been a dermatological paradox that those most seriously blighted by skin disease seem least concerned with their appearance the victims of what are now old-fashioned degrees of lupus vulgaris were often less apparently perturbed than the young man with relatively insignificant scars of acne

FAT AND FERTILE

IN a contribution to the proceedings of the Third International Congress of Nutrition, Widdowson[7] made some stimulating comments on reproduction in relation to obesity She stated that fat women (whether prediabetic or not) had large fat babies who grew big, reached an early puberty, still ahead of the field, and in due course completed the cycle by becoming fat mothers The additional risk which their obesity conferred in pregnancy (largely that of toxæmia) was compensated in the puerperium by the facility with which they fed their children, for the large women with large breasts pro duced more milk than their slender sisters, even to the extent of having lactorrhœa[8] It is safe to say that much of this is in opposition to what many clinicians believe Thus, it is widely held that the fat child is likely to be sexually immature, or late to mature Spence,[9] discussing obesity accompanied by delay in the onset of puberty, noted that nearly all these patients were suffering from simple obesity (though a craniopharyngioma had to be excluded) Yet there is now much evidence which seems to refute the very existence of such an association Wolff[10] has published the most recent of several studies all of which suggest that the obese girl reaches puberty no later and probably earlier than normal The opposite impression may have grown from wide acquaintance with the rare but more publicised endocrine disorders associated with the names of Frohlich and Cushing, and also from a knowledge that obesity and hypomenorrhœa are commonly associated in young adults At least, such evidence as there is (and there is little) goes to show that women with simple obesity may often have amenorrhœa which can be relieved by weight reduction Swyer[11] described irregular or scanty periods in overweight women, in whom restriction of diet restored menstrual regularity and improved fertility From a different approach, Rogers and Mitchell[12] found that a

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[1] Iverson P C *Plast reconstr Surg* 1947 2 427
[2] Kromayer E *Derm Z* 1905 12 26
[3] Kurtin, A *Arch Derm Syph, Chicago* 1953 68 389
[4] Wilson J W Luikart R Ayers S *Ibid* 1955 71 523
[5] Rattner, H Rein C R *J Amer med Ass* 1955 159 1299
[6] Robinson M M *Med Ann D C* 1955, 24, 17
[7] Widdowson E M *Amer J clin Nutr* 1955, 3 391
[8] Sheldon J H *Lancet* 1949 ii, 869
[9] Spence A W *Practitioner*, 1952, 169 260
[10] Wolff O H *Quart J Med* 1955 24 109
[11] Swyer G I M *Brit J Nutr* 1949 3 100
[12] Rogers J Mitchell G W *New Engl J Med* 1952 247 53

Special Articles

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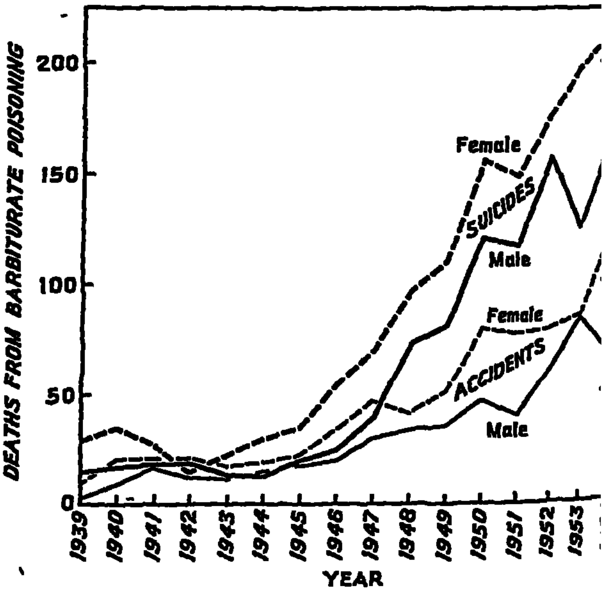

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	F	1 35	1 62	1 25	0 65	1 02	1 39	1 61	2 46	3 16	4 29	4 85	[illegible]	6 40	7 70	8 70	10 01

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[1] Geffen D H Report on the Health of the Metropolit Borough of Hampstead 1954

Points of View

A MATTER OF SCIENCE AND ETHICS

Reflections on the B M A. Committee's Report on Homosexuality and Prostitution *

ALEX COMFORT
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HON RESEARCH ASSISTANT, DEPARTMENT OF ZOOLOGY, UNIVERSITY COLLEGE, LONDON

THE Departmental Committee now taking evidence on the laws which affect homosexuality and prostitution is a potentially important body In the legal interpretation of sexual behaviour the psychological and biological sciences have for some years been increasingly persistent interrupters from the floor, and this committee is one of the first, in England, to invite them, together with their opponents, on to the platform Like most interrupters so treated, some workers who have much to contribute to the subject have fallen silent many of them have scientific scruples against presenting as evidence what they know to be only opinion But this is a field where the law has long been formed by disturbed minorities, and these scruples are not shared by the opponents of social science

The most important testimony which the committee requires to consider comes in all probability, not specifically from medicine, or even from psychiatry as it is usually understood but from comparative human biology on the one hand, and the social psychology of prohibitive legislation on the other But medicine has a number of important comments to make and doctors—who should, no doubt, be both human biologists and social psychologists—have a chance of being heard on the occasions when "scientists" are being shouted down by common sense, practical geoplanarians appealing to the self evident As there will be no lack of Wilberforces in any such debate, it is clearly someone's business to accept the unpleasantness of being a Huxley

A number of medical bodies are, in fact, giving their views One of these is a special committee set up by the council of the British Medical Association It has just made public the evidence which it proposes to submit, in the form of a report, accompanied by some well-calculated publicity

There are two reasons which make this document worthy of separate discussion The first is political A report endorsed by the B M A might easily turn out to be a microcosm either of the departmental committee's ultimate findings, or of future legislation The considered views of such professional bodies have great attractions for politicians facing unpopular topics the B M A is a conservatively inclined body with a high lobbying potential, which can be set as the exponent of the practical and human in contrast to the extremist or "egg-headed" conclusions of science There is nothing in its title or record to alarm the most disturbed or anti intellectual Member of Parliament, he may never have met a social anthropologist, but he has often met a doctor or two A Minister forced to advocate some changes in the law, unwilling to make many, and faced with an organised and paranoid minority campaign against any at all, will look instinctively for a body, quotable in support of his intention, to which the word "responsible" can be applied

One reason for the importance of the report, then, is that it could provide an opportunity for intelligent medical opinion to comment on the basis of new knowledge, and to encourage the reform of laws which are widely held to be bad There is, however, another Under the influence of modern research and thought, the psychology of law and government is undergoing changes as radical as is the psychology of individual behaviour science is beginning to assume the duty of replacing political ideology with research Our own generation has before it two excellent object lessons in the interplay of emotion, fact, reason, and prejudice in legislation, and of the relation between law-making and personality structure one is the attempt to abolish the death penalty, and the other the attempt to reform the law regarding sex offences In each case there are superficially substantial arguments on both sides, in each case there is intense emotional motivation on both sides, and in each case there are signs of a bimodal distribution of opinion by personality type, one type being commoner among legislators and executive officers, the other among social scientists This is a fascinating and important study—terrifying to those who think that legislatures can be trusted to accept expert advice, or that experts can be trusted to govern It is therefore intensely interesting to see how medical opinions, official and unofficial, scientific and administrative, distribute themselves on this scale In this respect, the B M A 's committee is offering itself for study by its sociological colleagues

* * *

A report of this kind was bound to be difficult to write One source of difficulty is evident if we compare the two matters with which it was to deal Prostitution is a practice which may offend but its discussion disturbs only those who are disturbed by sexuality in general Its control, and even its merits, can be, and have been, discussed with a realism bordering on the cynical Homosexuality is quite another matter. The reaction of our culture to it is so violent, and so disproportionate to any demonstrable importance of the behaviour concerned, that even if a committee is itself quite unaffected by this reaction (an unlikely event, if it is representative) it is bound still to decide how much insight it ought to try to give to those it addresses It could be argued that since doctors have no special claim to be arbiters of the *mores* of their culture, rational or irrational, such a committee should take the public attitude as it finds it This view, very properly, the committee rejects "Doctors," it says, "can influence, by instruction and example, the development of the moral and social environment of their patients, and discourage them from behaviour which may adversely affect their health" They will do so, no doubt, both from their own common sense and from any special insights they derive from the discipline of human biology In valiantly assuming this duty to an emotionally loaded subject, however, the Committee undertakes the responsibility both of showing what those insights are, and of writing intelligently about their application to ethics, and it has clearly found this no light assumption

This report had the opportunity of doing three things—of indicating the weaknesses and inhumanities of the present law regarding homosexuality, which it does with some success, of showing how modern social product Attempts were made to infect some egg albumen artificially with salmonella organisms To produce comparable conditions, it was important to contaminate the centre of the crystals, and to do this albumen had to be dissolved, infected, and re-crystallised Unfortunately, the resultant crystal formation was so different from the original albumen crystals that this method was abandoned All experiments were thereupon carried out on imported crystals known to be heavily infected with *S thompson*

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* The report was issued on Dec 16, and a long summary appeared in the Supplement of the *British Medical Journal* for Dec 17, 1955 It was prepared as a memorandum of evidence for the Departmental Committee, by an expert committee (set up by the council of the British Medical Association) whose members were Dr RONALD GIBSON (chairman), Dr T H BLENCH, Dr DENIS CARROLL, Dr T C N GIBBENS, Prof J GLAISTER, M D , Mr AMBROSE KING, F R C S , Dr J A MOODY, Dr DORIS ODLUM, Dr T P REES, Dr S L SIMPSON, and Dr R D SUMMERS with Dr E E CLAXTON as secretary On Nov 4 the council of the B M A agreed that the memorandum should go forward as the report of the committee, for on so controversial a subject it was not to be expected that the profession or any large body within it could be in agreement in detail

The experiments can roughly be divided into six different stages Full details are not given here, but will appear when the full report is published

Certain of the egg albumen crystals were powdered by crushing, and comparisons made between the effect of heat-treatment on this powdered material

First Stage

Initially, experiments were designed to find the effect of a wide range of temperature and time A total of 52 samples of both crystalline and powdered egg-albumen known to be heavily infected with *S thompson* was tested

Results varied considerably, and some samples withstood temperatures of 165°F for 10 hours, and 190°F for 3 hours, without the salmonella organisms being completely killed It was noticed that the relatively low temperature of 130°F for 3 days produced negative bacteriological results At first, the significance of this was not fully realised

Second Stage

Tests were continued to examine the effect of high temperatures of 180°F and 200°F for $^1/_2$–5 hours Initially, the results seemed promising, for periods of heat-treatment of 180°F for $1^1/_2$–2 hours and of $^1/_2$-hour at 200°F gave repeated negative results for both crystals and powdered samples

This experiment emphasised that powdered material was much more easily heat-treated than the crystalline products The significance of this finding increased as the investigations proceeded

Up to this point, all experiments had been carried out in an experimental oven, but difficulties appeared when attempts were made to treat large quantities A heat-processing machine, capable of dealing with 200–300 lb of material at a time was used Heat was provided by hot air, but it was found impossible to maintain in all parts of the chamber an even temperature of 180°F for 3–5 hours There were areas at which the temperature never exceeded 110°F, while at the heat inlet a charring of albumen occurred Quite apart from this difficulty, it was estimated that this process was too costly

Third Stage

The effect of long-continued low temperature was next investigated

Initial experiments showed that heat treatment at 120°F was uncertain, for salmonella organisms persisted after 4 days in approximately 1 out of every 5 samples tested By raising the temperature to 130°F, however, all salmonella organisms were killed *after four days'* treatment

Fourth Stage

The next experiment was designed to test this method (130°F for 1–5 days) in conditions similar to those likely to be experienced commercially Samples of crystalline albumen known to be very heavily infected with *S thompson* were wrapped in 'Cellophane' packets

For each test for every cellophane packet of egg albumen which was *heat-treated, another sample* was set aside for bacteriological examination as a control

The samples to be tested were placed in the centre of (*a*) 1-cwt bag of albumen crystals, (*b*) 100 lb wooden case of albumen crystals, (*c*) 28 lb tin of albumen crystals The results are given in the accompanying table

These results were then checked, using ten samples at each temperature with similar results no organisms survived after 4 days at 130°F with crystalline material, or after 2 days at 130°F with powdered albumen

These large scale experiments and all subsequent ones were carried out in a hot room measuring 11 × 12 × 9 ft As it was a converted refrigeration room, heat insulation was very good, and it was heated during these experiments by three radiant electric heaters An electric fan ensured complete circulation of air The temperature was thermostatically controlled, and a Cambridge temperature recorder was installed outside (see figure)

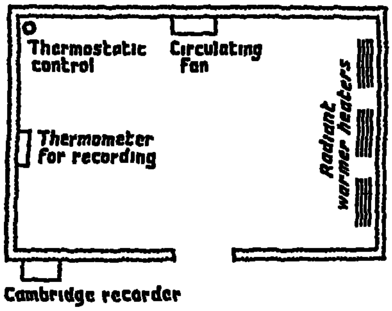

Diagram of the hot room

Fifth Stage

This experiment was designed to test the effect of placing 100-lb wooden containers at various parts of the hot room It was found that each container had to be placed at least 2 ft from the floor, otherwise the hot air circulating did not heat the centre sufficiently When raised 2 ft from the floor, and provided a free air space separated different containers, a temperature of 130°F was reached in the centre of the container within 36 hours, with an air temperature of 110°F (provided the fan was used)

Thus, with 100-lb containers, 36 hours must be added to the time of the earlier experiments

The cost of heating the room with the three electric heaters was roughly *1s* a day

Sixth Stage

The final test was to measure the effect of heat-treatment on solubility

It was found that with the crystalline product 4 days at 130°F was satisfactory but after 5 days at 130°F, changes reducing the solubility were demonstrated Heat-treatment on the powdered material showed less effect on solubility

DISCUSSION

These results suggest that the final solution of the problem of infected egg albumen will probably be mass low temperature heat treatment

To make treatment easier, all material should first be powdered The aim of heat treatment should be to ensure that a temperature of 130°F is maintained in the albumen in the centre of the container for 1–5 days It is estimated that in a *hot room* devised for this purpose, it would be necessary to have an air temperature of 140°F for $5^1/_2$–$6^1/_2$ days after the albumen is first placed in the room It is most important to maintain free circulation of the heated air, and to stand the cases at least 2 ft off the ground

RESULTS OF HEAT TREATMENT OF INFECTED CHINESE EGG ALBUMEN UNDER VARIOUS CONDITIONS AT 130°F

	Samples heated at 130°F				Unheated control samples		
			Result			Result	
Samples in centre of	No of samples	Time (days)	Positive	Negative	No of controls	Positive	Negative
(*a*) 1 cwt bag	[illegible]	1	[illegible]	0	[illegible]	[illegible]	0
	[illegible]	2	0	[illegible]	[illegible]	[illegible]	0
	5	3	0	[illegible]	[illegible]	[illegible]	0
	5	4	0	[illegible]	[illegible]	5	0
	5	5	0	[illegible]	[illegible]	5	0
(*b*) 100 lb case	[illegible]	1	[illegible]	0	[illegible]	5	0
	[illegible]	2	[illegible]	2	[illegible]	[illegible]	0
	[illegible]	3	0	[illegible]		5	0
	[illegible]	4	0	[illegible]	[illegible]	[illegible]	0
	[illegible]	[illegible]	0	[illegible]	[illegible]	[illegible]	0
(*c*) 28 lb tin		1	1	1	5	[illegible]	0
	[illegible]	2	0	[illegible]		[illegible]	0
	5	3	0	[illegible]			0
	5	4	0		[illegible]		0
	5	[illegible]	0	[illegible]	[illegible]		0

All positive samples yielded *S thompson* or endocrine correlations. The reactions of these various cultures range from complete toleration to intense emotional disturbance, and from admiration to severe punishment for individuals so behaving. Similar behaviour between females, however, only exceptionally evokes any intense reaction.

At no point does the B.M.A. report mention this comparative background. Yet the comparative study of sexual behaviour in man and animals is perhaps the fundamental contribution of modern biology to this whole question. A summary of mammalian work, or even an account of the attitudes of some other human societies, would probably have been more useful to the Departmental Committee than a long appendix describing the effects of evangelism on homosexual persons, while the lack of any paragraph dealing with phylogeny makes nonsense of a good deal of the discussion of causation neither genetics, endocrine imbalance, nor processes of parent-identification contribute detectably to the causation of homosexual play between dogs, sticklebacks, or rats, so far as the literature indicates—though they may begin to do so in higher primates, the complexity of whose sexual behaviour forshadows our own. One might punish these lower animals, but there would be little point in consulting a veterinary surgeon about their behaviour.

* * *

But the real importance of comparative studies is in their effect on our attitude, and I suspect that it is for this reason that they have been omitted.

If the authors of the report were tired of ethical judgments on human behaviour drawn from white rats and Trobriand islanders, they have most reasonable men on their side. Comparative and descriptive studies in animals or in man have no direct ethical meaning. The distribution of homosexuality in mammals and in cultures is not very different from that of fights to-the-death between males as a feature of mating behaviour, yet only the German duellists of the 1930s invoked phylogeny to prove the natural merit of this kind of competition. Nevertheless a background of comparative study does and should condition our response, and that of the Departmental Committee, to the magical propaganda regarding the unnatural, the diabolistic, and the loathsome, which plays such a large part in preventing the sensible discussion of sexual deviations, and even of the normal range of sexual behaviour. However harmful to society homosexual behaviour may be in man, the biologist, surrounded day in and day out by the homosexual activities of his healthy laboratory animals, finds it hard to muster convincing indignation at its unnaturalness.

It would, I think have been extremely valuable to the Departmental Committee's judgment—and, for that matter, my own—if this report had included a serious discussion of evidence that homosexual conduct has, in fact, social or psychiatric ill effects other than those due to the reaction it evokes in society in societies which encouraged it, did it become a self-propagating emotional disability? If, as the B.M.A. Committee believes (on evidence of the kind which has so long bedevilled the attempt to trace an authentic instance of instinct in human psychology) there are "essential" homosexuals, is it beneficial to their mental health to prohibit or discourage their activity? Does the same apply to persons who display both homosexual and heterosexual behaviour? Many would think that psychiatrists with a sufficiently wide comparative insight are among the people best qualified to answer these questions.

The committee says that it proposes to base its advice in ethical matters upon the effects of behaviour upon health and welfare it also devotes much time to the administrative arrangements for treating homosexuals instead of punishing them. The evidence its presents tends to indicate (1) that in man apart from the supposedly "essential" cases which it postulates, homosexuality is, like heterosexuality, a continuously distributed variable, and (2) that while its association with certain forms of psychological upset is evident in many of the individuals who come for treatment, there are probably circumstances under which it is no more a psychiatric problem than any of the wide range of sexual manifestations which may be displayed by "normal" human beings. In regard to homosexual play between adolescents, the committee takes this view it also lays stress on the need to assess each case upon its merits. There is, I believe, no virtue in treating people for symptoms which are not pathological or in punishing them savagely for crimes which are of no social importance, and there is a risk that the courts will grudgingly accord treatment to subjects who engage in homosexual behaviour and are mentally disturbed about it, while discharging the whole weight of frustrated righteousness on those who are not. It is not so long, after all, since adolescent masturbation was solemnly quoted as a cause of mental disorder, blindness, and pimples.

* * *

Medicine could help at this point, if it were willing to risk some legislative unpopularity by pointing out the differences between public law and personal ethics. The B.M.A.'s committee has felt itself unable to recommend that homosexual offences involving neither violence scandal, nor seduction should be recognised as outside the province of the law. It may be right in this, but I cannot help feeling that its views would have been more respected if their presentation and logic had been less confused in the ethical passages of the report. Perhaps the crux of the matter lies in the committee's own summary

> "The apparent increase in homosexual practices and in prostitution is attributable to the weakening of the sense of personal responsibility with regard to social and national welfare in a significant proportion of the population. It is illogical that homosexual practices receive greater condemnation than promiscuous heterosexual intercourse."

One could equally argue that there is a sense in which the increase, if real, represents the reverse of such a weakening, because the climate in which it occurs has sprung largely from the impact of new knowledge on society, leading to a rejection of pontifical and magical regulations upon conduct, and a search, often very confused and beset by rationalisations, for reasons for or against particular modes of behaviour. The teenage boy or the grown man who is no longer disturbed by the memory of a homosexual experiment has not unless he is exceptional, read widely in comparative social anthropology though he may have read Kinsey, or a distortion of Kinsey's findings in the Sunday Press. His lack of disturbance is, to my mind, a gain rather than a loss to the mental health and morale of the future.

I suspect that the author of the passage dealing with salacious posters would even the discrepancy between homosexual and heterosexual offences by increased punishment of the second. Others would incline to do so by presenting to public opinion rational grounds for responsible sexual behaviour. It is not surprising if doctors, like the rest, are confused between these two views they represent two kinds of person, at least as different in their reactions as are homosexual and heterosexual individuals, and probably determined in much the same manner, genetic and environmental. There may even be "essential" punishers and prohibitors. But we should bring the existence of this confusion of counsel to the notice of others explicitly, not implicitly, if our professional sincerity and insight are to be respected.

Relatives have to be interviewed the whole time, not so much with the idea of imparting information as to ascertain the aberration in themselves which precipitated the patient's trouble However, I had to sympathise with the husband who told me how it all began with his daughter's blinking eyes The school nurse said it was a cold, the doctor conjunctivitis, and the optician short sight They went to a specialist in Harpole Street who said it was astigmatism and ordered reading glasses, but another specialist in Wimley Street ordered distance glasses, while a third specialist at the hospital said that no glasses were needed at all "The wife has been confused ever since," he explained

* * *

As a devotee of this column, I may be excused for taking a special interest in Berwick-upon-Tweed, which might suitably have chosen "In England Now" for its motto—at least since the Reform Act of 1885 Before then the citizens must have had great difficulty in knowing when they were and when they were not in England The town changed hands between England and Scotland thirteen times from 1147 to 1482 it then became semi-independent, so that it had to be specially mentioned in all Acts of Parliament Berwick was included in the declaration of war on Russia before the Crimea, but this was forgotten when peace was made It will be interesting to see whether Mr Krushchev travels the Great North Road when he pays his promised visit to this country

Berwick is an anomalous place altogether It has its being in Northumberland but gives its name to a Scottish county Its Royal Border Bridge crosses the Tweed but not the border It is Scottish in speech and in appearance Its football team, Berwick Rangers, play in the Scottish League There has long been a movement for a return to Scotland, but it seems unlikely that this will be achieved For one thing, the difficulty of redrafting all the statutes suggests that Berwick will continue to provide a typical example of British compromise Cynical Scots may take pleasure in pointing out that it is no compromise to leave Berwick a few miles on the English side of the Border, but it has its uses The Scotsman who is wise enough to take the East Coast road to England is offered a gradual introduction to his new environment Strengthened by the sight, as he passes through Berwick, of Scotsmen everywhere, the peripatetic Scots graduate will be helped to withstand the shock, as he journeys further South, of meeting an occasional English doctor

* * *

At first sight the Mitsukoshi looks like any other chain store The lower floors are full of American style goods, but when you climb to the fifth you find good lacquer, damascene, cloisonné, pottery, and prints I spent an interesting hour watching the Japanese shoppers Some of the men were dressed in ready-made American-type lounge suits, some in the Oriental fashion, and some in a mixture of the two—an American overcoat and plug hat surmounting the dignified and well-tailored Japanese garments, with slippers or clogs on the feet Japanese women wearing kimonos carry their babies in a kind of sling upon their backs The babies are curiously submissive, too good to be true, and when they fall asleep their heads loll alarmingly as though about to fall off, though I never actually saw this happen

Japan is still a man-run country Father strides ahead of mother who carries not only the baby but most of the parcels When father grows tired he sits on some convenient seat, but mother remains standing respectfully beside him, and in the restaurant he is served first

* * *

I speak of bulimic obesity,
Of energy output and calories,
Of whether or not a disease pretty
Closely related to salaries,
Greed, and the middle aged spread
Deserves differential prognosis
From that of the vast overfed
Example of grave neurosis
In psychosomatic tomes
I search in vain for prediction
Which of today's gastronomes
Are tomorrow's victims of eating addiction?

Letters to the Editor

POLIOMYELITIS A BAFFLED LAYMAN

SIR,—As a layman I have recently had to decid whether or not to keep my child away from school aft a classmate had contracted poliomyelitis I learned that paralytic poliomyelitis has a 40% death or disabl ment rate, that the death-rate is highest in the young age groups, that the disease is probably transmitted b personal contact in a narrow stream of the populatio that there are many unrecognised cases which can pa on the infection, and that the chain of infection wa followed through for 31 out of 37 cases in the Isle o Wight epidemic of 1950 I therefore decided to keep m child at home for at least three weeks, arguing that while she might develop the disease as a result of th exposure to infection which she had already experienced she would at least not be exposed to possible infectio from any further cases (recognised or unrecognised which might develop

I am, however, very puzzled about the differen attitudes of the various authorities both in my distric and over the country as a whole

The school doctor here says "keep the children awa from crowded places (e g, cinema, parties)," but apparentl does not go on to make what seems to me the logical extensio by saying that they should be kept away from the crow in which the virus is known to be circulating (i e, school)

At a nursery school in my district mothers were informe when the older sister of one of the little ones had poliomyeliti and told to keep their children at home if they wished However, I was not notified by my daughter's infant school of th case in her class, and in fact subsequently discovered tha there had been a previous case in the school two weeks before In spite of this the headmistress said it is "perfectly absurd" to keep the children away from school Yet in some othe parts of the country, when a case of poliomyelitis occur schools are closed or the parents told to keep their childre at home if they wish

In my area not only does the public health departmen consider it unnecessary to keep children away from school but a health visitor is reported as having told the mothe of a child with poliomyelitis not to tell people what was th matter I cannot believe that a policy of secrecy is righ unless there is absolutely no knowledge of how the diseas is transmitted, and, if my understanding of the medica literature is correct, the position is by no means so black as that

In this district the fathers of both the cases of which we know continued going to work, but when one of my office colleagues contracted the disease the friend with whom he shared a flat was kept from work for three weeks, while my office in London was notified of the case by the local medical officer

Should there not be a consistent policy over the whole country? If medical opinion is too divided for this to be possible, could not the public be told the known facts and left to make their own individual decisions as to what precautions they take [1]

R H Daw

BREAD

THE WIDDOWSON-MCCANCE INVESTIGATION

SIR,—In your leading article of July 30 last you said that nothing in the Sanderson-Wells lecture [2] or in the Widdowson-McCance report [3] had altered your preference for high extraction or National flour as opposed to enriched white flour, and, in support of your conclusion, you quoted figures suggesting that the 70% white flour used in the investigation was in fact not a 70% flour at all, but one approximating to an 80% National flour In your issue of Sept 3 I pointed out that this suggestion was incorrect, and therefore misleading The detailed evidence which you then gave in a rejoinder to my letter or endocrine correlations. The reactions of these various cultures range from complete toleration to intense emotional disturbance, and from admiration to severe punishment for individuals so behaving. Similar behaviour between females, however, only exceptionally evokes any intense reaction.

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[1] E g Agerholm M *Lancet* 1953 ii 287, and subsequent correspondence
[2] McCance R A Widdowson E M *Lancet* 1955 ii, 205
[3] *Spec Rep Ser med Res Coun Lond* no 287 1954

At no point does the B.M.A. report mention this comparative background. Yet the comparative study of sexual behaviour in man and animals is perhaps the fundamental contribution of modern biology to this whole question. A summary of mammalian work, or even an account of the attitudes of some other human societies, would probably have been more useful to the Departmental Committee than a long appendix describing the effects of evangelism on homosexual persons, while the lack of any paragraph dealing with phylogeny makes nonsense of a good deal of the discussion of causation: neither genetics, endocrine imbalance, nor processes of parent-identification contribute detectably to the causation of homosexual play between dogs, sticklebacks, or rats, so far as the literature indicates—though they may begin to do so in higher primates the complexity of whose sexual behaviour forshadows our own. One might punish these lower animals, but there would be little point in consulting a veterinary surgeon about their behaviour.

* * *

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It would, I think, have been extremely valuable to the Departmental Committee's judgment—and, for that matter, my own—if this report had included a serious discussion of evidence that homosexual conduct has, in fact, social or psychiatric ill effects other than those due to the reaction it evokes in society. In societies which encouraged it, did it become a self-propagating emotional disability? If, as the B.M.A. Committee believes (on evidence of the kind which has so long bedevilled the attempt to trace an authentic instance of instinct in human psychology) there are "essential" homosexuals, is it beneficial to their mental health to prohibit or discourage their activity? Does the same apply to persons who display both homosexual and heterosexual behaviour? Many would think that psychiatrists with a sufficiently wide comparative insight are among the people best qualified to answer these questions.

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Medicine could help at this point [illegible] to [illegible] some legislative [illegible] differences between [illegible] The B.M.A.'s committee [illegible] mend that homosexual [illegible] scandal, nor seduction [illegible] the province of the law. [illegible] I cannot help feeling that the [illegible] more [illegible] if they [illegible] less confused in the ethical [illegible] the crux of the matter [illegible] summary:

> "The apparent [illegible] of persons [illegible]

One could argue [illegible] the increase, [illegible]

[illegible]

SIR,—As the B-vitamin section of the Widdowson-McCance investigations was carried out and reported by me,[1] and as my interpretation of the analytical values for the 70%-extraction flour differs in some important respects from that suggested in your leading article of July 30, it seems desirable that my own views should also be made known

Your article takes no account of the fact that the chemical method I used for nicotinic acid gave considerably higher values for the 70%-extraction flour (though not for the flours of higher extraction) than did the microbiological method employed at the Cereals Research Station When reporting the results of the investigations [1] I gave the microbiological as well as my own values (see p 97), but pointed out (p 108) that the German children's nicotinic acid intakes appeared to be adequate whichever value was used in the calculations

Comparisons of nicotinic acid content should be based on results obtained by the same analytical method Since the values for laboratory milled flours [2] to which you refer were obtained at the Cereals Research Station, it follows that this Station's value for the experimental 70% flour should be taken to compare with them When this is done there is nothing to suggest that the 70% flour used in Germany was considerably richer than other flours of this type Moreover, a comparison between the Cereals Research Station's value of 10 μg per g for the 70% flour used in Germany and their value of 16 μg per g for National 80% flour [3] (see table 12) indicates that the former was in no way comparable with the latter

With regard to vitamin B_1, the method I used gave values for the flours which were slightly higher than the corresponding values obtained at the Cereals Research Station by a different method Both were chemical methods, but, since metabolic studies on the children formed the main subject of the B vitamin investigations in Germany, mine was a procedure applicable to mixed diets, urine, and fæces The Cereals Research Station method was a method designed specifically for flour and was not applicable to other types of biological material

I concluded,[1] from a comparison of my values with data from the general literature (see p 97), that the 70% extraction flour used in the experimental periods was within the normal range with respect to vitamin-B_1 content, but was at the upper end of the range When the Cereals Research Station value of 1 1 μg per g for the German 70% extraction flour (p 98) is compared with their values of 0 7–0 8 μg per g for other flours of this type [2] a similar conclusion is reached Since the Cereals Research Station values were all obtained by the same method of analysis and since their values for laboratory-milled 80% extraction flours were 1 8–2 0 μg per g,[2] and for National 80%-extraction flour 2 4 μg per g,[3] it seems clear that the 70% extraction flour used in Germany was slightly richer than average, but was in no way comparable with an 80% extraction flour as regards vitamin-B_1 content

The riboflavine in the 70% extraction flour used in Germany was not discussed in your leading article, and as an index of the B-vitamin status of flours is admittedly less useful than the concentrations of vitamin B_1 and nicotinic acid, because the difference in riboflavine content between flours of 70 and 80% extraction is relatively small It is of interest however, to note that there was good agreement, on the whole, between my values for the experimental flours obtained by a chemical method and the corresponding values obtained microbiologically at the Cereals Research Station, and that the Cereals Research Station value of 0 47 μg per g for the 70% extraction flour was not only lower than the values of 0 8 μg per g [2] and 0 7 μg per g [3] reported from this station for 80%-extraction flour, but was also lower th the values of 0 6–0 7 μg per g they obtained for oth 70%-extraction flours [2]

Medical Research Council
Department of Experimental Medicine,
Cambridge

W I M HOLMAN

*** There are two issues here

(1) Had the 70%-extraction flour used by McCan and Widdowson an unusually high vitamin-B conten Dr Moran says that its thiamine (vitamin B_1) w "slightly high but still within the range for a 70 flour", but the difference even between his average f the two main consignments (1 15 μg per g) and th figures given by the Ministry of Food (0 7 or 0 8 μg seems to us substantial

(2) Did this flour (as we said) approximate, as regar thiamine and nicotinic acid, to "the National flour this country"? In the table at the end of his lett Dr Moran shows that (according to his analyses) it d not come near the standard laid down for 80%-extracti flour by the Flour Order, but is he prepared to say th National flour itself reaches this high standard? In h current report (1955, p 19) the Government Chemi gives figures for the thiamine content of non-importe National flour (straight run) that range from 1 9 to 2 1 μ but are always below the 2 4 μg specified by the Minist of Food

In view of the apparent difficulty of estimating thiamin in flour, we doubt whether any more exchange of vie will be profitable until Dr Moran, Dr Holman, and th Government Chemist have made, and published, analyse of the same samples of National flour It would b interesting to know precisely how much thiamine, nicotini acid, and riboflavine would now be found in sampl of National flour purchased at random in various par of the country, and how much agreement betwe different analyses can be expected —ED L

CONVULSIONS FOLLOWING PUDENDAL BLOCK BY LIGNOCAINE

SIR,—I read with interest Mr Dutton's article i your issue of Dec 31

It is a great pity that Goldberg's [1] work on the toxicit of lignocaine is so often quoted out of its context

This worker found that when he injected this drug in mice in 0 5% solution, it was equally toxic with procain though it was more toxic when stronger solutions were use Goldberg's LD50 for procaine was 1 02 g per kg, and for ligno caine 1 07 g per kg It is not, however, generally realis that the giving of this dose of any drug to a 20 g mouse i 0 5% solution requires the administration of just over 4 m of solvent—which may be presumed in this case to have bee water This amount of fluid is one fifth of the animal's tota weight, or four times its entire blood volume It will therefo be apparent that the circumstances of these experiments ar in no way comparable to the injection of ordinary amount of local anæsthetic in man, where the total volume of flui given is rarely more than 1/50 of the total blood volume Indeed it would seem possible that at the high dilutions use in Goldberg's experiments the animals succumbed to acut water intoxication before significant amounts of lignocain or procaine could be absorbed

There is a second factor which modifies the toxicit of lignocaine

I found that when this drug was injected prior to thoraco plasty it had virtually no modifying effect on the vaso constrictor action of adrenaline added to its solutions Pro caine, Cyclaine,' and even more so amethocaine antagonis vasoconstriction under comparable circumstances Becau the vascularity of the tissues remains relatively unalte when these latter agents are used the addition of adrenalin to their solutions does not markedly modify their toxic for absorption continues at a rate only slightly slowed by th vasoconstrictor In the case of lignocaine however th adrenaline greatly delays the absorption of the local an thetic drug, whose concentration in the blood stream i

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[1] Spec Rep Ser Med Res Coun, Lond no 287 1954

[2] Biochem J 1915 39 213

[3] Bread London 1951

[1] Goldberg L Svensk tandläk Tidskr 1947, 40 816

TABLE III—ACTUAL NUMBERS OF SUICIDES COMPARED WITH THOSE EXPECTED AT THE 1945 LEVEL

Suicidal agent		Males 1945	Males 1947	Males 1950	Males 1954	Females 1945	Females 1947	Females 1950	Females 1954
Barbituric acid and derivatives	Actual	20	32	122	161	35	70	156	230
	Expected		24	26	25		41	39	46
Other analgesic and soporific drugs	Actual	29	58	64	61	47	72	89	82
	Expected		35	115	126		55	126	145
Other solid and liquid poisons	Actual	121	120	110	82	99	113	83	51
	Expected		146	79	87		116	85	42
Gases	Actual	744	939	1058	1395	685	858	762	1077
	Expected		896	959	1037		803	759	892
Hanging and strangulation	Actual	483	582	569	612	130	165	128	125
	Expected		581	623	686		152	144	169
Drowning	Actual	295	301	330	290	267	234	221	178
	Expected		355	350	419		313	296	348
Firearms	Actual	184	241	195	197	22	13	9	6
	Expected		222	237	261		26	24	29
Cutting and piercing instruments	Actual	222	216	198	160	41	44	40	27
	Expected		267	280	315		48	45	53
Jumping from heights	Actual	52	70	84	76	61	68	51	51
	Expected		63	67	74		72	68	79
Others	Actual	88	128	162	144	45	43	47	35
	Expected		106	113	125		53	50	59
Total (actual)		2238	2694	2885	3178	1432	1680	1586	1865

means were used have decreased, supports Dr Geffen's views Aspirin is another easily obtainable drug and recently suicide-rates for this agent have increased somewhat, though they are low compared with those for the other two methods: this may be because it is not generally known that a sufficiently large quantity of aspirin is lethal and also because of the large number of tablets which must be swallowed to ensure a fatal dose

The actual and expected deaths (suicides and accidents) due to barbiturate and aspirin poisoning during 1946–54 are shown in table v, the expected deaths having been calculated on the assumption that these forms of poisoning account for the same proportion of the total deaths due to poisoning by solids and liquids as they did during 1939–45 (see fig 2)

The sex age suicide-rates from barbiturate poisoning for 1942, 1948, and 1954 are shown in table vi

The increase in rates is apparent in each age-group shown but is more pronounced at ages 45–64 and 65 and over—i e, from the age of the climacteric onwards It is in these age-groups that we should expect to find most of those cases of depression and insomnia for which barbiturates might be prescribed

TABLE IV—CRUDE SUICIDE RATES PER MILLION LIVING, ACCORDING TO THE METHOD USED, 1944–54

Suicidal agent	Males 1944	Males 1946	Males 1948	Males 1950	Males 1952	Males 1954	Females 1944	Females 1946	Females 1948	Females 1950	Females 1952	Females 1954
Poisoning analgesics and soporifics	2	3	7	8	11	10	3	5	10	11	13	14
Poisoning domestic gases	46	46	54	49	52	64	28	36	40	33	34	47
Poisoning other solids and liquids	7	7	6	5	5	4	5	5	3	4	3	2
Hanging and strangulation	24	32	29	27	25	29	5	8	6	6	5	6
Drowning	19	18	17	16	13	14	11	12	11	10	8	8
Firearms and explosives	12	11	10	9	8	9	*1*	*0*	*1*	*0*	*0*	*0*
Cutting and piercing instruments	15	15	9	9	7	8	2	3	2	2	1	1
Jumping from high places	4	4	5	4	3	4	2	3	3	2	2	2
Other and unspecified means	6	7	7	8	7	[illegible]	2	3	3	2	1	2

That barbiturates are dispensed on a fairly large scale is shown from two analyses which have been made of prescriptions on form E C 10 Dunlop et al[2] analysed a sample of 11,435 of these forms comprising 17 301 prescriptions issued during September, 1949, and found 1636 or 9 4% were for barbiturates In an analysis made by the Ministry of Health[3] of 106,295 prescriptions on form E C 10 issued during October, 1954 8 8% were for barbiturates or preparations containing barbiturates The difference between the percentages may have been influenced by the absence of a predominantly rural area from Dunlop's sample, which covered three types only—prosperous residential, industrial, and mixed suburban—as well as by the disparity in size of the samples, but there have also been material changes in prescribing since 1949 and these may provide a better explanation The percentages are believed to be calculated on similar bases but it should be recognised that some of the preparations containing barbiturates contain only small amounts The percentage of all prescriptions in which barbiturates were the sole or principal therapeutic agent in October, 1954, was 6 4, the balance of 2 4% consisting among other things of anticonvulsants, sex hormones, and sedatives and hypnotics other than barbiturates which would be classed in these groups and not as barbiturates

As the samples were for September and October, 1954, the proportion of barbiturates to other drugs as between these two months should not be greatly affected by the seasonal variations in drugs prescribed The selection of September and October as sampling months may, however, have resulted in an unduly high proportion of barbiturates, and had February and March, for example, been selected, no doubt the proportions would have been much less From estimates made by the Ministry of Health, based on samples in different months, the amount of barbiturates prescribed annually during the last few years may have varied between 80 000 and 100 000 lb, but these estimates should be treated with considerable reserve owing to the large sampling errors involved and the difficulty of knowing how far any particular month's prescriptions may be regarded as representative of dispensing during the year

TABLE V—BARBITURATE AND ASPIRIN POISONING

—		Barbituric acid Suicides Actual	Barbituric acid Suicides Expected	Barbituric acid Suicides A % of E	Barbituric acid Accidental deaths Actual	Barbituric acid Accidental deaths Expected	Barbituric acid Accidental deaths A % of E	Aspirin Suicides Actual	Aspirin Suicides Expected	Aspirin Suicides A % of E	Aspirin Accidental deaths Actual	Aspirin Accidental deaths Expected	Aspirin Accidental deaths A % of E
1946	M	24	17	141	20	17	118	20	15	133	5	7	71
	F	54	29	186	34	23	148	51	32	159	14	8	175
1948	M	73	24	304	34	23	148	56	21	267	16	10	160
	F	96	39	246	41	29	141	101	43	235	16	10	160
1950	M	122	26	469	47	22	214	42	22	191	14	9	156
	F	156	44	355	80	41	195	75	48	156	17	15	113
1952	M	157	32	491	61	30	203	74	28	264	24	13	185
	F	176	48	367	79	41	193	106	52	204	26	15	173
1954	M	161	28	575	67	29	231	49	24	204	18	12	150
	F	230	49	469	117	48	244	64	53	121	14	17	82

Not all cases of barbiturate poisoning are fatal, and the non-fatal ones may require inpatient hospital treatment, or, if less severe and not requiring overnight care, may be dealt with in the outpatients department In hospital cases it is usually difficult for the statistician to ask for a distinction to be made on a large scale between cases of

drip, and a transient rise in blood-pressure will assure him that the correct treatment is being given

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[2] Dunlop D M. Henderson T L Inch R S *Brit med J* 1952 i 292

[3] Ministry of Health Personal communication

Following 2 deaths from postoperative collapse which had been treated with noradrenaline drips and high bed-blocking, which at necropsy showed acute heart failure with pulmonary œdema, I employed as a routine in such cases digitalis, aminophylline, and even Fowler's position The results were most gratifying and were certainly not attended by the hazards of bed-blocking and hypertensive drips

In conclusion, I submit the following observations which may give thought to others who are often called on to treat postoperative collapse

(1) Central failure is a more common cause of postoperative collapse than peripheral failure, in those patients who have received infusions during operation This is the result of overloading and (if the infusion is not blood) of cardiac anoxia due to hæmodilution This especially applies to the aged and to those with cardiac disease

(2) The treatment of central failure in mistake for peripheral failure is exceedingly dangerous but the reverse is not so

(3) Hypertensive additives are lethal drugs and, I believe, have very little place in treating postoperative collapse except when hypotensive anæsthesia is employed

(4) A falling blood pressure does not necessarily indicate peripheral failure

(5) *We all appear to be too "drip conscious,"* without *stopping to realise why we are employing them*

London, S W 1 C Landon Smith

HEALTH CENTRE OR GROUP PRACTICE?

Sir,—I am much interested in the correspondence on this subject I should like to strongly support Dr Stephen Taylor (Dec 31) In 1942 I wrote [1]

> "*Health Centres* A glance at the Diagrams shows that here the Doctor has at his immediate beck and call a trained staff He is in close touch with his côlleagues and all the Welfare Workers *Example* Mrs Smith *comes to consult* the Doctor and is *ordered home to bed* Mrs Smith replies 'I *cannot possibly do that Doctor* I have *my* husband and family to *look after*' *The Doctor here is able to reply* 'that is easy take this note over to the welfare workers' room they will fix things up for you' What a vast improvement is here on the decaying past"

Is not this truer even today than when it was written many years ago?

Worthing Harold Leeson

CONSULTANTS IN DERMATOLOGY

Sir—Dr Franklin's letter (Dec 31), in which he states that I am wrong about young trainees qualified to practise both dermatology and venereology (Dec 17), is interesting, but obviously his counter statement refers to only one clinic Surely the fact that the respective groups of dermatologists and venereologists are against dual appointments and the endorsement of this opinion by the Central Consultants and Specialists Committee, proves an overwhelming majority

Dr Franklin's further allegation that higher academic qualifications, whilst required in dermatology, are not in venereology is entirely fallacious *In 1948* some long-established venereologists, just as similar practitioners in dermatology and other special subjects, were accepted as consultants by virtue of their standing *in the* profession and amongst their colleagues although they did not hold higher qualifications Nowadays no applicant for a consultant post in any subject including venereology would be considered by any appointing committee unless he held a higher qualification and my experience as an external assessor on various regional board committees leaves me in no doubt as to this statement I would further challenge Dr Franklin by stating that up and down the country the directors of the majority of venereal disease departments hold higher qualifications

As a past president of the Medical Society for th Study of Venereal Diseases, which publishes what now the only journal on venereal disease in the Engli language, and is *mainly* responsible for postgraduat teaching *in this country*, I cannot recall ever havin enjoyed the presence of Dr Franklin or any of hi assistants at the society's deliberations

Sheffield Douglas J Campbell

ACUTE CHYLOUS PERITONITIS

Sir,—Mr Walker (Jan 14) gives an interestin description of a non filarial chylous peritonitis H states that blockage of the main lymph ducts by micr filaria causes stasis, &c Surely the blockage is due t an inflammatory reaction around adult filaria now mor correctly known as wuchereria?

Department of Tropical Medicine
University of Edinburgh

Fred'k J Wright

"MUNCHAUSEN'S SYNDROME"

Sir,—*The tallish man*, aged 20, with a right faci palsy and a "crew" hair cut, described by Mr Mawson last week, presented himself at the casualty departmen of the West London Hospital on Dec 20

He said *that he had had a right mastoid operation in Dublin* a week before, but he could no longer *afford to pay the hospital* bill and had discharged himself *two days* before and cam over on the boat the previous night He added that he had a headache and that the facial palsy had developed since he had discharged himself from hospital

He had a right endaural incision with the sutures still in position There were several palpable glands on the right side of the neck, but his temperature was 98°F and there was no neck rigidity He was advised to attend an E N T hospital in the morning A penicillin injection was refused ver firmly

West London Hospital,
W 6

A R Bearn
Casualty Officer

"SOCIAL VALUES"

Sir,—As *The Lancet* arrives some five weeks after publication, I do not know whether you have commented on the proposed ban on heroin If the letter in the *Times* of Nov 30 signed by Sir Russell Brain and other eminent signatories has not astonished you as it has me I would like to comment on an important implication of this letter The signatories escape responsibility whether or not the ban on heroin is justified, by saying that the use of heroin must be decided by social values

To me such a view is totally abhorrent The same argument led to attempts to murder the insane in the asylums of Nazi Germany, fortunately frustrated by public opinion led by the Director of Bethel-Bielefeld

Many things may be socially good (and I freely admit that the relief of suffering is) But "love thy neighbour as thyself" is the second Commandment—the first is "love the Lord thy God with all thy heart " Medicine relieves pain because it is *good to do so in the sight* of a Force greater than man secondarily man benefits The motivation is paramount Medicine derives it ethos from natural law, its value is absolute

To admit the social motivation *of* medicine will degrade it to a mere service to the Welfare State (or may be, the Welfare World) *Of course*, all sensible physicians will agree with precautions to prevent heroin addiction, but they cannot admit the *right of the State* (a social organisation) to ban their use of it to relieve pain (a divinely imposed duty) Nowadays social consequences are too often given *as a reason for medical* research and action Only a few weeks ago Dr Bronte Stewart and his colleagues (Nov 26) sought *to justify* their investigation into the relation of coronary heart disease and diet by saying that coronary disease kill or injures 'men our community can little afford to lo

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[1] Leeson H H State Medicine or What High Wycombe 1942

ABLE III—ACTUAL NUMBERS OF SUICIDES COMPARED WITH THOSE EXPECTED AT THE 1945 LEVEL

Suicidal agent		Males				Females			
		1945	1947	1950	1954	1945	1947	1950	1954
arbituric acid and derivatives	Actual	20	39	122	161	35	70	156	230
	Expected		24	26	28		41	39	46
ther analgesic and soporific drugs	Actual	29	58	54	61	47	72	89	82
	Expected		35	115	126		55	126	148
ther solid and liquid poisons	Actual	121	120	110	82	99	113	83	51
	Expected		146	79	87		116	55	42
ases	Actual	744	939	1058	1395	685	858	762	1077
	Expected		896	959	1057		803	759	892
Hanging and strangulation	Actual	483	582	569	612	130	165	128	128
	Expected		561	623	686		152	144	169
rowning	Actual	295	301	330	290	267	234	221	178
	Expected		355	380	419		313	296	348
irearms	Actual	184	241	198	197	22	13	9	6
	Expected		222	237	261		26	24	29
utting and piercing instruments	Actual	222	216	198	160	41	44	40	27
	Expected		267	286	315		48	45	53
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Total (actual)		2238	2694	2885	3178	1432	1680	1586	1865

means were used have decreased, supports Dr Geffen's views Aspirin is another easily obtainable drug and recently suicide rates for this agent have increased somewhat, though they are low compared with those for the other two methods this may be because it is not generally known that a sufficiently large quantity of aspirin is lethal and also because of the large number of tablets which must be swallowed to ensure a fatal dose The actual and expected deaths (suicides and accidents) due to barbiturate and aspirin poisoning during 1946–54 are shown in table v, the expected deaths having been calculated on the assumption that these forms of poisoning account for the same proportion of the total deaths due to poisoning by solids and liquids as they did during 1939–45 (see fig 2)

The sex age suicide-rates from barbiturate poisoning for 1942, 1948, and 1954 are shown in table vi

The increase in rates is apparent in each age group shown but is more pronounced at ages 45–64 and 65 and over—i e , from the age of the climacteric onwards It is in these age-groups that we should expect to find most of those cases of depression and insomnia for which barbiturates might be prescribed

TABLE IV—CRUDE SUICIDE RATES PER MILLION LIVING, ACCORDING TO THE METHOD USED, 1944–54

Suicidal agent	Males						Females					
	1944	1946	1948	1950	1952	1954	1944	1946	1948	1950	1952	1954
Poisoning analgesics and soporifics	2	3	7	8	11	10	3	5	10	11	13	14
Poisoning domestic gases	46	46	54	49	52	64	28	36	40	33	34	47
Poisoning other solids and liquids	7	7	6	5	5	4	5	5	3	4	3	2
Hanging and strangulation	24	32	29	27	25	29	5	8	6	6	5	6
Drowning	19	18	17	16	13	14	11	12	11	10	8	8
Firearms and explosives	12	11	10	9	8	9	*1*	*0*	*1*	*0*	*0*	*0*
Cutting and piercing instruments	15	15	9	9	7	8	2	3	2	2	1	1
Jumping from high places	4	4	5	4	3	4	2	3	3	2	2	2
Other and unspecified means	6	7	7	8	7	7	2	3	3	2	1	2

That barbiturates are dispensed on a fairly large scale is shown from two analyses which have been made of prescriptions on form E C 10 Dunlop et al [2] analysed a sample of 11,435 of these forms comprising 17,301 prescriptions issued during September, 1949, and found 1636 or 9 4% were for barbiturates In an analysis made by the Ministry of Health [3] of 106,295 prescriptions on form E C 10 issued during October, 1954, 8 8% were for barbiturates or preparations containing barbiturates The difference between the percentages may have been influenced by the absence of a predominantly rural area from Dunlop s sample, which covered three types only —prosperous residential industrial, and mixed suburban —as well as by the disparity in size of the samples, but there have also been material changes in prescribing since 1949, and these may provide a better explanation The percentages are believed to be calculated on similar bases but it should be recognised that some of the preparations containing barbiturates contain only small amounts The percentage of all prescriptions in which barbiturates were the sole or principal therapeutic agent in October, 1954, was 6 4 the balance of 2 4% consisting, among other things of anticonvulsants, sex hormones, and sedatives and hypnotics other than barbiturates, which would be classed in these groups and not as barbiturates

As the samples were for September and October, 1954, the proportion of barbiturates to other drugs as between these two months should not be greatly affected by the seasonal variations in drugs prescribed The selection of September and October as sampling months may, however, have resulted in an unduly high proportion of barbiturates , and had February and March, for example, been selected, no doubt the proportions would have been much less From estimates made by the Ministry of Health, based on samples in different months, the amount of barbiturates prescribed annually during the last few years may have varied between 80 000 and 100,000 lb , but these estimates should be treated with considerable reserve owing to the large sampling errors involved and the difficulty of knowing how far any particular month's prescriptions may be regarded as representative of dispensing during the year

TABLE V—BARBITURATE AND ASPIRIN POISONING

		Barbituric acid						Aspirin					
		Suicides			Accidental deaths			Suicides			Accidental deaths		
—		Actual	Expected	A % of E	Actual	Expected	A % of E	Actual	Expected	A % of E	Actual	Expected	A % of E
1946	M	24	17	141	20	17	118	20	15	133	5	7	71
	F	54	29	186	34	23	148	51	32	159	14	8	175
1948	M	73	24	304	34	23	148	56	21	267	16	10	160
	F	96	39	246	41	29	141	101	43	235	16	10	160
1950	M	122	26	469	47	22	214	42	22	191	14	9	156
	F	156	44	355	80	41	195	75	48	156	17	15	113
1952	M	157	32	491	61	30	203	74	28	264	24	13	185
	F	176	48	367	79	41	193	106	52	204	26	15	173
1954	M	161	28	575	67	29	231	49	24	204	18	12	150
	F	230	49	469	117	48	244	64	53	121	14	17	82

Not all cases of barbiturate poisoning are fatal, and the non fatal ones may require inpatient hospital treatment, or, if less severe and not requiring overnight care, may be dealt with in the outpatients department In hospital cases it is usually difficult for the statistician to ask for a distinction to be made on a large scale between cases of values ranging from 10 to 14 mg. per day; 1 male patient had values around 18 mg. per day. When chlorpromazine treatment was started in the females the values decreased between the first and eighteenth day to levels near zero, whereas those in the male patient decreased in the first ten days of treatment to levels of 0·6–6 mg. per day. Later the levels in all the patients returned to those before treatment, though chlorpromazine medication was continued. There was a concomitant, but insignificant, decrease of 17-hydroxycorticoid excretion. During the period of extremely low 17-ketosteroid excretion, we sometimes, but not always, found a gradual increase of blood corticotrophin which however returned to normal levels when the 17-ketosteroids in the urine returned to normal.

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[2] Dunlop D M., Henderson T. L Inch R S *Brit med J* 1952 i 292

[3] Ministry of Health Personal communication

Somatotrophic Hormone (S.T.H.)

In patients treated for two months, no acromegalic changes were discerned in photographs taken in profile, but their weight increased noticeably.

In rats treated for over two months with chlorpromazine (10 mg. per kg. body-weight), a definite stunting of growth and development was discernible. 5 female and 5 male rats were given daily injections of chlorpromazine 10 mg. per kg. and their growth curve was compared with that of 5 male and 5 female control rats. Whereas no difference in weight was noted between the initial weights of 30–90 g., obvious impairment of growth became visible later on. Within two months the female control animals reached a weight of 125 g., while the treated animals reached a maximum weight of 95 g. Similar results were obtained in male animals, in which the weight of the controls rose to 200 g., whereas the treated animals remained at 125 g. Then they were given daily 10 R.U. growth hormone subcutaneously, whereupon they attained the weight of the control animals within a further two months.

Thyroid-stimulating Hormone (T.S.H.)

2 patients had their basal metabolic rate (B.M.R.) checked weekly before and during treatment. Before treatment their B.M.R. was + 35% and + 12% respectively. The weekly readings of B.M.R. were as follows:

Case 1 from + 35% to + 20%, + 30%, + 22%, and + 35%.
Case 2 from + 12% to + 18%, + 6%, + 5%, and + 17%.

Thus, there was a slight tendency of the B.M.R. to decrease during the first one to three weeks of treatment. The significance of these results needs further investigation.

Discussion

The mechanism of the endocrine disturbances observed has not yet been clearly defined, since it involves impairment of the hypothalamus or the formatio reticularis as well as peripheral effects which may be humoral, vegetative, or toxic.

The temporary inhibition of the hypothalamus may be explained as follows:

The hypothalamus through its portal veins as well as through its cholinergic and adrenergic fibres regulates the anterior lobe of the pituitary gland. The six tropins cause production of hormones in the peripheral glands by the "push and pull" principle. Thus F.S.H. stands in reciprocal relation to œstrone, L.H. to progesterone and testosterone, corticotrophin to the cortical steroids, and T.S.H. to thyroxine and tri-iodothyronine. These tropins should be called "balanced tropins" since they are permanently kept in balance by the peripheral hormones which they produce. On the other hand, there exist two "unbalanced tropins" which apparently do not produce secondary hormones, but instead exert a direct hormonal effect: thus prolactin produces milk, and S.T.H. has an anabolic effect on bone and muscle growth. It is obvious that neither milk nor muscles can balance their respective tropins.

The theory of the balanced and unbalanced tropins proposed by us would explain the surprisingly high prevalence of lactation in female patients under chlorpromazine treatment. It is possible that a similar effect of growth hormone can be recognised behind the anabolic effect regularly found in all patients under chlorpromazine treatment—namely, rapid gain in weight.

Our hypothesis of the balanced and the unbalanced tropins explains also the temporary fluctuations in hormonal output described by us. It is well known that stunting of the hypothalamus is followed by impaired function of the peripheral hormones. It has been shown in our experiments with chlorpromazine that the imbalance is ended in the case of the balanced tropins within two to three weeks. There is, however, no ready readjustment in the case of the unbalanced tropins.

In addition to the balancing effect within the hypothalamus/pituitary/peripheral gland axis there obviously exist additional peripheral effects which are directly engendered by chlorpromazine. Thus the prolonged effect of progesterone on the rabbit uterus could also be explained as a humoral effect (acetylcholine antagonism), the immediate depression of the 17-ketosteroid excretion as a vegetative effect, and the stunting of growth in rats as a toxic effect (interference with metabolic enzyme systems).

In summary, the manifold effects of chlorpromazine can be largely explained by partial block of the hypothalamus followed by impairment of most of its functions. The effects of hormonal inhibition thus produced in man and animals result in temporary increase of production of the so-called "balanced tropins"—F.S.H. and L.H., as well as corticotrophin and T.S.H. On the other hand there is a prolonged increase of the "unbalanced tropins," especially prolactin resulting in *production of colostrum or galactorrhœa*. In addition to these central effects *there exist peripheral effects* which may be humoral, vegetative, or toxic.

Our thanks are due to our colleagues, Dr. A. Jarus, Mr. A. Evjatar, and Mr. N. Ben Hur, for their help.

Department of Applied Pharmacology F. G. SULMAN

Department of Psychiatry, H. Z. WINNIK
Hebrew University—Hadassah
Medical School, Jerusalem, Israel.

A RARE COMPLICATION OF CHLORPROMAZINE TREATMENT

SIR,—Gäde and Heinrich[1] have reported the unusual complication of secretion from the mammary glands in three female patients who were taking chlorpromazine. We would like to report a similar occurrence in a virgin aged 21 years.

The patient had long been subject to generalised jerky choreiform movements attributed to thrombosis in or about the basal ganglia following diphtheria at the age of 4½. These movements were made worse by anxiety or emotional disturbance, and disappeared or became less during relaxation, during sleep, or after the ingestion of a moderate quantity of alcohol. Secondary sexual characters were normally developed for her age. Her sexual history was unremarkable. Her periods were regular every twenty-eight days, lasted for three days, and were uncomplicated by pain. She had variable premenstrual tension with some depression.

She was admitted to a neurosis unit on Sept. 10, 1955, and was treated with chlorpromazine 25 mg. t.d.s. Her breasts began to enlarge, and on Oct. 14 began to secrete sufficiently for her to have to wear pads to prevent staining of the clothes. The quantity of daily secretion was unknown, but the fluid was milky and contained fat globules. She failed to menstruate on the expected date (Oct. 30), but menstruated normally at the next period. Gynæcological examination showed no apparent abnormality apart from the secreting breasts. The chlorpromazine was stopped on Nov. 2 and secretion ceased on Nov. 16. Administration was resumed on Nov. 21, and secretion again occurred on Nov. 30 and has continued. Chlorpromazine has helped her movements and disturbed emotional state considerably, and the beneficial action is considered by the patient to outweigh the disadvantage of some breast secretion.

Apart from the three cases already mentioned, no other examples of this effect of chlorpromazine seem to have been reported. This is somewhat surprising in view of the very extensive use of this drug.

W. K. MARSHALL
D. M. LEIBERMAN

Bexley Hospital, Kent.

1. Gäde, F. B., Heinrich, K. Nervenarzt, 1955, 26, 49.

TABLE III—ACTUAL NUMBERS OF SUICIDES COMPARED WITH THOSE EXPECTED AT THE 1945 LEVEL

Suicidal agent		Males 1945	Males 1947	Males 1950	Males 1954	Females 1945	Females 1947	Females 1950	Females 1954
Barbituric acid and derivatives	Actual	20	39	122	161	35	70	156	230
	Expected		24	26	28		41	39	46
Other analgesic and soporific drugs	Actual	29	58	54	61	47	72	89	82
	Expected		35	115	126		55	126	148
Other solid and liquid poisons	Actual	121	120	110	82	99	113	83	51
	Expected		146	79	87		116	35	42
Gases	Actual	744	930	1058	1397	685	858	762	1077
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	Expected		581	623	686		152	144	169
Drowning	Actual	295	301	330	290	267	234	221	178
	Expected		355	380	419		313	296	348
Firearms	Actual	184	241	198	197	22	13	9	6
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Poisoning domestic gases	46	46	54	49	52	64	28	36	40	33	34	47
Poisoning other solids and liquids	7	7	6	5	5	4	5	5	3	4	3	2
Hanging and strangulation	24	32	29	27	25	29	5	8	6	6	5	6
Drowning	19	18	17	16	13	14	11	12	11	10	8	8
Firearms and explosives	12	11	10	9	8	9	*1*	*0*	*1*	*0*	*0*	*0*
Cutting and piercing instruments	15	15	9	9	7	8	2	3	2	2	1	1
Jumping from high places	4	4	5	4	3	4	2	3	3	2	2	2
Other and unspecified means	6	7	7	8	7	7	2	3	3	2	1	2

That barbiturates are dispensed on a fairly large scale is shown from two analyses which have been made of prescriptions on form E C 10 Dunlop et al [2] analysed a sample of 11,435 of these forms, comprising 17,301 prescriptions issued during September, 1949, and found 1636 or 9.4% were for barbiturates In an analysis made by the Ministry of Health [3] of 106,293 prescriptions on form E C 10 issued during October, 1954, 8.8% were for barbiturates or preparations containing barbiturates The difference between the percentages may have been influenced by the absence of a predominantly rural area from Dunlop's sample, which covered three types only—prosperous residential industrial, and mixed suburban—as well as by the disparity in size of the samples, but there have also been material changes in prescribing since 1949, and these may provide a better explanation The percentages are believed to be calculated on similar bases, but it should be recognised that some of the preparations containing barbiturates contain only small amounts The percentage of all prescriptions in which barbiturates were the sole or principal therapeutic agent in October, 1954, was 6.4, the balance of 2.4% consisting, among other things, of anticonvulsants, sex hormones, and sedatives and hypnotics other than barbiturates, which would be classed in these groups and not as barbiturates

As the samples were for September and October, 1954, the proportion of barbiturates to other drugs as between these two months should not be greatly affected by the seasonal variations in drugs prescribed The selection of September and October as sampling months may, however, have resulted in an unduly high proportion of barbiturates, and had February and March, for example, been selected, no doubt the proportions would have been much less From estimates made by the Ministry of Health, based on samples in different months, the amount of barbiturates prescribed annually during the last few years may have varied between 80,000 and 100,000 lb, but these estimates should be treated with considerable reserve owing to the large sampling errors involved and the difficulty of knowing how far any particular month's prescriptions may be regarded as representative of dispensing during the year

TABLE V—BARBITURATE AND ASPIRIN POISONING

		Barbituric acid: Suicides Actual	Barbituric acid: Suicides Expected	Barbituric acid: Suicides A % of E	Barbituric acid: Accidental deaths Actual	Barbituric acid: Accidental deaths Expected	Barbituric acid: Accidental deaths A % of E	Aspirin: Suicides Actual	Aspirin: Suicides Expected	Aspirin: Suicides A % of E	Aspirin: Accidental deaths Actual	Aspirin: Accidental deaths Expected	Aspirin: Accidental deaths A % of E
1946	M	24	17	141	20	17	118	20	15	133	5	7	71
	F	54	29	186	34	23	148	51	32	159	14	8	175
1948	M	73	24	304	34	23	148	56	21	267	16	10	160
	F	96	39	246	41	29	141	101	43	235	16	10	160
1950	M	122	26	469	47	22	214	42	22	191	14	9	156
	F	156	44	355	80	41	195	75	48	156	17	15	113
1952	M	157	32	491	61	30	203	74	28	264	24	13	185
	F	176	48	367	79	41	193	106	52	204	26	15	173
1954	M	161	28	575	67	29	231	49	24	204	18	12	150
	F	230	49	469	117	48	244	64	53	121	14	17	82

Not all cases of barbiturate poisoning are fatal, and the non-fatal ones may require inpatient hospital treatment, or, if less severe and not requiring overnight care, may be dealt with in the outpatients department In hospital cases it is usually difficult for the statistician to ask for a distinction to be made on a large scale between cases of

values ranging from 10 to 14 mg per day, 1 male patient had values around 18 mg per day When chlorpromazine treatment was started, in the females the values decreased between the first and eighteenth day to levels near zero, whereas those in the male patient decreased in the first ten days of treatment to levels of 0 6–6 mg per day Later the levels in all the patients returned to those before treatment, though chlorpromazine medication was continued There was a concomitant, but insignificant, decrease of 17-hydroxycorticoid excretion During the period of extremely low 17 ketosteroid excretion, we sometimes, but not always, found a gradual increase of blood corticotrophin which, however, returned to normal levels when the 17 ketosteroids in the urine returned to normal

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[2] Dunlop, D M Henderson, T L Inch R S *Brit med J* 1952 i 292

[3] Ministry of Health Personal communication

Somatotrophic Hormone (S T H)

In patients treated for two months, no acromegalic changes were discerned in photographs taken in profile, but their weight increased noticeably

In rats treated for over two months with chlorpromazine (10 mg per kg body-weight), a definite stunting of growth and development was discernible 5 female and 5 male rats were given daily injections of chlorpromazine 10 mg per kg and their growth curve was compared with that of 5 male and 5 female control rats Whereas no difference in weight was noted between the initial weights of 30–90 g, obvious impairment of growth became visible later on Within two months the female control animals reached a weight of 125 g, while the treated animals reached a maximum weight of 95 g Similar results were obtained in male animals, in which the weight of the controls rose to 200 g, whereas the treated animals remained at 125 g Then they were given daily 10 R U growth hormone subcutaneously, whereupon they attained the weight of the control animals within a further two months

Thyroid-stimulating Hormone (T S H)

2 patients had their basal metabolic rate (B M R) checked weekly before and during treatment Before treatment their B M R was + 35% and + 12% respectively The weekly readings of B M R were as follows

Case 1 from + 35% to + 20% + 36%, + 22%, and + 35%
Case 2 from + 12% to + 18% + 6%, + 5%, and + 17%

Thus, there was a slight tendency of the B M R *to decrease* during the first one to three weeks of treatment The significance of these results needs further investigation

Discussion

The mechanism of the endocrine disturbances observed has not yet been clearly defined, since it involves impairment of the hypothalamus or the formatio reticularis as well as *peripheral effects which may be humoral,* vegetative, or toxic

The temporary inhibition *of the hypothalamus* may be explained as follows

The hypothalamus through its portal veins as well as through its cholinergic and adrenergic fibres regulates the anterior lobe of the pituitary gland The six tropins cause production of hormones in the peripheral glands by the "push and pull" principle Thus F S H stands in reciprocal relation to œstrone, L H to progesterone and testosterone, corticotrophin to the cortical steroids, and T S H to thyroxine and tri iodothyronine These tropins should be called "balanced tropins" since they are permanently kept in balance by the peripheral hormones which they produce On the other hand, there exist two "unbalanced tropins" which apparently do not produce secondary hormones, but instead exert a direct hormonal effect, thus prolactin produces milk, and S T H has an anabolic effect on bone and muscle growth It is obvious that neither milk nor muscles can balance their respective tropins

The theory of the balanced and unbalanced tropins proposed by us would explain the surprisingly high prevalence of lactation in female patients under chlorpromazine treatment It is possible that a similar effect of growth hormone can be recognised behind the anabolic effect regularly found in all patients under chlorpromazine treatment—namely, rapid gain in weight

Our hypothesis of the balanced and the unbalanced tropins explains also the temporary fluctuations in hormonal output described by us It is well known that stunting of the hypothalamus is followed by impaired *function of the peripheral hormones* It has been shown in our experiments with chlorpromazine that the imbalance is ended in the case of the balanced tropins within two to three weeks There is, however, no ready readjustment in the case of the unbalanced tropins

In addition to the balancing effect within the hypothalamus/pituitary/peripheral-gland axis, there obviously exist additional peripheral effects which are directly engendered by chlorpromazine Thus the prolonged effect of progesterone on the rabbit *uterus could also be* explained as a humoral effect (acetylcholine antagonism) the immediate depression of the 17-ketosteroid excretion as a vegetative effect, and the stunting of growth in rat as a toxic effect (interference with metabolic enzyme systems)

In summary, the manifold effects of chlorpromazine can be *largely* explained by *partial block of the hypothalamus* followed by impairment of most of its functions The effects of hormonal inhibition thus produced in man and animals result in temporary increase of production of the so called "balanced tropins" F S H and L H, as well as corticotrophin and T S H On the other hand, there is a prolonged *increase of the "unbalanced tropins,"* especially *prolactin resulting in production of colostrum or galactorrhœa* In addition to *these* central effects, there exist peripheral effects which may be humoral, vegetative, or toxic

Our thanks are due to our colleagues, Dr A Jarus, Mr A Eviatar, and Mr N Ben Hur, for their help

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A RARE COMPLICATION OF CHLORPROMAZINE TREATMENT

SIR,—Gäde and Heinrich [1] have reported the unusual complication of secretion from the mammary glands in three female patients who were taking chlorpromazine We would like to report a similar occurrence in a virgin aged 21 years

The patient had long been subject to generalised jerky choreiform movements, attributed to thrombosis in or about the basal ganglia following diphtheria at the age of $4^{1}/_{2}$ These movements were made worse by anxiety or emotional disturbance, and disappeared or became less during relaxation, during sleep, or after the ingestion of a moderate quantity of alcohol Secondary sexual characters were normally developed for her age Her sexual history was unremarkable Her periods were regular every twenty eight days, lasted for three days, and were uncomplicated by pain She had variable premenstrual tension with some depression

She was admitted to a neurosis unit on Sept 19, 1955, and was treated with chlorpromazine 25 mg t d s Her breasts began to enlarge, and on Oct 14 began to secrete sufficiently for her to have to wear pads to prevent staining of the clothes The *quantity of daily secretion* was *unknown*, but the fluid was milky and contained fat globules She failed to menstruate on the expected date (Oct 30), but menstruated normally at the next period Gynæcological examination showed no apparent abnormality apart from the secreting breasts The *chlorpromazine* was *stopped on Nov 2, and secretion* ceased on Nov 16 Administration was resumed on Nov 24, and secretion again occurred on Nov 30 and has continued Chlorpromazine has helped her movements and disturbed emotional state considerably, and the beneficial action is considered by the patient to outweigh the disadvantage of some breast secretion

Apart from the three cases already *mentioned, no* other examples of this effect of chlorpromazine seem to have been reported This is somewhat surprising in view of the very extensive use of this drug

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[1] Gäde E B Heinrich K *Nervenarzt*, 1955 26 49

TABLE III—ACTUAL NUMBERS OF SUICIDES COMPARED WITH THOSE EXPECTED AT THE 1945 LEVEL

Suicidal agent		Males 1945	Males 1947	Males 1950	Males 1954	Females 1945	Females 1947	Females 1950	Females 1954
Barbituric acid and derivatives	Actual	20	39	122	161	35	70	156	230
	Expected		24	26	25		41	39	46
Other analgesic and soporific drugs	Actual	29	58	54	61	47	72	89	82
	Expected		35	115	126		55	126	148
Other solid and liquid poisons	Actual	121	120	110	82	99	113	83	51
	Expected		146	79	87		116	35	42
Gases	Actual	744	939	1058	1395	685	858	762	1077
	Expected		896	959	1057		803	759	892
Hanging and strangulation	Actual	483	582	569	612	130	165	128	128
	Expected		581	623	656		132	144	169
Drowning	Actual	295	301	330	290	267	234	221	178
	Expected		355	380	419		313	296	348
Firearms	Actual	184	241	198	197	22	13	9	6
	Expected		222	237	261		26	24	29
Cutting and piercing instruments	Actual	223	216	198	160	41	44	40	27
	Expected		267	286	315		48	45	53
Jumping from heights	Actual	52	70	84	76	61	68	51	51
	Expected		63	67	74		72	68	79
Others	Actual	88	128	162	144	45	43	47	35
	Expected		106	113	125		53	50	59
Total (actual)		2238	2694	2885	3178	1432	1680	1586	1865

means were used have decreased, supports Dr Geffen's views Aspirin is another easily obtainable drug, and recently suicide rates for this agent have increased somewhat, though they are low compared with those for the other two methods this may be because it is not generally known that a sufficiently large quantity of aspirin is lethal and also because of the large number of tablets which must be swallowed to ensure a fatal dose The actual and expected deaths (suicides and accidents) due to barbiturate and aspirin poisoning during 1946–54 are shown in table V, the expected deaths having been calculated on the assumption that these forms of poisoning account for the same proportion of the total deaths due to poisoning by solids and liquids as they did during 1939–45 (see fig 2)

The sex age suicide-rates from barbiturate poisoning for 1942, 1948, and 1954 are shown in table VI

The increase in rates is apparent in each age group shown but is more pronounced at ages 45–64 and 65 and over—i e, from the age of the climacteric onwards It is in these age groups that we should expect to find most of those cases of depression and insomnia for which barbiturates might be prescribed

TABLE IV—CRUDE SUICIDE RATES PER MILLION LIVING, ACCORDING TO THE METHOD USED, 1944–54

Suicidal agent	Males 1944	Males 1946	Males 1948	Males 1950	Males 1952	Males 1954	Females 1944	Females 1946	Females 1948	Females 1950	Females 1952	Females 1954
Poisoning analgesics and soporifics	2	3	7	8	11	10	3	5	10	11	13	14
Poisoning domestic gases	46	46	54	49	52	64	28	36	40	33	34	47
Poisoning other solids and liquids	7	7	6	5	5	4	5	5	3	4	3	2
Hanging and strangulation	24	32	29	27	25	29	5	8	6	6	5	6
Drowning	19	18	17	16	13	14	11	12	11	10	8	8
Firearms and explosives	12	11	10	9	8	9	1	0	1	0	0	0
Cutting and piercing instruments	15	15	9	9	7	8	2	3	2	2	1	1
Jumping from high places	4	4	5	4	3	4	2	3	3	2	2	2
Other and unspecified means	6	7	7	8	7	7	2	3	3	2	1	2

That barbiturates are dispensed on a fairly large scale is shown from two analyses which have been made of prescriptions on form E C 10 Dunlop et al[2] analysed a sample of 11,435 of these forms comprising 17 301 prescriptions issued during September, 1949, and found 1636 or 9 4% were for barbiturates In an analysis made by the Ministry of Health[3] of 106,295 prescriptions on form E C 10 issued during October, 1954, 8 8% were for barbiturates or preparations containing barbiturates The difference between the percentages may have been influenced by the absence of a predominantly rural area from Dunlop's sample, which covered three types only—prosperous residential, industrial, and mixed suburban—as well as by the disparity in size of the samples, but there have also been material changes in prescribing since 1949, and these may provide a better explanation The percentages are believed to be calculated on similar bases but it should be recognised that some of the preparations containing barbiturates contain only small amounts The percentage of all prescriptions in which barbiturates were the sole or principal therapeutic agent in October, 1954, was 6 4, the balance of 2 4% consisting, among other things, of anticonvulsants sex hormones, and sedatives and hypnotics other than barbiturates, which would be classed in these groups and not as barbiturates

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—		Barbituric acid Suicides Actual	Barbituric acid Suicides Expected	Barbituric acid Suicides A % of E	Barbituric acid Accidental deaths Actual	Barbituric acid Accidental deaths Expected	Barbituric acid Accidental deaths A % of E	Aspirin Suicides Actual	Aspirin Suicides Expected	Aspirin Suicides A % of E	Aspirin Accidental deaths Actual	Aspirin Accidental deaths Expected	Aspirin Accidental deaths A % of E
1946	M	24	17	141	20	17	118	20	15	133	5	7	71
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Cutting and piercing instruments	Actual	222	216	198	160	41	44	40	27
	Expected		267	280	315		48	45	53
Jumping from heights	Actual	52	70	84	76	61	68	51	51
	Expected		63	67	74		72	68	79
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Poisoning domestic gases	46	46	54	49	52	64	28	36	40	33	34	47
Poisoning, other solids and liquids	7	7	6	5	5	4	5	5	3	4	3	2
Hanging and strangulation	24	32	29	27	25	29	5	8	6	6	5	6
Drowning	19	18	17	16	13	14	11	12	11	10	8	8
Firearms and explosives	12	11	10	9	8	9	*1*	*0*	*1*	*0*	*0*	*0*
Cutting and piercing instruments	15	15	9	9	7	8	2	3	2	2	1	1
Jumping from high places	4	4	5	4	3	4	2	3	3	2	2	2
Other and unspecified means	6	7	7	8	7	7	2	3	3	2	1	2

That barbiturates are dispensed on a fairly large scale is shown from two analyses which have been made of prescriptions on form E C 10 Dunlop et al[2] analysed a sample of 11,435 of these forms, comprising 17,301 prescriptions issued during September, 1949, and found 1636 or 9 4% were for barbiturates In an analysis made by the Ministry of Health[3] of 106,295 prescriptions on form E C 10 issued during October, 1954, 8 8% were for barbiturates or preparations containing barbiturates The difference between the percentages may have been influenced by the absence of a predominantly rural area from Dunlop's sample, which covered three types only—prosperous residential, industrial, and mixed suburban—as well as by the disparity in size of the samples, but there have also been material changes in prescribing since 1949, and these may provide a better explanation The percentages are believed to be calculated on similar bases, but it should be recognised that some of the preparations containing barbiturates contain only small amounts The percentage of all prescriptions in which barbiturates were the sole or principal therapeutic agent in October, 1954, was 6 4, the balance of 2 4% consisting, among other things, of anticonvulsants, sex hormones, and sedatives and hypnotics other than barbiturates, which would be classed in these groups and not as barbiturates

As the samples were for September and October, 1954, the proportion of barbiturates to other drugs as between these two months should not be greatly affected by the seasonal variations in drugs prescribed The selection of September and October as sampling months may, however, have resulted in an unduly high proportion of barbiturates, and had February and March, for example, been selected, no doubt the proportions would have been much less From estimates made by the Ministry of Health, based on samples in different months, the amount of barbiturates prescribed annually during the last few years may have varied between 80,000 and 100,000 lb, but these estimates should be treated with considerable reserve owing to the large sampling errors involved and the difficulty of knowing how far any particular month's prescriptions may be regarded as representative of dispensing during the year

Not all cases of barbiturate poisoning are fatal, and the non fatal ones may require inpatient hospital treatment, or, if less severe and not requiring overnight care, may be dealt with in the outpatients department In hospital cases it is usually difficult for the statistician to ask for a distinction to be made on a large scale between cases of

TABLE V—BARBITURATE AND ASPIRIN POISONING

—		Barbituric acid Suicides Actual	Barbituric acid Suicides Expected	Barbituric acid Suicides A % of E	Barbituric acid Accidental deaths Actual	Barbituric acid Accidental deaths Expected	Barbituric acid Accidental deaths A % of E	Aspirin Suicides Actual	Aspirin Suicides Expected	Aspirin Suicides A % of E	Aspirin Accidental deaths Actual	Aspirin Accidental deaths Expected	Aspirin Accidental deaths A % of E
1946	M	24	17	141	20	17	118	20	15	133	5	7	71
	F	54	29	186	34	23	148	51	32	159	14	8	175
1948	M	73	24	304	34	23	148	56	21	267	16	10	160
	F	96	39	246	41	29	141	101	43	235	16	10	160
1950	M	122	26	469	47	22	214	42	22	191	14	9	156
	F	156	44	355	80	41	195	75	48	156	17	15	113
1952	M	157	32	491	61	30	203	74	28	264	34	13	185
	F	176	48	367	79	41	193	106	52	204	26	15	173
1954	M	161	28	575	67	29	231	49	24	204	18	12	150
	F	230	49	469	117	48	244	64	53	121	14	17	82

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[2] Dunlop D M Henderson T L Inch R S *Brit med J* 1952 i, 292

[3] Ministry of Health Personal communication

appreciable reduction in the 50–70 death rate from diseases of the respiratory system other than cancer, while during the same period the corresponding death rate from lung cancer has increased more than four times The complementary death-rates below age 50 show that the reduction for diseases of the respiratory system other than cancer has been very substantial, while the increase in the corresponding rate for lung cancer, although substantial up to 1945, has since remained practically constant

A similar division has been made of the death-rates for women, but this merely confirms the superiority in its resistance to disease of the respiratory system of the female compared with that of the male The 50–70 death-rate from diseases of the respiratory system other than cancer has fallen by half over the period, while the corresponding death-rate from lung cancer has only doubled In 1953 the 50–70 death-rate from lung cancer for men was over eight times that for women I am not sending the figures for women as I do not wish further to encroach on your space

London, W 1 F L BRADSHAW

URETERIC CATHETERISATION

SIR,—I was very interested in Mr Tresidder's method, described in your issue of Dec 24 For many years, at St Bartholomew's Hospital, gum elastic ureteric catheters have been placed in a cotton container in the form of a tube 1 cm in diameter, and sterilised in a formalin cabinet When the catheter is boilable, however, Mr Tresidder's innovation of Penrose rubber-tubing seems excellent

I would like, however, to sound a note of warning about the plastic ureteric catheter The instrument has not yet been perfected, and the tip is quite liable to break off at the first hole Should this happen in the bladder, the fragment can of course be easily removed with suitable forceps, but if it breaks off in the pelvis of the kidney or ureter the consequences may well be troublesome I have not so far seen this misadventure in the upper urinary tract, but suggest that each catheter should be carefully examined before it is introduced along the cystoscope, and if there is any doubt about its reliability it should be discarded

London, W 1 A W BADENOCH

PRODUCTION OF CODEINE

SIR,—The increased world production of morphine for therapeutic purposes is, according to the report of the U N Permanent Central Opium Board,[1] due to the requirements of codeine This accounts for 80–90% of the morphine manufactured, which amounted to 84 tons in 1954 Although this figure is small compared with that for illicit opium, it is none the less remarkable, since codeine is a drug of such little therapeutic value

Codeine is used universally, but illogically, for the relief of pain

Thus during the last year 200 oz of codeine was dispensed in the London Hospital as tab codein co (800,000 tablets), 190 oz as mixture of aspirin, phenacetin, and codeine, and $31^1/_2$ oz as the linctus This is untidy and extravagant therapeutics because the amount of the drug in two codeine compound tablets or in half an ounce of the mixture contributes negligibly to its analgesic effect, even morphine gr $^1/_6$ given by mouth is less effective than aspirin gr 10[2] Presented in this way codeine only constipates, and the amount in a drachm of linctus codeinæ will not even do this Very little was used for the relief of diarrhœa, and for this purpose there are suitable alternatives

It seems reasonable to end the world production of codeine

London Hospital, E 1 EIRIAN WILLIAMS

BLOOD-TRANSFUSION

SIR,—I fully support Dr Shillitoe's statement (Jan that "experience shows that in reading difficult doubtful agglutinations the opinion of the technici of a few years' experience is greatly superior to that o doctor who has only been doing the job for a few month

At this centre I have been privileged to teach ABO and grouping, preparation of compatible blood, and care a maintenance of a blood bank to several hundred doctors a technicians in the past few years Each course of instructi lasts 5 days[1] As was pointed out in your leading arti (Dec 31), fear of a mismatched transfusion has made jun staff, both medical and technical, unwilling to take t responsibility of declaring compatibility This fear can o be overcome by adequate training and experience, and t technicians and junior pathologists I have met are try very hard to get the experience necessary to give th confidence in their results

As Race and Sanger[2] so aptly put it "to achie accuracy a long apprenticeship of error seems necessa A friendly but silent atmosphere is essential Given silen there is still danger of the mind wandering, this it must n be allowed to do, however routine the tests may be *It is useless to expect reliable blood grouping* and co patibility tests unless staff are given relief from their routi work in order to undertake proper training in simple bloo group work After a basic course, experience is best achiev by repeating the work of a more practised worker Increasi experience will reveal personal shortcomings and the limit tions of the technique and the materials used, and, possib most important of all, teach when to refer problems f advice

When sufficiently experienced, all staff responsible for t supply of compatible blood have one main problem—t lack of time necessary for full safety From the many d cussions during the courses held here it is obvious that high proportion of the urgent requests for blood suppli are due to lack of planning and/or consideration for the path logical laboratory Given the time, and the training, both t technicians and the assistant pathologists can supp compatible blood

Meanwhile, if I required a blood-transfusion I would pu my faith in the trained and experienced technician for th compatibility test Those who perform only an occasion blood grouping, under pressure for an emergency cas cannot hope to possess the technical skill or the abilit of interpretation necessary for the selection of compatib blood Indeed the internal organisation of each un should be such that this is never necessary

Finally it must be stressed that the possession o an academic qualification may automatically comman a certain salary but does not necessarily indicate abilit to undertake compatibility tests Similarly, unqualifie laboratory workers may well have had the necessar training and experience to make their results safe an acceptable This is a decision which can only be mad by the pathologist in charge of the laboratory in th light of his knowledge of the individual, and the issu must not be confused by administrative or politica red-herrings

Regional Transfusion Centre,
Sheffield

I DUNSFORD
Senior Scientific Officer

SIR,—In your leading article (Dec 31) you mentio the Danish cards for simultaneous ABO and Rh grouping[3,4] and quote from the article referred to[3] 6 error out of 15,000 groupings on the cards And you con tinue "Unfortunately an error of 4 per 1000 canno be disregarded when blood grouping is involved "

An error of 6 per 15,000 does not correspond to 4 pe 1000, but to 4 per 10,000 Furthermore, the 6 error

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[1] *Daily Telegraph*, Jan. 9, 1956
[2] *Lancet*, 1955 ii, 26

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[1] Dunsford, I, Bowley, C C Techniques in Blood Grouping Edinburgh 1955, p 83
[2] Race, R R, Sanger, R Blood Groups in Man Oxford, 1950 p 163
[3] Eldon K *Dan med Bull* 1955, 2 33
[4] Jordal, K *Ibid* p 40

Further experiments are being carried out to ascertain whether the 5½ day method has a sufficient safety margin It will be a great advantage to reduce the time as far as possible, so that the effect on solubility will be slight

Because of the dangers of machines becoming infected during the process of powdering, it is suggested that it should be obligatory on all exporters in China and elsewhere, to powder the product before shipment The 100-lb cases could then be dealt with by this method of heat treatment without any danger The control of this heat-treatment could best be supervised by the medical officer of health at the port of importation in the same way as pasteurised milk is supervised

The bakery and confectionery trades want Chinese crystalline egg-albumen as an ingredient, and it is doubtful whether at present we can depend on this product being handled in such a way in China as to ensure its freedom from harmful pathogenic organisms Therefore, as with milk, we must fall back on some form of pasteurisation to ensure that such pathogens are not consumed by the British public

SUMMARY

Six months' experimental work into the heat-treatment of imported egg-albumen has suggested a practical cheap, and effective method of heat treating bulk supplies of egg-albumen crystals at 130°F for 5½–6½ days

It is recommended that steps be taken to make it obligatory for all imports of egg albumen from China to be powdered and heat treated on arrival in this country

We are grateful to Messrs Goldrei Foucard, Aintree, Liverpool, for their coöperation and generous supplying of material for experiments, and for the experimental facilities provided at their factory Our sincere thanks are also due to Prof D T Robinson and Dr E C Armstrong, of the Public Health Laboratory Service, Liverpool, for performing the extensive bacteriological sampling

REFERENCE

Newell K W, Hobbs B C Gordon Wallace E J (1955) *Brit med J* ii 1296

Influenza

On Jan 17 influenza-A virus was identified from 2 cases in the Ipswich area New claims for sickness benefit in the week ended Jan 10 were much above average at the Ipswich, Stowmarket Felixstowe, and Woodbridge offices of the Ministry of Pensions and National Insurance There is a lot of influenza-like illness in East Suffolk and virus A may well be responsible

Epidemic Respiratory Illness in Children

As we reported last week, there has been an outbreak of acute respiratory illness among children in Liverpool The total number of cases traced up to Jan 16 was about 300, although many patients treated at home have probably not been included Last week 61 patients were admitted to Liverpool hospitals with a diagnosis of bronchopneumonia A second child died last week and post-mortem specimens have been sent to the M R C Virus Reference Laboratory. It is difficult to know whether the peak of the epidemic has passed but there are many indications that it has Health-visitors are at present seeking information about the health of family contacts

In the past fortnight there was a definite increase in the amount of illness generally in Liverpool, and in the week ending Jan 10, 5700 new claims for sickness benefit were received for the Liverpool area It is rare for the weekly figure to exceed 5000 Figures for all deaths in the past two weeks are as follows

	Week ending	
	Jan 14	*Jan 7*
Total deaths	211	222
Deaths due to respiratory disease		
At all ages	50	56
Under 2 years	5	7

In England Now

A Running Commentary by Peripatetic Correspondents

The New Gentlewoman's Toilet Guide was in the sixpenny secondhand tray. Although it may not have the intrinsic value of the Ebers papyrus, it is much more legible and is equally a mirror of the medical and cosmetic practice of its age The illustrations and a fleeting reference to Garrison Hair Dye suggest the end of the first world war, the text a pre-Coward nostalgic effort to recapture the spirit of Cavalcade I do not claim to keep abreast of current neckline adjectives, but observation without palpation would describe the models to be sagging rather than plunging The Mesopotamian campaign seems to have influenced the nomenclature of toilet preparations Fatima Balsam from a clean saucer was just the thing for an emancipated generation of free-limbed and graceful girls Pummelling it into the bosom for ten minutes every night increased the bust to operatic dimensions If joy through strength was overzealous a slap or two with Zorida Lotion would secure retraction within the limits of the corsage Such an Alice-in-Wonderland touch would be handy nowadays to enhance woolly sweaters in the daytime and minimise the catastrophic insecurity of modern evening dress But whether Madame was coming up or the gown was slipping down appeared to be of no great moment when Mimi Creme achieved the lustre of a snowy-breasted pearl, and Taj Mahal Emulsion had whipped the acne pimples off her back Venus de Milo's marble must have looked adolescent by comparison

The pink and white complexion of an Edwardian intact world could be restored with a couple of bottles of Lait Virginal, made from an old prescription described rather cynically as favoured by the beautiful women at the court of Charles II Whatever disillusionment the war had brought, the situation could be retrieved with a pot of Maiden's Blush "Please send me two dozen" runs one testimonial, but a discreet veil is drawn over the cause for her blushes Do maidens blush today? It's so long since I tried to make one that the section on salts for suppressed gout looks more my line It conjures up mental pictures of the North West Frontier and my paternal grandfather A bookmarker keeps the place for alternate generations, and my big toe tingles expectantly

Even with para-professional privilege and the odd thankoffering of gin at New Year I cannot get a dental appointment for my fillings under a couple of months In the good old days of *The Gentlewoman's Guide* a highly recommended Tooth Stopping Cement kept the family masticating and free from halitosis I suppose it was pushed in with a hat-pin The chapter on self-massage looked promising I tried upward traction on my wrinkled forehead kneading my double chin according to directions, firmly but not violently, smoothing out the bags below my eyes The snag was that without a bottle of Shalimar Enamel the whole dissipated lot flopped back like the flews of a bloodhound I am off to the bookshop in search of *The New Gentleman's Guide*

* * *

The somatic physician who goes digging in the psychiatrists' garden is in for a bewildering experience. It is like groping one's way in a darkroom with both feet off the floor, and as one's eyes become accommodated to delicate shades of grey, one surprise follows another

Ward rounds are particluarly strange Instead of moving from bed to bed inquiring "How are you," I now pass from chair to chair asking for the name of the Prime Minister One patient gave me a cheery "Good morning!", but when I told the psychiatrist, he said "I know, poor soul, she is very disturbed" Several mornings are spent in the production of convulsions and coma, and I find it difficult to keep my thoughts from the many sleepless nights I had doing the opposite Apparently the TV is the biggest boon to psychiatrists since electricity was invented, all programmes from the interludes to "Puzzle Corner" are followed with rapt attention *Punch* is heavily subscribed to, and even in the doctors' mess a pile of copies holds pride of place next to *The Lancet*

The authors often give quotations from the literature of the last century, and when they do not condemn them *they appear to subscribe to them*

Thus, firstly, the emphasis on functional disability and the denial that the "vasomotor system is primarily at fault" tend, I feel, to obscure the importance *of the autonomic* system This may well be not primarily—or even secondarily—deranged But, as research increasingly indicates, it certainly acts as a mediator-effector for corticosubcortical *integration in* all *psychogenic symptoms*, whether they be called hysterical or psychosomatic That is why the *dictum* "I cannot = I cannot will" is confusing, since it brings in volition

Secondly, the reported "striking feature of concreteness of expression" is indeed characteristic, yet not as such, but in the sense of some symbolism *which invariably underlies such* disorders The idea of "dirt," for instance, in its dual sense, is often clearly depicted by psychosomatic skin lesions One can hardly agree with the authors that it amounts to thought disorder (mostly seen in schizophrenia) unless it *had* been *tested* with the usual *proverb tests, &c* *To me, it appears as* part and parcel of the pathogenesis, and I feel that it should simply give food for thought on the psychology and ontogenetic evolution of language rather than be given a sinister significance

Thirdly, *the statement that* the patients wish for amputation "may be regarded as a degree of *self mutilation amounting* to partial suicide" would seem somewhat nugatory unless it is meant to support the view that these patients were mentally ill To call such a wish (not the act !) suicide—even "partial"—is at least *inappropriate*, *for while* on the one hand we know little of the psychology of suicide, on the other the concept of dissociation offers a much more likely psychological explanation

Fourthly, it is suggested that "cases of œdème bleu illustrate the early *stages* of mental illness," and *I think* it is *with this view that the authors* have *raised the neurotic* "inaccessibility to objective evidence and reassurance," to the status of delusions—even though not "frank" ones I think that this is not supported by the facts A psychosis may indeed *mimic all so* called "neurotic" states, but there is no particular reason to consider such states as a prelude to insanity If we agree, as the authors do, that the psychogenic symptoms are vital to psychic *economy*, we cannot mistake the patients' desperate loyalty *to* such symptoms as delusion, while we can appreciate *that the so called "secondary gains"* and "motives" are but the *altera pars* of these symptoms There are as many psychic economics as there are individuals at any given moment, and if they occasionally result in disabilities one cannot readily speak of mental illness

Finally, I would like to join with the authors in their protest against the confusion caused by *that* misnomer, "hysteria" I used, above, *the term* "*the hysterias*", *yet, unlike the schizophrenias*, the epilepsies, and other such "plural" conditions, these possess nothing that is not to be found, rudimentarily at least, in the normal, they are as protean in their psychopathology as life itself

If we all make a point of using terms like "psychosomatic," "immature and unstable personality," "conversion syndromes," and "regression states," there will be no room for so bad a name as hysteria

The National Hospital for Nervous Diseases London W C 1 — G M Jacobides

DANGER—CLINICIANS AT WORK

Sir,—One of the most stimu*lating aspects of medicine* is the inability of its *practitioners to agree on* any topic whatsoever It is no surprise to hardened readers of *The Lancet* to see (Jan 7) that the diets so beloved and acclaimed by our distinguished elders are quite useless in the treatment of peptic ulcer As everybody knows, ulcer is caused by stress which is a *condition found* in prosperous, civilised communities Ulcer is seldom seen in Afghans, who have no worries (and no X-ray machines), and was unknown to our ancestors, who suffered from famine, plague, war, and poverty but never from stress

A few pages further on we read *that the time* honoure abduction splint for paralysis of the *shoulder* muscl should be abandoned Of course it should, and as f repairing hernia by sewing the conjoined tendon to t inguinal ligament (Mr Doran, Dec 24)—it's useless, m dear fellow and if you're thinking of that chap yo *operated on a couple of years ago* forget it ! He isn' *really cured, as you would know if you'd shoved in a fe* radio opaque markers Talking *of radio opaque* marker Mr Doran's lower pair of photographs *repays* a secon glance It will be seen that the outer marker in th conjoined tendon has not only separated from its opposi number in the inguinal ligament, but has moved twic as far from its fellow in the conjoined tendon as it was i *the beginning* How come ? Has the tendon suddenl *doubled in length*, or has the "marker," like any othe foreign body in muscle, *moved around a bit* ?

Don't let's stop There *must* be *plenty of other* useles procedures going on in London What about fracture of the collar-bone ? We usually treat them with som elegant modification of the "three handkerchief sling Why ? Is it to relieve pain ? Try it and see Is it t correct the displacement ? X-ray it and see Why, then Perhaps if I may misquote Pascal, we "have reason *that Reason itself* knows nothing of"

South Mimms, Herts — V J Downie

X RAYS FROM TELEVISION SETS

Sir,—I was interested in Dr Chisholm's query (Jan 7 regarding the possibility of dangerous X-ray emanation from television tubes

Recently I and three other members of our hospita staff carried out experiments on our four television sets Small fast dental X-ray films were placed on the glas immediately in *front of the tubes*, on *the* sides of th *sets, and at other positions up to 2 feet away from th front of the set* A *small disc of metal* was inserted between the sensitive side and the tube, the films being kept in position by 'Sellotape' The films were developed after periods varying from 1 to 8 weeks, and in no cas was there any evidence *of* the films having been sensitised The sets are standard ones with tubes ranging from *14 to 17* inches

This *test seems a fairly easy one to apply*, and as a *result I personally have ceased to worry about* any dangerous television X radiation

Sutherland Dental School,
Newcastle upon Tyne — G E M Hallett

MODIFIED QUECKENSTEDT TEST

Sir,—Dr Belton's *comments* last week cannot be *allowed to pass unchallenged, for apart* from their *theoretical inaccuracy* they contain implications of practical danger His belief that the rise in cerebrospinal fluid (C S F) pressure on jugular compression is due to the slowing of absorption is surely shared by very few This rise in pressure, which takes place within a few seconds, is in *fact* due *to* an increase in the *total* contents of the virtually *inelastic meninges* which enclose blood and nerve tissues as well as C S F Obstruction of the venous outflow whilst arterial inflow continues results in a rapid rise of cerebral blood-volume with consequent rise in C S F pressure The possible alteration in C S F-absorption rate cannot contribute materially to this rapid change

Dr Belton's practical advice is *that jugular* compression *should* be abandoned in *favour of forced* expiration *against* the closed *glottis* by the patient But this manœuvre is precisely that required as a contrast to the effects of jugular compression when one wishes to demonstrate an obstruction to the normal C S F dynamics either in the lateral sinuses or in the *spinal theca*, for it increases intra *abdominal tension, compresses* the howed a confusion of thought to which I was tempted o reply, but at the time it seemed more appropriate o prepare a report on the matter for the Cohen Committee, and this was done However, I now find that at least one other medical journal has apparently accepted your objection as correct As it would be regrettable if the scientific implications of the Widdowson-McCance investigation, unique of its kind, were restricted by any ill-founded criticism, I feel that a further reply is imperative

Before discussing the actual composition of the flours, I should mention that they were not milled under ideal circumstances

At that time (1947–48) the extraction of National flour was 85%, and in the ordinary way the clothing of the sifters in the mills would have been changed for the milling of 70% flour This was impossible, but the milling was carried out under the supervision of experienced staff of the Cereals Research Station, and in the case of the 70% flour several runs were made and the flours analysed before the final flour was regarded as satisfactory The difficulty—as mentioned in the Widdowson McCance report—was to prevent too much powdered scutellum and bran from getting into the flour, this possibility was due to the relatively wide mesh of the silks covering the several flour sieves

Three consignments of flour were supplied (1) a quantity of 70% for the preliminary period only (i e, before the experiment proper began), (2) the first main consignment, and (3) the second main consignment The two main consignments were carefully sampled and analysed at the Cereals Research Station before dispatch. and the results are contained in two letters to Professor McCance, then in Germany, dated May 20, 1947 and Jan 2, 1948 The figures for the 70% (unenriched), 85%, and 100% flours were

Flour extraction	Vitamin B_1 (µg per g)	Nicotinic acid (µg per g)	Iron (mg per 100 g)	Protein (%)
First consignment				
70%	1.2	10	0.99	10.9
85%	3.2	36	2.26	11.8
100%	3.9	48	3.65	11.95
Second consignment				
70%	1.2		1.1	
85%	3.3	30	1.8	
100%	4.2	50	3.6	

When we later analysed for vitamin B_1 a sample of 70% flour from the first consignment that was sent to us from Germany the figure obtained was 1.1 µg per g (report, p 98) The average analysis of the 70%-extraction flour as determined at the Cereals Research Station may therefore be taken as

Vitamin B_1	1.15 µg per g
Nicotinic acid	10 µg per g
Iron	1.05 mg per 100 g

It was on these figures that the degree of enrichment of the other flours used in the investigation was calculated

For a 70–72%-extraction flour the Ministry of Food's *Manual of Nutrition* (1945) gives the following figures

Vitamin B_1	0.7 µg per g
Nicotinic acid	11 µg per g
Iron	1.4 mg per 100 g

In February, 1953, the Ministry adopted the following revised figures

Vitamin B_1	0.8 µg per g
Nicotinic acid	8 µg per g
Iron	1.25 mg per 100 g

All the vitamin-B_1 figures so far mentioned, including those adopted by the Ministry of Food, were obtained by the method in use at the Cereals Research Station since the outbreak of the war[4] The nicotinic acid was assayed by the microbiological method also developed at the station, and in experiments carried out in the last few months, on a wheat mixture similar to that used in the Widdowson-McCance investigation, two flours of 70% extraction milled in different ways gave nicotinic-acid figures of 11.3 and 11.4 µg per g, whilst a 65%-extraction flour gave the figure of 10.2 µg

The conclusion is that the nicotinic acid and iron contents of the 70% flour used in the German investigation were normal for a 70% flour the B_1 content is slightly high but still within the range for a 70% flour Thus, in one of the important papers by Dame Harriette Chick and her colleagues[5] showing the effects of flours of different extraction-rate on the growth of rats the 70% flour had a B_1 content of 1.09 µg per g (the value was determined at the Cereals Research Station) Kent Jones[6] also gives 1.1 µg per g as the average figure for a white flour of about 72% extraction

Your leading article quoted some of the published data on the composition of flour without apparently appreciating how most of these data were obtained The composition of 80% National flour, for example was laid down by the Conference on the Post-War Loaf This definition which forms the basis of the Flour Order, 1953, give the following *minimum* figures for the three nutrients

Vitamin B_1	2.4 µg per g
Nicotinic acid	16 µg per g
Iron	1.65 mg per 100 g

It is of course easy to mill an 80% extraction flour which would have lower levels of these three nutrients, but such a flour would not conform to the prescribed standards for National flour (which in fact is relatively difficult to mill) For this reason the 80% flour quoted by you, which was obtained in a laboratory investigation[7] in which no attempt was made to mill the flour to the Post-War Loaf standards, cannot properly be used as a standard of comparison

Furthermore, one cannot compare data obtained by different methods unless these methods have been shown to give reproducible and identical results on the same sample of material (flour) Thus, the figures for B_1 and nicotinic acid quoted by Dr. Holman in the report were obtained by entirely different methods, the first using adsorption on Decalso with an internal standard and which is held to give higher values than the conventional thiochrome method for flour used at St Albans,[8] whilst the nicotinic-acid figures were obtained by a chemical method in contrast to the microbiological method used for the figures obtained originally on the two consignments of flour

The protein figure of a flour from a given wheat is also an index of its extraction-rate It is our experience that on the average the difference in protein content between a 70% flour and the whole wheat is about 1%, and between 80% and the whole wheat about 0.5% Below, therefore, are listed the characteristics of the 70% flour used in the Widdowson-McCance investigation, with those which would have been expected for an 80% National flour from the same wheat mixture The methods of assay are of course the same for both flours

—	70% flour (as found)	Corresponding National 80% flour
Vitamin B_1	1.15 µg per g	2.4 µg per g
Nicotinic acid	10 µg per g	16 µg per g
Iron	1.05 mg per 100 g	1.65 mg per 100 g
Protein	10.9%	11.5%

From these figures it is certainly difficult to see any justification for your statement of June 30 that the 70% flour was comparable to National 80%-extraction flour

Cereals Research Station
St Albans

T MORAN

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[4] Ridyard H N J Soc publ Analysts 1949 74 18

[5] Chick H, Copping, A M Slack, E B Lancet 1946, i 196

[6] Kent Jones D W J roy Soc Arts Jan 13 1950

[7] McCance R A, Widdowson, E M Moran T Pringle, W J S Macrae, T F *Biochem J* 1945 39 213

[8] Ridyard, H N *J Soc publ Analysts* 1950, 75 634

JAMES MEADOWCROFT TURNER

M B Lond, F R C S

Mr J M Turner, consulting orthopædic surgeon to Brighton Municipal Hospital and orthopædic surgeon to the Royal Sussex County Hospital, died on Jan 6 at the age of 52

He was born at Oldham and took his medical training at Guy's Hospital, qualifying in 1920 and taking his M B with honours and distinction in surgery in the following year After holding house-appointments at Guy's he was for a time in general practice in Streatham, but his interest in orthopædics had already been aroused by his work under Trethowan and Lambrinudi, and after holding a clinical assistantship in the orthopædic department at Guy's he became surgical registrar at the Royal National Orthopædic Hospital He took the F R C S in 1928 In the early '30s he settled in Brighton and quickly established a large consulting practice During the late war he served in Persia with the R A M C as an orthopædic specialist, holding the rank of major

R B writes "By nature Turner was shy and retiring, and it was only rarely that he could be persuaded to contribute to the medical journals As an operating surgeon he was conservative, and he preferred to confine his work to the more simple and straightforward cases, but when occasion arose he tackled an exacting and difficult problem with certainty and skill In obscure cases his opinion was invaluable Those who knew him came to depend on his quiet sympathy and surgical skill"

WILLIAM HAROLD ROWE JEREMY

M B Camb, D O M S

Mr Jeremy, ophthalmic surgeon to the West of England Eye Infirmary, died at his home at Pinhoe, near Exeter, on Dec 27 at the age of 46 He was the only son of the late Harold Rowe Jeremy, ophthalmic surgeon to the London Hospital

William Jeremy studied medicine at Cambridge and St Bartholomew's Hospital, and after graduating M B he became ophthalmic house-surgeon at Barts and later house-surgeon at the Royal Westminster Ophthalmic Hospital During the late war he served as an ophthalmic specialist with the rank of squadron-leader in the R A F V R In 1943 he took the D O M S In 1946 he was appointed assistant surgeon to the West of England Eye Infirmary, Exeter, becoming surgeon two years later He was also ophthalmic surgeon to the North Devon Infirmary, Barnstaple, and to the West of England Institution for the Blind in Exeter

M D B writes "Jeremy was always a most conscientious and competent oculist, and soon acquired a flourishing private practice He was at his best in his outpatient work and in the operating-theatre Refractions he endured but never enjoyed, relishing them even less than most ophthalmic surgeons Particularly in his earlier years at Exeter he was keen to try new operations, but in the end he as often as not fell back on old and well-tried methods His patients liked him, and he was essentially friendly and kind-hearted if he had a fault it was that he was too kind and found it difficult if ever he had to break bad news to a patient

"He was a perfect colleague, and my affection for him grew with the years Absolutely loyal, of a genial temper, and with a happy sense of humour, he would have been an asset to the staff of any hospital It is hard to believe that there will be no more of those pleasant breaks on Monday mornings when we three surgeons forgathered for coffee, not really for the sake of the coffee but for the pleasure of being together and of talking about anything or nothing—about a difficult case (and none of us was ashamed to admit before the others that we didn't know the answer), about our patients (William always seemed to have the most extraordinary ones), about infirmary problems and difficulties, or possibly a little scandal, if only we could hear of any Or there were the occasional evenings in Southernhay when he came for a drink, with the inevitable attaché case, and, like Heraclitus, we 'tired the sun with talking and sent him down the sky' until dinner could be kept waiting not a moment longer and William was gonged out"

Mr Jeremy leaves a widow and three young children

OSCAR HILTON

B A, D M Oxfd

Dr Hilton, who was for many years in practice Northwood, Middlesex, died on Jan 8, at the age of 7 He was born in Dundee but was educated in Londo at St Paul's School He was an exhibitioner of Magdale College, Oxford, and after taking his B A with first-cla honours in physiology in 1899 he went to St Thomas' Hospital to complete his medical studies He qualifie in 1902, and held house-appointments at St Thomas and at Great Ormond Street, where he fell under the spel of the late Sir Frederic Still He also held a post at th Children's Hospital, Shadwell, before he settled i general practice on the edge of the Chilterns at Northwood, then a small village With the years Northwoo became a large urban area, and his practice grew an prospered He was one of the founders of the Northwood and Pinner Hospital His experience in general practic led him to publish a monograph on the commone children's diseases, which carried a foreword from Si Frederic Still He retired to Dorset in 1947

"Outside his happy family circle," writes W R "Hilton's two greatest loves were children and hi garden Children could not resist him, nor he them This, combined with his exceptional knowledge o children's diseases, and his broad common sense, were the basis of his success Like all men of character he could sometimes fail He had a short and brusque way on the telephone which occasionally scared away even his friends, but those who knew him loved and forgave this very pardonable fault He will be remembered alwa with affection and gratitude"

D M B, who took over his practice, describes Hilton as "a man of great humanity and charm and endowed with unusual clinical judgment While intolerant of fools and of those who thought themselves much more ill than they really were, to those in trouble or severe illness he gave all his skill and kindness and wise counsel His memory was prodigious, and up to the last there were few details in the family histories of his Northwood patients which he could not recall I used to send him bulletins every three or four months, in which he seemed to delight, and the letters he wrote in answer were full of wisdom and humour"

Dr Hilton leaves a widow, three sons, and a daughter

Professor LERICHE

Mr David Patey writes

May I add a note to your excellent obituary notice on Professor René Leriche to mention the great influence on Leriche of Halsted, an influence probably secondary only to that of Claude Bernard Leriche never seemed to tire of acknowledging this indebtedness as illustrated for example by the famous obituary notice he wrote on Halsted's death, the numerous references in his book *La philosophie de la chirurgie*, and his oration at the Halsted centenary celebrations in Baltimore in 1952 At his first visit to Baltimore as a young man, Leriche was captivated not only by Halsted's contribution to surgical technique in his doctrine of gentleness in the handling of tissues, but also by his surgical philosophy in regarding surgery as a branch of experimental biology

On Leriche's oratory and writing, the charm of which all acknowledge, I once took the opportunity of asking him which French writer had most influenced him I hazarded the guess that it was Flaubert, who was noted for the extreme care with which he polished and repolished every word and sentence, but Leriche told me that this was not so In fact he found Flaubert rather tedious and he said that the writer who had had the greatest influence on him had been Anatole France

Perhaps you will have space for a final characteristic littl story When I was introduced to Leriche at Baltimore in 1952 it was mentioned that we had met at the International Society of Surgeons meeting in Paris in 1951, of which Lerich was president I diffidently added that he would not remember me as I had been just a 'simple soldat" while he was the 'général" Straight away Leriche replied "Il vaut mieux être simple soldat et jeune, que général et vieux" And at once he proceeded to put me at ease with graciousness and charm ever allowed to reach a dangerous level Relatively much arger quantities of it can therefore be tolerated It is probably or this reason that all the accidents which have been eported [2-7] after the use of lignocaine have occurred in atients in whom no adrenaline has been used Mr Dutton's ase is no exception in this respect

It would therefore seem that the best results with ignocaine will be obtained by those who accept 300 mg as a maximum safe dose, and who use the solutions containing adrenaline These conditions in fact impose little limitation on the use of the drug, which is effective for long periods in 0 25% solution Further, though Carnegie and Hewer [8] found that the best vasoconstriction was obtained with 1 250,000 adrenaline it is still possible, in the scalp at least, to obtain pronounced vasoconstriction with as little as 1 1 000,000 There should therefore never be any necessity to exceed the maximum safe total dose of adrenaline which is 0 5 mg

I trust that these facts will help to dispel much of the confusion which has arisen concerning lignocaine, and in future make safer the use of this most valuable agent

Department of Neurosurgery
Royal Infirmary
Manchester

A R HUNTER

DOMICILIARY CONSULTATION IN PSYCHIATRIC PRACTICE

SIR,—Dr Denis Leigh (Dec 17) expresses the opinion that the "family doctor is well advised to steer clear of psychotherapy other than simple supportive measures" no doubt for the reason that "the present generation of practitioners is almost untrained in psychiatry" Yet in discussing the figure for outpatient referrals from general practitioners he observes, perhaps rather naively, that "it seems that the general practitioner himself deals with most of his psychiatric patients"

Clearly Dr Leigh regards psychiatry as a field for the expert only This follows inevitably from a view of mental illness, held by many well known psychiatrists, according to which the symptoms are random physical expressions of the disorder, interesting to assess in relation to other bodily events but without meaning in themselves

There is, however, another view of the psychiatric patient, according to which he is a "living," changing person, reacting to other people who are reacting to him, whose symptoms are an essential part of his whole being and a means of communicating his "shut out" feelings and emotions to others, including his doctor This view is frightening to those whose need is to keep everything "scientific"—i e, in their control—and fear recognising their own emotional responses to the patient But it does provide some sort of approach to an understanding of how the general practitioner manages to help his psychiatrically ill patients

All my clinical experience has confirmed that people *do* react to one another, that the patient with a symptom is no exception and neither is his doctor It might be platitudinous to repeat *this were it* not for the existence of an influential body of psychiatric opinion whose need seems to be to deny the existence of these emotional relations, or, admitting to their existence, to deny that they have any significant rôle in the cause or course of the illness

The mechanistic view, which regards the symptom as a manifestation of the patient's 'neuroticism,' precludes acceptance of the view that the symptom is a means of communication, and that its very existence depends on the response which it secures from the "other person" A patient may have asthma, by means of which symptom the "other person" is made aware of his distress and emotionally compelled to act to relieve it The symptom can be the patient's way of saying to the other person 'I am in a desperate state and only your loving concern can save me, but, make no mistake about it, the situation is deadly and if you do not recognise that and treat it as such then I shall die' If a child *is dying of hunger although there is milk beside him* the *spontaneous* reaction is to feed the child before scolding him or even treating him In my view, if he fails to appreciate the emotional significance of the symptom, which I consider the mechanistic view makes inevitable, the psychiatrist may be putting his patient in grave peril

Fortunately most people not expert in psychiatry including general practitioners, do react quite spontaneously to their patients' demands for help and give it to them in one way or another True, not every doctor has the "feel" for helping psychiatric patients fully developed, but a great many do

Here then, is a possible explanation of Dr Leigh's puzzling referral figures When one remembers that minor psychiatry represents a third of all general practice it is encouraging to realise that the rank and file of our profession can and do help their patients—even their neurotic ones I wish to associate myself with the views expressed in the excellent letters by Dr Balint and Dr Hopkins (Dec 31), that general practitioners can and should be helped to develop their innate capacities for psychotherapy, for they alone have the numbers sufficient to cope with the needs

London, N W 3

N CHISHOLM

DANGERS OF RAISING FOOT OF BED

SIR,—Raising the foot of the bed is undoubtedly of value in true peripheral circulatory failure (from hæmorrhage or vasomotor collapse) or in profound anæmia where cerebral anoxia is causing distress Under these circumstances, bed blocking aims at increasing venous return and hence cardiac output *from a healthy heart* and/or increasing cerebral blood flow Before the use of infusions and controlled respiration, bed-blocking as a measure of resuscitation in postoperative collapse was both safe and effective With the advent of both these adjuncts to surgery, however, I submit that bed-blocking in a patient who has received an intravenous infusion with or without controlled respiration is a dangerous if not on occasions a lethal procedure

The difficulty of estimating blood-loss during an operation tends to make replacement therapy err on the side of excess Furthermore, controlled respiration changes a normal negative thoracic pressure to a positive one, causing a greater or lesser degree of venous pooling in the great subthoracic venous tree During an operation, these two factors may well act in opposition, thus maintaining a relatively normal physiology When, however, voluntary breathing becomes established and the patient returns to the ward, the change to a normal thoracic pressure will release the venous pool, and may, in a heart whose reserves are limited by disease or old age cause incipient right sided heart-failure In a case of this nature, bed blocking may tip the balance into severe acute cardiac failure, which may be unrecognised and fatal

The first indication of central failure will be a falling blood-pressure and a rising pulse We have all been taught that this state of affairs in a postoperative patient represents peripheral failure, for which bed-blocking is part of the treatment It may of course be peripheral failure, but if it is treated as such when it is in fact central failure, it will almost certainly be fatal

The practical aspect of all this is fairly obvious It is not easy to distinguish central from peripheral failure in the semiconscious or unconscious patient More often than not, a drip trolley is ready by the time the house surgeon arrives, and treatment aimed at combating peripheral failure is rigorously pursued without a complete appraisal of the situation The rather more imaginative houseman may well use hypertensive additives in the

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[2] Ansbro F P Blundell A E Sweeney J C, Bodell B Andorko J E *Curr Res Anesth* 1954 33 406
[3] Crawford O B *Anesthesiology* 1953, 14 228
[4] Gordh T *Anæsthesia* 1949 4 4
[5] Grimshaw C *Brit med J* 1952 i 488
[6] Powell W E Nowill W K *Curr Res Anesth* 1953 32 350
[7] Safar P *Ibid* 1954 33 98
[8] Carnegie D D Hewer A J H *Lancet* 1950 ii 12

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on Jan 9, with Prof Stanley Graham, the president, in the chair, the following were admitted fellows of faculty

Ali Muhammad Nasim Almaly, William Brodie, W D Roberts

College of General Practitioners

Butterworth Gold Medal—The subject for this year's essay is the Care of the Elderly in General Practice Essays should be sent, not later than Sept 17, to the chairman of the awards committee of the college, 14, Black Friars Lane, London, E C 4, from whom further particulars may be had

Central Middlesex Group H M C

Dr Peter Friedlander has been awarded a prize of £50 from the research fund of this group for his thesis on the physiological response of the stomach to fat in duodenal ulcer The work of Dr J S Crawford on obstetrical anæsthesia was commended

Microcirculatory Conference

The theme of the third Microcirculatory Conference, which is to be held on April 3, at Milwaukee, Wisconsin, will be regulation of blood flow Further information may be had from the chairman, Mr George P Fulton, PH D, department of biology, Boston University, 675, Commonwealth Avenue, Boston 15, Massachusetts

Child and Family Psychiatry

The department of child psychiatry of the Ipswich Group Hospitals is holding a refresher course on this subject from April 9 to 13 Further information may be had from 11, Fore Street, Ipswich

Oliver Prize

The 1955 award of this prize (£50) has been made to Dr W d'A Maycock for his contributions to the development of blood transfusion

Liverpool University Medical Students Society

The annual dinner for past and present members of this society is to be held at the Adelphi Hotel, Liverpool, on Feb 8, when the guest of honour will be Sir Clement Price Thomas Tickets (25*s*) may be had from the medical dinner secretary, Medical School, University, Liverpool, 3

Eli Lilly Medical Research Fellowship

Applications are invited before April 30 from doctors registered in South Africa for this fellowship for medical research in the United States The value of the fellowship is $250 a month for twelve months, with return travelling expenses Further particulars can be had from Dr H A Shapiro, P O Box 1010, Johannesburg

Society of Chemical Industry

On Wednesday, Jan 25, at 6 30 P M, the third meeting in the series on Nutritional Requirements and Food Fortification will be held at Burlington House, Piccadilly, London, W 1 The speakers will be Miss E M Widdowson, D SC, and Miss D L Hollingsworth, and the subject will be Calcium and Iron

Salon des Médecins

An art exhibition for doctors, dentists, pharmacists, and veterinary surgeons will be held from March 4 to 25 at the Musée d'Art Moderne, Paris British doctors are invited to send details of name, address, qualifications, and titles of exhibits to Dr Malet, 67, Avenue Pierre Larousse, Malakoff (Seine), France, without delay Exhibits should bear the same information and should be sent to Messrs Davies Turner, Ltd, 47, Graham Terrace, London, S W 1, and not direct to Paris

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A newspaper report on the use of 2 phenyl 3 methyl tetra hydro 1, 4 oxazine hydrochloride as a slimming pill says that the medical advisers of the firm (Messrs Pfizer) which has introduced it are satisfied that it is "safe enough to be sold over the chemists counter" Dr R K Phillips informs us that "the advice of myself and of my medical colleagues and that of the firm has always been that the drug should be taken only under medical supervision"

Directory of Convalescent Homes—King Edward's Hospital Fund have published the 1956 edition of their directory of homes serving Greater London Copies may be had from the Fund, 10, Old Jewry, E C 2 (7*s* 6*d* post free)

Diary of the Week

JAN 22 TO 28

Monday, 23rd

MANCHESTER MEDICAL SOCIETY
9 P M (Medical School University of Manchester) *Gen Practice* Dr J Blair Hartley The Radiologist and General Practitioner

Tuesday, 24th

ROYAL SOCIETY OF MEDICINE 1, Wimpole Street, W 1
8 P M *Medicine* Prof Andrew Wilson, Dr Sidney Lo Dr Denis Williams, Dr R M Mason Recent Adva in Treatment
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P M Mr V B Green Armytage *The Dramatic in Obstet and Gynæcology*
INSTITUTE OF DERMATOLOGY, Lisle Street London, W C 2
5 30 P M Dr R H Meara *Bullous Diseases*

Wednesday, 25th

ROYAL SOCIETY OF MEDICINE
5 P M *Endocrinology* Prof Melville Arnott, Dr A C Cro Mr H Donovan, Prof S H Taylor Total Adrenalecto for Hypertension
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S W 3
5 P M Dr F H Young *Management of the Tubercul Patient after leaving Hospital*
INSTITUTE OF DERMATOLOGY
5 30 P M Dr Henry Haber Clefts, Vesicles, and Bullæ
BRITISH PSYCHOLOGICAL SOCIETY
8 10 P M (1 Wimpole Street W 1) *Medical Section* P T Ferguson Rodger The Other Man's Point of View
BIRMINGHAM MEDICAL INSTITUTE 154, Gt Charles Street B mingham 3
8 P M Dr C L O Burns Experience and Reflection
NOTTINGHAM MEDICO-CHIRURGICAL SOCIETY, 64, St Jame Street, Nottingham
8 30 P M Prof R L Tunbridge Disorders of the Biliary Tra
MANCHESTER MEDICAL SOCIETY
4 30 P M *Pathology* Dr Lois Stent Some Aspects of Clini Pathology (Presidential address)
ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St Vinc Street, Glasgow, C 2
5 P M Prof D F Cappell The Kidney in Hypertension

Thursday, 26th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn Fiel W C 2
5 P M Mr B B Milstein Cardiac Arrest and Resuscitati (Hunterian lecture)
UNIVERSITY OF LONDON
5 15 P M (University College Hospital Medical School, Univers Street, W C 1) Prof Gordon King (Hong Kong *Advanced Extra-uterine Pregnancy*
ROYAL SOCIETY OF MEDICINE
8 P M *Urology* Mr D S Poole Wilson, Mr A W Badenoc Urethral Injuries
UNIVERSITY OF ST ANDREWS
5 P M (Queen's College, Dundee) Dr H J Deuel (Los Angeles Fat as an Essential Component of the Diet

Friday, 27th

ROYAL SOCIETY OF MEDICINE
5 P M *Pædiatrics* Dr Kenneth Cross, Mr J B Blaikle Dr George Abercrombie Asphyxia in the Newborn
8 15 P M *Obstetrics and Gynæcology* Miss Gertrude Dearnle Mr H G E Arthure, Mr D B Fraser Place of Myomec tomy in the Treatment of Primary Infertility
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road W C 1
7 30 P M Mr S I Birdsall *Chronic Otitis Media*
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEAS 11, Chandos Street, W 1
7 30 P M Dr A Grimble Prognosis of Cardiovascular Syphilis

Appointments

DRUMMOND, JAMES, M B Edin, D I H deputy M O H and principa school M O, East Ham
MANSON W G C, M B Aberd appointed factory doctor, Alford Aberdeen

The Hospital for Sick Children, Great Ormond Street, London
ELOART, MARY E M B Lond M R C P part time M O, depart ment of dermatology
MYERS N A A M B Melb F R C S F R A C S surgical registra to the thoracic unit
STROUD C F, M B Wales, M R C P, D C H asst medica registrar

Births, Marriages, and Deaths

BIRTHS

KELSALL—On Jan 10, in London, the wife of Dr A R Kelsall—a daughter

MULCAHY—On Dec 8, at Hatch Street Nursing Home, Dublin to Aileen (née Hanlon), wife of Dr R Mulcahy, 58 Fitzwillia Square, Dublin—a son, Richard Mary rue, these authors quickly recovered themselves, but e remark ought never to have been made Inquiries nto the cause of disease are good just because it is good save the individual human being from suffering hat is a sufficient and full justification

Department of Social Medicine
and Public Health,
University of Malaya

T A Lloyd Davies

ECLAMPSIA

Sir,—I would like to answer Dr Salzmann (Jan 7) y referring him to an account, just published, by rofessor Lambillon, concerning his experience with oxæmia and eclampsia in the Belgian Congo [1]

While visiting the U S A Professor Lambillon was struck y the high frequency (10%) of severe toxæmia among the oloured women everywhere in the southern States These ere getting the same antenatal care as their white sisters n the North, among whom eclampsia is very rare but latent re eclampsia (according to Professor Lambillon) is still very ommon although their diet is high in protein

In the Belgian Congo until twenty years ago eclampsia as unknown among natives, but nowadays the frequency f this disease is rising in towns, where people from the ural districts are getting plenty of European food, to which heir constitution must adapt itself Even now there is a istrict, with a population of two million, where not a single ase of toxæmia has ever occurred, here, according to radition, pregnant women drink only water, their diet is egarded by Professor Lambillon as inadequate, yet it eems to suit expectant mothers better than the adequate European diet

The *ratio of boys to girls* born in the Belgian Congo s the same as elsewhere in the world

Amsterdam

R Schuurmans

FOOD-POISONING

Sir,—Your editorial last week will be widely welcomed by most medical officers of health, and, representing the medical practitioner's viewpoint, must command attention

I am a little disappointed that you did not stress two factors which contribute to the over-large figure of 39% of all incidents reported as "cause unknown"

As a medical officer of health of a borough many of whose residents spend their working day in the city and partake there of midday meals in hotels, cafés, and restaurants, I find many incidents which cannot be investigated This must be the experience of other medical officers in the Home Counties and outside other great towns

Another factor is that, in this antibiotic age, many patients have recovered before notifications are forwarded to the local medical officer Sometimes the notifications are sent in with the monthly accounts Investigations at this stage are, of course, quite useless, and the medical officer must feel unhappy at the loss of so much opportunity of adding to his local knowledge of the essential causes of food-poisoning

I do not think that legislation has run ahead of public opinion I was recently approached by the secretary of a local women's citizens association to take action with regard to the sale, on open fish counters, of certain food which would not be cooked, and in many other instances public opinion is rebelling against careless practice No one can incriminate cigarette ash, though cigarette ends in bread are rather revolting, but surely let us first get the hygiene right and then tackle the bigger question of the unknown "virus"

I quite agree with on-the spot investigation by the medical officer of health, provided he has the assistance of a team with local knowledge, and a "free" hand to investigate

Public Health Department
Town Hall Beckenham,
Kent

L R L Edwards

HORMONAL EFFECTS OF CHLORPROMAZINE

Sir,—Treatment of 200 psychiatric cases with chlorpromazine ('Largactil') has shown us that this drug produces far reaching endocrine changes, commonly including galactorrhœa,[1] which are apparently due to transient partial impairment of the hypothalamus We describe here the effect of chlorpromazine on secretion of anterior-pituitary tropins in man and animals

Method

Chlorpromazine was administered to the patients thrice daily in doses ranging from 25 to 100 mg, together with vitamins of the B complex

Chlorpromazine was administered subcutaneously to 35 rats at a dosage level of 10 mg per kg body-weight, and to 20 rabbits at a dosage level of 1 mg per kg

Results

Follicle stimulating Hormone (F S H) and Luteinising Hormone (L H)

One patient, a 16 year old girl with a long standing psychic disorder, probably schizophrenic, had increased gonadotropin values before treatment was started These values increased, together with those for œstrone, at the fifteenth to twenty-fifth day of treatment (see accompanying table) Another patient, a male who was a borderline case of schizophrenia, before treatment excreted F,S H 100 rat units (R U) per litre of urine and no L H On the eleventh day of treatment the values went up to F S H 200 R U per litre and L H 100 R U per litre This increased hormone production was maintained for another fourteen days

URINARY EXCRETION OF HORMONES, BEFORE AND DURING TREATMENT WITH CHLORPROMAZINE, IN A 16 YEAR OLD GIRL

Day of treatment	F S H (R U per litre)	L H (R U per litre)	Œstrone (I U per litre)
Before	200	100	10
1st–14th	200	100	10
15th–25th	1000	500	50
26th–36th	200	100	10

In 15 mature female rats vaginal smears were examined daily In 10 there were typical and regular patterns of the sexual cycle, averaging one day œstrus followed by four day anœstrus After this cycle was clearly established, subcutaneous injections of chlorpromazine were started From that day onwards the pattern of the cycle changed to five day œstrus followed by five day anœstrus This periodicity prevailed even in animals which had shown an irregular pattern of cycle before treatment was started When injections were discontinued after 8 weeks, the former pattern of cycle gradually returned in all the rats Intraperitoneal injections of chlorpromazine produced permanent anœstrus

Prolactin

25 female patients were daily examined for production of colostrum or milk Before chlorpromazine treatment no colostrum could be obtained from their nipples Within two weeks after treatment was begun, 17 showed colostrum on pressure or even pronounced galactorrhœa The remainder produced colostrum for a short period, lasting three to seven days, 6 had only unilateral secretion of colostrum

10 immature female rabbits, after being primed with œstrogen, received subcutaneous progesterone 0 5 mg daily, together with chlorpromazine 10 mg per kg body weight After time intervals varying from 17 to 34 days they were killed and the generative phase of the uterus was determined microscopically Whereas in control animals the second phase disappeared spontaneously after seventeen days of continued progesterone injections, the second phase was maintained in rabbits which had chlorpromazine added to the progesterone So far we have been able to keep up the second phase for thirty-four days, which may indicate endogenous production of prolactin The mechanism of this effect is being studied

Corticotrophin

4 patients were checked daily for urinary 17 ketosteroid output in the urine Before treatment 3 female patients had

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[1] Lambillon J *Ciba Symp* 1955 3, 138

[1] Winnik H Z Tennenbaum, L *Pr méd* 1955, 63, 1093

blood-pressure accurately in patients with aortic-valve disease, and the pulse-pressure, which averaged 27 mm Hg (109/82), is apparently not always a reliable measure of the degree of aortic stenosis The second heart sound was normal in 5, diminished in 9, and not heard in 2 cases on auscultation in the aortic area, though probably it could have been found by phonocardiography we do not think it is a helpful sign in the diagnosis or in the assessment of the severity of aortic stenosis

The heart was little if at all enlarged, the cardiothoracic ratio averaging 51 5% and being between 47% and 55% in all but cases 7, 9, and 11 Large hearts were uncommon, mainly because there were no patients with much aortic incompetence, but this did not exclude concentric hypertrophy of the left ventricle, which was found in the patients who died Some prominence of the left ventricle was seen on radioscopy, even in the smaller hearts, and there was some prominence of the first part of the aorta in most of the cases with congenital lesions Calcification of the aortic valves was seen in all the patients except the 2 children

The electrocardiogram always showed severe left-ventricular strain and deep T wave inversion in leads I, V5, and V6, and often in leads II and V4 as well, except in case 7 in which there was right bundle branch block

It was the symptoms that decided us to advise surgery in these 16 patients 11 had syncopal attacks and 5 had them very frequently, 13 had anginal pain and this was often the main reason for their incapacity All had dyspnœa and several had cardiac asthma, showing that the left ventricle was failing, and 2 developed congestive failure after the decision to operate but before their admission to hospital The time between the onset of significant symptoms and operation was not very long, and in those cases where there was delay it was generally a rapid increase of symptoms that led us to advise operation

Results of Operation

All these patients were operated on by Sir Russell Brock, to whom we should like to express our thanks Before discussing the results, the first patient will be described Although he died two years after operation, the amount he could do during these two years showed that he had derived much benefit

Case 1 —When he was 27 he fainted and was told he had a heart murmur He had no symptoms except a tendency to faint, and he carried on a busy general practice When he was 59 he became increasingly dyspnœic, with burning mid sternal pain on even slight exertion, soon followed by loss of consciousness unless he stopped at once Aortic stenosis was diagnosed

His work was proving impossible, so, after two years, aortic valvotomy was performed He resumed his practice without any more attacks of loss of consciousness, but six months later, on a fishing holiday in Scotland, he had some cardiac asthma He continued his practice for another year, but there were increasing episodes of cardiac asthma and finally congestive failure, and he died two years after operation

At necropsy there was much concentric hypertrophy of the left ventricle The aortic valve was bicuspid with severe calcification, and the opposed, rigid cusps were almost closed The other valves were normal, and there was only slight atheroma of the coronary arteries

GOOD RESULTS

Good results were achieved in 5 of the 16 patients—a boy with congenital stenosis (case 11), and 4 adults All have been followed for a year or more

The systolic and diastolic pressures on each side of the aortic valve before and after operation are recorded in table II Fleming (personal communication) has pointed out, however, that the fall in the mean systolic gradient after valvotomy is generally much less than the fall in the peak systolic gradient

In those cases with good results the pressure gradient was greatly reduced after operation—in 3 cases it fell to about half of what it was before and in 2 cases (9 and 11) it was almost abolished Only 1 of these (case 9) developed significant aortic regurgitation In 2 the electrocardiogram was improved, and in 1 the heart became smaller 1 patient (case 8), however, has died from her cardiac condition, and another (case 7) from carcinoma of the bronchus

TABLE II—PRESSURE GRADIENT ACROSS THE AORTIC VALVE BEFORE AND AFTER OPERATION

Case no	Blood pressure before valvotomy (mm Hg)				Blood pressure after valvotomy (mm Hg)			
	Clinical	In left ventricle	In aorta	Systolic gradient	Systolic gradient	In left ventricle	In aorta	Clinical
1	105/80				70	130/?	60/?	120/80*
2	106/71	96/9	48/34	48	60	130/12	70/52	115/80
3	120/80	216/36	112/76	104	Little change	Little change	Little change	Died
4	102/85	172/8	70/50	102	60	104/8	44/34	Died
5	95/65	192/34	72/53	120	100	205/30	103/58	Died
6	110/80	200/12	77/62	123	132	222/17	92/68	135/85*
7	100/85	125/30	55/37	70	40	100/23	60/43	115/85*
8	120/70	180/8	70/40	110	55	139/12	84/52	120/70*
9	122/100	215/15	73/47	142	20	110/16	90/64	140/80
10	102/77	188/3	94/79	94	59	155/7	96/68	130/90
11	95/65	220/18	92/74	128	12	105/15	93/71	110/65
12	110/80	165/4	83/60	82	31	125/25	95/37	98/55†
13	113/91	153/10	66/52	87	52	114/22	62/39	130/85
14	140/100	115/17	69/58	46	15	87/14	73/38	†
15	96/74	175/15	53/42	122	14	72/9	58/32	Died
16	115/85	145/9	51/37	94	60	145/17	85/57	

* Died one or two years later † Died some months later

Case 7 —At the age of 38 this man became breathless and within a year he had gross congestive failure After months in hospital this was eventually controlled with thiouracil, digitalis, and mersalyl, but he easily slipped back into congestive failure At 46 he had a large heart, right bundle branch block, severe aortic stenosis without incompetence, but no mitral stenosis

At aortic valvotomy, the pressure gradient was reduced from 70 to 40 mm Hg He returned to work, which he had not been able to do for years A year after operation his condition was excellent and his heart was smaller with a cardiothoracic ratio of 58% compared with 66% before operation He then developed fresh symptoms and a lump appeared on his chest wall On biopsy this proved to be an undifferentiated carcinoma, and necropsy confirmed the cause of death as carcinoma of the bronchus

Case 8 —A woman, aged 40, had had few symptoms until two years previously, although she knew she had a rheumatic heart She had then become dyspnœic and had anginal pain on exertion, she had lost consciousness a dozen times and would have done so more often if she had not been careful to stop at the first hint of pain Finally she could walk no more than 200 yards There was an aortic diastolic murmur and slight mitral stenosis as well as aortic stenosis Her attacks of unconsciousness showed the urgent need for aortic valvotomy, but her aortic incompetence and high pulse pressure (120/70 mm Hg) were against it

At operation the aortic valve was found to be fibrocalcareous but could be split readily, the pressure gradient across it was reduced from 110 to 55 mm Hg, the mitral valve, which was slightly narrowed (1 0 × 1 25 cm), was divided A year later she was leading a normal life, she was able to walk 2 miles and never felt faint, although she did all the household tasks, such as shaking rugs and polishing, that gave her attacks before There was no increase in the aortic incompetence or in the size of the heart The T waves were biphasic instead of deeply inverted in leads V4, V5, and V6, and upright instead of biphasic in V3 She remained well for another six months but then died suddenly While walking with her husband she had severe sternal pain, and she was only able to utter a few words before she became unconscious and died within five minutes

Case 9 —A woman, aged 48, had been incapacitated with angina for eight years and had had syncopal attacks and cardiac asthma for two years After aortic valvotomy, the pressure gradient across the aortic valve was reduced from 142 to 20 mm Hg She has less dyspnœa and angina, and

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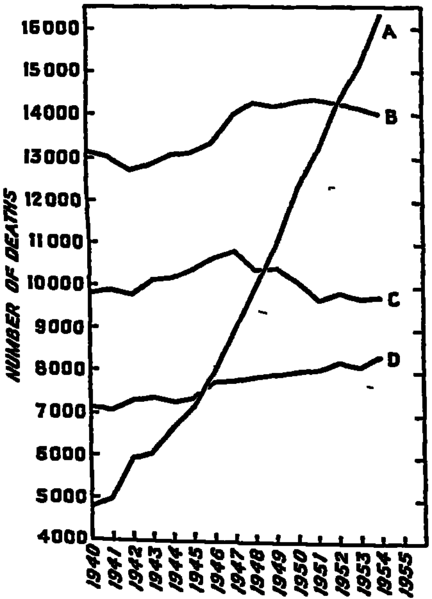
The mere setting out of the yearly consumption of obacco, without relating this to the methods of smoking, eglects the most important change in our habit during he past fifty years It is probable that we in this country ed the world in the number of cigarettes smoked per ead of population until 1925 Certainly we were far head of the United States until then Between 1910 and 925 there was an increase of 100% in cigarette con umption in this country The deaths from carcinoma of the bronchus that clinicians have seen in the past five years occurred mainly in men who commenced smoking in the 1914–18 war Smoking habits are acquired before he age of 30 and seldom change in an individual after this This factor merited investigation in New Zealand



Deaths from cancer of lung and bronchus (A) stomach (B) intestine (C), and heart (D) England and Wales 1940–54

We are faced with a very serious epidemic of lung cancer here, as the accompanying figure shows This contrasts the deaths with those from cancer in other common sites I know of no scientific publications which have shown any change of urbanisation sufficient to explain this alarming rise It is explicable on the vast increase of cigarette consumption, and herein lies hope of dealing with the epidemic Articles purporting to be scientific but which fail to analyse this aspect do a great disservice to those who have shed light on this problem by patient research The peak of the epidemic is not in sight, but its height can surely be diminished if we will act on the ascertained facts and ensure that the public is informed constantly of the risks of cigarette smoking The Government is not prepared to do this yet, but surely, Sir, we can expect informed medical writing not to neglect it

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ATMOSPHERIC POLLUTION

SIR,—Your article of Jan 7 on the Investigation of Atmospheric Pollution makes one ask whether industrial smoke and the smoke from domestic coal fires is really all there is to the heavy pollution and contamination of the air we breathe Has the time not come for directing our attention also to other common sources of air pollution? Outdoors it is the ever-increasing admixture of exhaust fumes from motor vehicles, particularly from Diesel oil driven vans and buses which deserves close study and efficient action Is it really beyond the wit of engineers and chemists to devise decontaminators, fitted to the exhaust pipes, which would absorb or render harmless the hydrocarbons and the carbon monoxide and possibly other poisonous constituents of these dangerous gases? In the meantime it might not be a bad idea if motorists waiting in traffic queues were compelled to switch off their engines which throw out unmeasured quantities of highly toxic exhaust fumes

Turning now to air contamination indoors, may I make a plea for air sampling and for research into the tobacco smoke pollution of the air we are compelled to inhale in buses, in picture and concert halls, in pubs, and wherever else people meet? It could perhaps be argued that smoke abatement (not unlike charity) should begin at home Whatever good is being done by the creation of smokeless zones and by wider application of technological knowledge to the reduction of coal smoke from factories and from home fires, much of it, I feel, is undone by the perpetual and *still* increasing air contamination with tobacco smoke

Apart from its irritating effect on the mucous membranes and on the air passages of both smokers and passive non smokers and its provocation of coughing, which naturally increases the bacterial content of the atmosphere in closed rooms, the burning of cigarettes and pipes takes up a considerable amount of oxygen from the air we are left to breathe Air-sampling and analysis of the O_2, CO_2, and CO content of the atmosphere in smoky rooms and public vehicles would, I believe, reveal a state of affairs that might shock the guardians of our public health

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MALIGNANT DISEASE OF THE RESPIRATORY SYSTEM

SIR,—In a statistical survey of this subject[1] I compared the death-rates below age 70 from (*a*) all diseases of the respiratory system except cancer, and (*b*) cancer of the respiratory system, and suggested that possibly the considerable increase in the death rate from lung cancer in the period under review had resulted partly from better treatment of other lung diseases as manifested by the substantial reduction in the death rate therefrom during the same period

It has been suggested that a split-up of these death-rates at the age of 50 could be of interest since it requires some 20–30 years of cigarette smoking to produce lung cancer, and thus if there is any statistical correlation between the two it will be apparent only in death-rates after the age of 50

DEATHS PER 100,000 MALE POPULATION OF ENGLAND AND WALES FROM DISEASES OF RESPIRATORY SYSTEM

Diseases	1932	1938	1948	1949	1950	1951	1952	1953
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Ages 50–70	419 7	360 2	412 3	470 2	403 1	530 2	377 3	404 4
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The death-rates for males up to age 50 and from 50 to 70 are set out in the accompanying table The results are quite remarkable and appear to establish a definite correlation between lung cancer and the tobacco habit This conclusion is of course supported by the fact that during the period reviewed there has been no incompetence The following data suggest that the greater the relief of the stenosis the greater is the risk of producing incompetence

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[1] Bradshaw, F L *Lancet*, 1955, i 861

In the 5 good results, the pressure gradient was reduced to 40, 55, and 59 mm Hg in the 3 cases where aortic incompetence was not produced or increased, and to 20 and 12 mm Hg in the 2 where it was produced (cases 9 and 11) though in case 11 (where there was congenital stenosis without calcification) it was only slight In the patients who were improved the pressure gradient was reduced only to an average of 75 mm Hg, but even in these cases aortic incompetence was produced in 2 and it was thought to be one reason why the patients were not much better Of the 6 who died, 3 died at once, in the other 3 the pressure gradient was reduced to between 14 and 31 mm Hg, but all developed free aortic incompetence, and this was probably the main cause of their deaths

This risk is increased when the valve is calcified, as it was in all our adult patients Except for young children with congenital or rheumatic disease, it seems unlikely that many patients will reach a stage of severe obstruction without calcification developing We have seen it as early as 18 and 24 years of age This difficulty will be hard to overcome, and McMillan (1955) finds that it is difficult to produce a satisfactory opening even in a necropsy specimen, which must be easier than in a living heart at operation

Our results, however, show that it is possible to get good results even with a calcified valve, and greater experience in surgical technique or in the selection of patients may overcome this obstacle

For example, a patient seen recently had moderate incompetence, so that much doubt was felt about aortic valvotomy, but, in view of the good result in case 8 and his increasing disability, the operation would probably have been advised if we had not had the results of left atrial puncture The left atrial mean pressure was high (22 mm) Analysis of the records according to the criteria of Gorlin et al (1955) suggested that the aortic stenosis and incompetence were of equal importance, and that the aortic valve area had a minimal size of 0 83 sq cm (Gorlin and Gorlin 1951) We thought, therefore, that any increase in size was likely to do more harm from additional incompetence than good from relief of the stenosis, and valvotomy was not advised We are indebted to Dr P R Fleming for these figures and calculations

Another reason why some of the results are disappointing is that the patients were chosen for operation at a late stage of their disease 9 of our 16 patients had left ventricular failure and 3 of these had progressed to right sided failure as well, and all had electrocardiographic signs of severe left ventricular strain Many had reached an age when independent coronary disease is possible, but we think that generally the signs were due not to this, but to changes in the muscle secondary to the aortic stenosis—changes that may become irreversible if the operation is delayed too long

Though the poor outlook without surgery made the decision to operate easier in most of these cases, it is clear that the best time for operation had passed The approach to the aortic valve through the wall of the left ventricle makes it imperative to operate before the muscle of that chamber is irreversibly damaged When the left ventricle shows signs of failure or pain and syncope denotes severe ischæmia, it may be too late for it to recover, even if its burden is relieved

If when severe symptoms are evident it may be already too late for successful surgery, we need signs that left ventricular failure is imminent, so that surgery can be considered sooner The physical signs that point so clearly to the diagnosis are of no help in prognosis because they are compatible with the patient's full activity for many years An increase in heart size would be a clear warning, but it may come too late Measurement of left ventricular pressure and the gradient across the aortic valve is difficult and not without danger, so that it has not been possible to accumulate evidence to correlate with clinical and electrocardiographic findings, as in pulmonary stenosis

The pattern of left ventricular strain in the electrocardiogram seems likely to be the most helpful sign, but more exact knowledge of its prognostic significance is needed This pattern does not prove that the changes are irreversible, because after pulmonary valvotomy it can often be reversed The fact that patients stand aortic stenosis well for so long may mean, however, that by the time symptoms appear important left ventricular strain has been present so long that the changes in the muscle are often irreversible This would suggest that the first sign of left ventricular strain is an indication for surgical treatment, but we think this far from certain, because in some patients it is already present or has been seen to develop gradually during several years while the patient is free from symptoms

This strain pattern is, however, seen more often in those who already have symptoms Thus of the 40 patients reported by Campbell and Kauntze (1953), 24 showed this pattern 17 of these had symptoms of moderate severity but there were few symptoms in 7, 4 of whom were children aged between 4 and 9, where the absence of symptoms is less decisive In contrast to this, among the 16 patients with no strain pattern, 9 had only slight symptoms, and 7 had none

The most hopeful cases seem to be the young patients with congenital aortic stenosis where the valve is not calcified, but many of these do well without operation, it should, therefore, be advised only when they are losing ground Of 2 such patients in this series, 1 died with free aortic incompetence, but 2 boys, aged 9 and 13 (cases 9 and 11, Campbell and Kauntze 1953), have since had operations with good results

The first had not changed much clinically during five years, but T wave inversion in lead V6 had developed in the electrocardiogram In this case the pressure gradient across the aortic valve was reduced from 72 to 24 mm Hg

The second boy was hardly disabled in 1950 but had lost ground in 1952, he was much the same in 1955 except for increasing left ventricular strain (T wave inversion in V4–V6) Operation was therefore advised and the systolic pressure gradient was reduced from 144 to 13 mm Hg without producing aortic incompetence

Patients with aortic stenosis who have symptoms or a left ventricular strain pattern must be watched closely They should be considered for surgery at the earliest sign of deterioration Some patients do well for a long time after the electrocardiogram has shown signs of left ventricular strain, but these signs in a growing child (Marquis and Logan 1955), or their progression in an older patient when symptoms are getting worse, probably indicate the best time for surgery The chances of success will be better if the valve is not calcified, but even then the risk of producing incompetence cannot be ruled out (case 15)

It is important to emphasise to patients that surgery can improve their prognosis and enable them to lead a fuller life, but that complete restoration of normal valve function and normal activity is unlikely Such complete restoration is what they naturally hope for, and, unless they are warned, they will expect it

Summary and Conclusions

In isolated aortic stenosis, valvotomy is less successful than it is in mitral or pulmonary stenosis

We report the results of aortic valvotomy in 16 patients 6 died and in only 5 were good results achieved Even among these 5, 1 died within eighteen months

The main danger of the operation is the production of aortic incompetence The reason for this is that in adults with advanced disease the aortic valve is calcified and deformed

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The mere setting out of the yearly consumption of tobacco, without relating this to the methods of smoking, neglects the most important change in our habit during the past fifty years It is probable that we in this country led the world in the number of cigarettes smoked per head of population until 1925 Certainly we were far ahead of the United States until then Between 1910 and 1925 there was an increase of 100% in cigarette consumption in this country The deaths from carcinoma of the bronchus that clinicians have seen in the past five years occurred mainly in men who commenced smoking in the 1914–18 war Smoking habits are acquired before the age of 30 and seldom change in an individual after this This factor merited investigation in New Zealand

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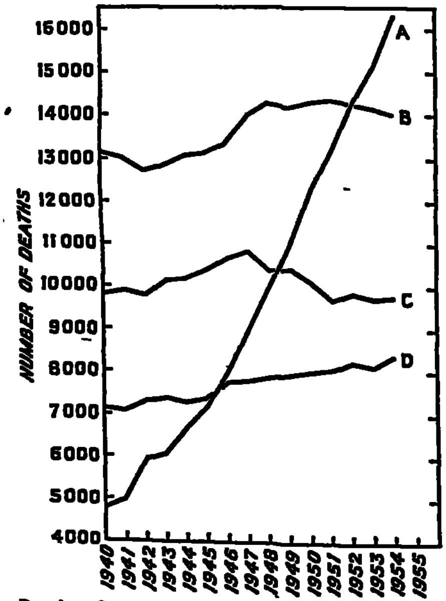

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The infecting organism in every instance examined was *Staphylococcus pyogenes* The in vivo sensitivity of the staphylococcus to antibiotics did not necessarily tally with its in-vitro sensitivity Although the resistance of superficial mastitis to penicillin therapy may have been due to the fact that the mother derived her staphylococci from the resistant strains commonly inhabiting hospitals, penicillin 1,000,000 units daily seemed to be less effective than would be expected on that score alone

There was a firm association with concurrent infection Of the 24 cases of superficial mastitis, either alone or preceding intramammary mastitis, in 14 infection which was, or may be presumed to have been, staphylococcal, was present either in the mother or in her baby or her husband, and in the 25th case an intramammary abscess had been incised Thus 60% may be said to have had concomitant staphylococcal infection (table I) Manual expression of colostrum after delivery appeared to have increased the incidence of this kind of mastitis, although it was not much practised in the wards 13 of the patients had used it

Treatment

Prevention evidently consists in avoiding infection of the skin of the areola, which is very vulnerable to trauma and chemical irritants Antiseptic applications have been avoided so far as possible, but, since the strong association with concurrent infection has been recognised, mothers who have pustules or whose babies have paronychia or staphylococcal conjunctivitis are recommended to use a bactericidal soap when washing their trunk The use of penicillin cream on the nipple or a spot seems quite unjustifiable Likely causes of pustules on the breast are also avoided where possible rubber linings to brassières are discouraged, and adhesive plaster is not used in dressing an abscess for fear of causing another Treatment usually consisted in giving an antibiotic and opening the abscess

Since several of these patients had already been treated elsewhere, the numbers allocated early enough to different forms of treatment are too small to show their relative merits Table II gives the numbers receiving each treatment and shows how many resolved and how long the unresolved took to reach the stage of incision or spontaneous discharge Of the 12 abscesses treated initially with penicillin only 1 resolved The 11 others seemed to take longer than usual to ripen for incision, and, since incision was in the end inescapable, the penicillin was of doubtful service The initial use of either aureomycin or chloramphenicol apparently cured the mastitis in 3 of 6 cases

Our present practice is that, if the lesion is still scarcely larger than a lentil when first seen, aureomycin 250 mg six-hourly is given The effectiveness of this treatment is visible within forty eight hours Where it is ineffective, or where the induration is already as large as a pea, antibiotics are considered less necessary, unless the infection appears to be exceptionally virulent, since evacuation of pus is sure to be necessary ultimately and has to be undertaken as soon as it is physically possible

TABLE I—CONCURRENT INFECTION ASSOCIATED WITH SUPERFICIAL MASTITIS

Type of mastitis	Superficial only	Intramammary only	Superficial succeeded by intramammary	Intramammary succeeded by superficial
Number of cases	20	104	4	1
Site of associated infection				
Baby				
Skin	3	4	1	
Conjunctiva	3	5		1
Abscess	0	1		
Mother				
Skin	5	2	1	
Conjunctivitis	0	1		
Vulval abscess	0	1		
Urine (staph)	0	1		
Father				
Barber's itch	1	0		
Total *no* of cases with infection	12 (60%)	15 (14%)	2	1

TABLE II—RESULTS OF ANTIBIOTIC TREATMENT OF SUPERFICIAL MASTITIS

Antibiotic	No of cases	No resolved without opening	Duration of mastitis before opening (days)
None	5	0	2–6
Penicillin alone	8	1	6–21
Aureomycin 1 g daily	4	2	1–4
Chloramphenicol 1 g daily	2	1	27
Penicillin followed by aureomycin	4	0	2–9
Unknown	2		
Total	25	4	

A stab incision under brief general anæsthesia and preservation of the cavity walls by refraining from using sinus forceps to open the cavity will, if undertaken early enough, enable the mother to continue breast-feeding, unless the incision is very close to the nipple The incision is best made at the margin of the areola It is of course absolutely essential for the breast to be emptied as often and as well as it had been before If emptying is impracticable, suppression of lactation must be started in good time to avoid unnecessary suffering and to prevent superimposed intramammary mastitis

INTRAMAMMARY MASTITIS

Intramammary mastitis is characterised by pain in the breast, a lump in the glandular tissue, a flush of the skin over the affected area, pyrexia, and reduction of secretion from the affected breast The most constant and important of these symptoms and signs is the lump Although a lump may be present in a lactating breast without amounting to mastitis, the other symptoms and signs have not been seen where there was no palpable lump in any case in this series or in the many other cases seen In the present 109 patients the criterion of mastitis was therefore taken to be the presence of at least one other symptom or sign besides the lump All 109 patients had pain, and 71 had pyrexia On this basis of diagnosis no difference could be drawn, in the early stages of intramammary mastitis, between the condition of the mother with intense engorgement and pyrexia which resolved entirely on emptying the breast and the case where resolution by emptying was not obtained and an abscess resulted

This preliminary stage, when intramammary mastitis is manifest yet resolvable, presents features which are hard to reconcile with the usual view of intramammary mastitis The assumption was often made in the past that the condition of the breast and the pyrexia were due in the first place to bacterial invasion, but Romanis and Mitchiner (1952) comment that engorgement of the breast may be regarded as the first stage in intramammary mastitis

In the present series 77 patients (71%) recovered completely without detectable residual induration, and a further 10 did not require incision (fig 1) Since most of the patients were given antibiotics, the defeat of the bacteria may have caused healing and restoration of the normal tissues of the breast, but antibiotics were not essential for this, because 4 patients had thirteen pyrexial attacks with retention which resolved entirely on emptying the breasts at home without other treatment. Recovery like this was often seen before the advent of antibiotics, as Isbister (1952) has remarked occurred during a period of two years, the material consisting, in fact, of 30,000 card groupings Of the 5 errors, 2 occurred because the cards at that time were not protected against moisture, and accordingly the reagents on some cards had been completely spoiled during a damp summer month Since then every card has been packed in a moisture proof envelope with control paper enclosed for an easy check on the effectiveness of the protection The other errors were due to grave disregard of the directions for use

Finally I should like to point out that the groupings in this material were carried out by a rather large number of doctors and technicians in various hospitals Thus, the results should not be directly compared with those published for other new methods, which usually relate to the worker's own laboratory only

Copenhagen KNUD ELDON

WERTHEIM'S HYSTERECTOMY

SIR,—I read with interest Mr Mills's account last week of his modified procedure based on the Howkins combined abdomino vaginal hysterectomy, as I have been using an exactly similar method for the last three years During that time I have treated in this way about fifteen cases of carcinoma of the cervix, though not, as yet, any of carcinoma of the body of the uterus

Mr Mills's statements as to the increased facility of isolation and division of the parametrium can be fully substantiated, while the use of a pack at the conclusion of the vaginal part of the operation, by raising the contents of the pelvis higher up into the abdomen, makes the abdominal part of the operation quicker and easier The reduced time spent in the Trendelenburg position is of value both to the patient and to the anæsthetist While the numbers are too small to be of statistical significance, the impression is that the incidence of ureteric fistula is diminished, though just why this should be so is not apparent

The chief disadvantage of the method is the necessity of being certain that the growth is operable, and it has been thought advisable, on one or two occasions, to open the abdomen before proceeding to the vaginal part of the operation

Rush Green Hospital
Romford Essex E GARLAND COLLINS

"INFECTIOUS ROSEOLA"

SIR,—Dr Fletcher describes in his letter (Jan 7) a small epidemic of "infectious roseola" in Palestine The disease he describes is well known to those with tropical experience as dengue fever, spread by aedes species In the former Netherlands East Indies the more popular name was *vyfdaagsche* or *van der Scheersche koorts* (five day fever or van der Scheer's disease)

The incubation period is generally 5–8 days with extremes of 3–10 days Acute onset, with muscle pains, pyrexia up to 104°F, pain on turning the eyes, slight conjunctivitis, and initial exanthema and enanthema, is common The exanthema may differ from case to case, but usually one can see against the background of large livid maculæ after 3–6 days small, dense, vivid red, spots or papulæ beginning on the chest, waistline, hands, feet, and arms, the face is generally spared Occasionally petechiæ are seen in the spots After defervescence the exanthema disappears, often with fine desquamation General lymphadenopathy is common, the spleen is not enlarged The tongue is coated, anorexia, nausea, and vomiting are common On lumbar puncture the cerebrospinal fluid is under high pressure, and contains an excess of albumin, glucose, and white blood cells A distinct leucopenia is valuable corroborative evidence In the well known Greek epidemic the mortality rate was 0 03%, but usually dengue fever is a benign, though temporarily incapacitating, disorder It has nothing to do with roseola infantum (Zahorsky) The virus of dengue, discovered by Ashburn and Craig, may be transferred to man and animals by injection of the patient's blood in the first days of fever The virus has not been cultivated from human blood, but by repeated passage in infected mice it can be grown There are several strains of dengue virus The infection does not confer immunity

Hilversum, Holland D P R KEIZER

"OEDÈME BLEU"

SIR,—Dr I Macalpine and Sir James Paterson Ross in their paper last week describe a syndrome better known to a past than to the present generation of neurologists They define it as "a not uncommon form of 'hysterical' affection of joints simulating medical or surgical disease"

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London W 1 F M R WALSHE

SIR,—One feels indebted to Dr Macalpine and Sir James Paterson Ross for their article, which was not only interesting but also very stimulating for further consideration of the "hysterias" However, there are, I think, several points that are open to debate

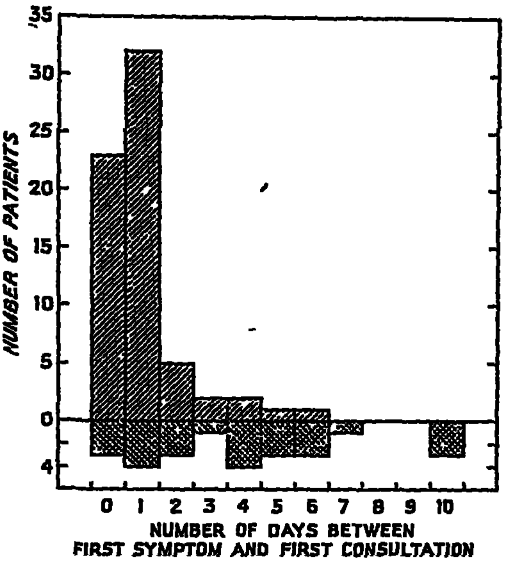

Fig 2—Importance of early treatment of intramammary mastitis *above line* complete resolution, *below line*, residual lump or scar from incision

else to have had a recurring cause—*e g*, temperamental babies—since between them they had forty-four attacks

Probably many women have transitory attacks—complete with pain, lump, and pyrexia—repeatedly during lactation Where the mother thinks little of the signs in her breast, the condition can easily be mistaken for influenza Mastitis should always be suspected when influenza is diagnosed in a woman who is, or who has been recently, lactating

Analysis of the incidence of mastitis shows that there was a preponderance of primiparity and of girl babies, which fact suggests that these factors may have contributed to the failure of emptying Primiparæ, whose breasts offer greater difficulty in suckling (Gunther 1955a), were in the ratio of 76 to 31 multiparæ, whereas the intake of the hospital was 1651 primiparæ to 1054 multiparæ ($\chi^2 = 4\ 67$, $p < 0\ 05$) Dean (1951) has shown that, in the first days of life, girls take less milk than boys do There were more girls than boys among the children of those who developed mastitis in the first ten days 20 girls to 10 boys ($\chi^2 = 3\ 99$, $p < 0\ 05$) But in the children of all the mothers who got mastitis there were only slightly more girls (55 girls to 50 boys from among 1247 girls and 1308 boys born) In an earlier investigation the mothers of small babies were found to be particularly at risk, but in this series that was not so, perhaps because the risk was known

Treatment

The most important part of treatment, as Walsh (1949) pointed out, is to begin early (fig 2) If infection comes, the organism will be *Staph pyogenes*, and antibiotic therapy, not sulphonamides, should be given for prevention Since the mastitis is due in the first place to failure of emptying, emptying must be maintained during treatment and while œstrogens take effect, if suppression is decided on The urgency of treatment depends not only on the threat of infection but also on the finding that the lump is likely to empty its contents in the first day or two of the disease, but that if it has not done so by the third day it is unlikely to do so at all

Since in the present cases and in many others : ill effects followed breast feeding in the first days, t obvious way of dealing with the secretion of m in the first two days was taken where the mother w willing to continue In a few cases the pain of feeding w too great, and, since this was worst when the draug reflex was strongly induced, the humalactor milki machine, which evokes a weaker reflex, was found to wi draw new secretion less painfully than the baby coul and by virtue of its being able to act for fifteen to twen minutes on a breast without causing trauma it wou sometimes withdraw the pent up secretion where the ba would lose interest in five minutes and fail in the job

It was found that, where the lump was not diminish by the third day, an abscess was likely to be formed, a then resolution would usually take place only if lactati was suppressed It seemed better to suppress lactati as soon as quick resolution became improbable In t way slow but complete resolution, a cold abscess, or worst a small abscess is likely to be the outcome In t series 3 patients had had penicillin for some days befo they came to us with a deteriorating mastitis, but who lactation had not been suppressed, and only in them d we see the extensive destruction of breast tissue, t copious pus, and the ugly scarring which is the terror mastitis The deleterious effects on mastitis of sucklin once infection has set in, may be partly due to t spread of infection by the pumping action of the draug reflex within the breast (Gunther 1955b)

The end-result may also be poorer if secretion is allow to persist until the time of incision, because fresh are of retention are then hard to avoid on the day aft incision Fig 3 shows the relation of the final outcom in cases where lactation was suppressed and antibioti were used, to the times when suppression and antibioti were started The interrupted line in the figure encircl the entries relating to patients where emptying was al done It will be seen that neither suppression of lactatio even if it precedes mastitis, nor antibiotic therapy give early is as effective as both procedures together wi emptying of the breast

The object of incision is of course to drain the absce with the least residual scarring not only of the skin bu also of the mammary tissue With the proviso that th secretion of milk should already have been largely su pressed, and that drainage is judged to be ultimatel necessary, the sooner the incision is undertaken the bette Much unnecessary destruction of the breast can resul from waiting to be confident of fluctuation, and, whe there is doubt about the presence of pus, the lump shoul be explored with a needle under general anæsthesia an

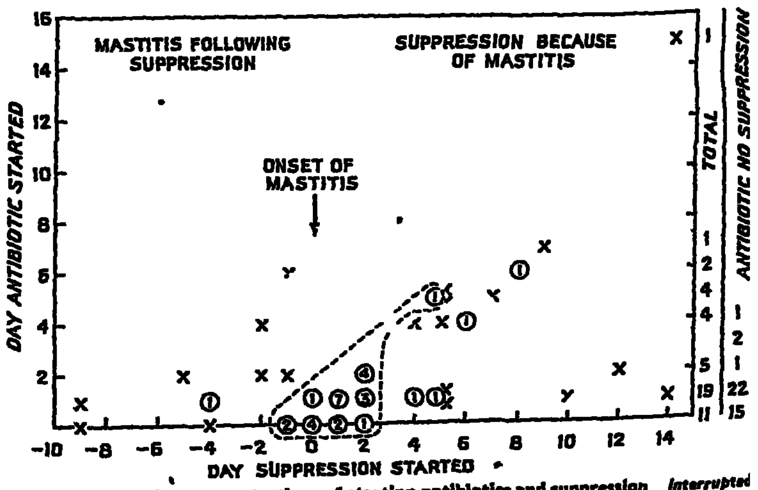

Fig 3—Relation of outcome to time of starting antibiotics and suppression *Interrupted line contains cases in which emptying was achieved*, X subsequently incised *numerals in rings denote number of cases which resolved*

occurred during a period of two years, the material consisting, in fact, of 30 000 card groupings Of the 3 errors 2 occurred because the cards at that time were not protected against moisture, and accordingly the reagents on some cards had been completely spoiled during a damp summer month Since then every card has been packed in a moisture proof envelope with control paper enclosed for an easy check on the effectiveness of the protection The other errors were due to grave disregard of the directions for use

Finally I should like to point out that the groupings in this material were carried out by a rather large number of doctors and technicians in various hospitals Thus, the results should not be directly compared with those published for other new methods, which usually relate to the worker's own laboratory only

Copenhagen   KNUD ELDON

WERTHEIM'S HYSTERECTOMY

SIR,—I read with interest Mr Mills's account last week of his modified procedure based on the Howkins combined abdomino-vaginal hysterectomy, as I have been using an exactly similar method for the last three years During that time I have treated in this way about fifteen cases of carcinoma of the cervix, though not, as yet, any of carcinoma of the body of the uterus

Mr Mills s statements as to the increased facility of isolation and division of the parametrium can be fully substantiated, while the use of a pack at the conclusion of the vaginal part of the operation by raising the contents of the pelvis higher up into the abdomen, makes the abdominal part of the operation quicker and easier The reduced time spent in the Trendelenburg position is of value both to the patient and to the anæsthetist While the numbers are too small to be of statistical significance, the impression is that the incidence of ureteric fistula is diminished, though just why this should be so is not apparent

The chief disadvantage of the method is the necessity of being certain that the growth is operable and it has been thought advisable, on one or two occasions, to open the abdomen before proceeding to the vaginal part of the operation

Rush Green Hospital
Romford Essex.   E GARLAND COLLINS

"INFECTIOUS ROSEOLA"

SIR,—Dr Fletcher describes in his letter (Jan 7) a small epidemic of "infectious roseola" in Palestine The disease he describes is well known to those with tropical experience as dengue fever, spread by aedes species In the former Netherlands East Indies the more popular name was *vyfdaagsche* or *van der Scheersche koorts* (five day fever or van der Scheer's disease)

The incubation period is generally 5–8 days with extremes of 3–10 days Acute onset, with muscle pains, pyrexia up to 104°F, pain on turning the eyes, slight conjunctivitis, and initial exanthema and enanthema, is common The exanthema may differ from case to case, but usually one can see against the background of large livid maculæ after 3–6 days small, dense, vivid red, spots or papulæ beginning on the chest, waistline, hands, feet, and arms, the face is generally spared Occasionally petechiæ are seen in the spots After defervescence the exanthema disappears, often with fine desquamation. General lymphadenopathy is common, the spleen is not enlarged The tongue is coated, anorexia, nausea, and vomiting are common. On lumbar puncture the cerebrospinal fluid is under high pressure, and contains an excess of albumin, glucose, and white blood-cells A distinct leucopenia is valuable corroborative evidence In the well known Greek epidemic the mortality-rate was 0 03%, but usually dengue fever is a benign, though temporarily incapacitating, disorder It has nothing to do with roseola infantum (Zahorsky) The virus of dengue, discovered by Ashburn and Craig, may be transferred to man and animals by injection of the patient s blood in the first days of fever The virus has not been cultivated from human blood, but by repeated passage in infected mice it can be grown There are several strains of dengue virus The infection does not confer immunity

Hilversum Holland   D P R KEIZER

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suppression stilbœstrol 5 mg thrice daily for three days, twice daily for three days, and then 1 mg thrice daily for two days, twice daily for two days, and once daily for two days

Summary

129 cases of acute mastitis were studied

Superficial mastitis was found to be associated with other forms of staphylococcal infection and, except for the very early stages, to resist antibiotic treatment

Reasons are put forward for ascribing the lump, pain, flush, and pyrexia of intramammary mastitis to retention of milk and not in the first place to infection At first, pyrexia does not signify pus, pyæmia, or poor prognosis

The outcome depends mostly on the time of starting treatment, which should consist of antibiotic protection, emptying of the breast, and local heat

Prevention is thought to consist in ensuring adequate emptying of the breasts, which can be assisted by antenatal care and by suggested methods of managing lactation until weaning is complete

The pyrexia of early intramammary mastitis is probably due to pyrogens not of bacterial origin

Sites holding stagnant colostrum or milk are commonly infected by *Staph pyogenes*

My thanks go to Mr J. D Martin, my surgical colleague in this work, and to Prof W C W Nixon and the staff of the obstetric hospital, University College Hospital

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ACUTE BARBITURATE POISONING

P M G BROUGHTON
B Sc Lond, F R I C

G HIGGINS
B Sc Oxfd

J R P O'BRIEN
M A, B Sc Oxfd

From the Department of Clinical Biochemistry, Radcliffe Infirmary, Oxford

ACUTE barbiturate poisoning has become a serious problem in many countries Several workers have commented on the increasing incidence of such poisoning, and the relatively large number of fatalities (Nilsson 1951, Moore et al 1952) The number of cases admitted to this hospital has increased from 3 in 1945 to 41 in 1954 Once such patients are admitted to hospital their chances of survival are greatly increased, and early diagnosis is probably the most important factor in reducing the number of deaths Biochemical analyses can be of great value in confirming the diagnosis rapidly, assessing the severity of the poisoning, and following its course

In the past, methods for the estimation and identification of barbiturates in biological material have been slow, tedious, and insensitive, and the rôle of the laboratory usually limited to confirming the diagnosis by qualitat tests on urine and gastric contents The introduction ultraviolet spectrophotometric methods (Walker et 1948, Goldbaum 1952) has enabled barbiturates to rapidly and specifically estimated in any material, b since the toxicity of barbiturates differs considerabl quantitative analysis is of limited value unless the dr can be identified (Wright 1954) A spectrophotomet method, by which barbiturates may be estimated a partially identified within an hour (Broughton 1956), n enables results to be available in time to aid in t treatment of patients

TABLE I—CLASSIFICATION OF BARBITURATES

Barbiturate	Proprietary names	Substituents on 55 position	Duration pharmaco gical actio (Martinda 1952)
Phenobarbitone	'Luminal'	Ethyl phenyl	Long
Barbitone	'Veronal' Medinal'	Ethyl ethyl	Long
Butobarbitone	Soneryl'	Ethyl *n* butyl	Intermedi
Amylobarbitone	'Amytal'*	Ethyl iso amyl	Intermedi
Cyclobarbitone	'Phanodorm'	Ethyl cyclohexenyl	Short
Quinalbarbitone	Seconal'*	Allyl 1 methylbutyl	Short
Pentobarbitone	'Nembutal'	Ethyl 1 methylbutyl	Short

* 'Tuinal is a mixture of amytal and seconal and its action "short"

We record here the results of analyses of specimens fro 36 patients, of whom 1 died, who were admitted to th hospital between March, 1952, and August, 1955, a from 10 persons found dead, after the ingestion commonly prescribed barbiturates

Materials and Methods

Most of the living patients in this series were unco scious on admission to hospital, and, with many, b chemical analysis was necessary to establish the dia nosis Samples of blood, urine, and gastric contents we analysed during recovery Necropsy specimens of bloo urine, cerebrospinal fluid (C S F), liver, kidney, a intestinal contents, taken from patients found dea were also examined

Blood-barbiturate levels were determined in 5 cas (nos 4, 5, 13, 14, 17) by the method of Walker *et a* (1948), and in the remainder by a modification (Broughto 1956) of Goldbaum's (1952) method The barbiturat ingested are listed in table I These were identified fro the patient's history, by measurement of the amount alkaline hydrolysis under standard conditions (Broughto 1956), or by the methods described by Turfitt (1948 Barbiturates may be prescribed as either the acid or th sodium salt, and all levels reported here are of the ac form of the particular *55'* disubstituted barbitura named

The degrees of consciousness of these patients a defined as follows

U=unconscious *does not respond to painful stimuli, suc as strong supra orbital pressure*

S=semiconscious responds to painful stimuli, moving a groaning, but unable to talk

D=drowsy answers simple questions, but falls asleep undisturbed

A=awake rational

Consciousness was said to have returned when th patient regained the ability to answer simple questions

Results

LIVING PATIENTS

The highest blood-barbiturate levels found in patient after their admission to hospital, together with the dos lumbar veins, and so increases the pressure in the spinal theca, irrespective of what may be happening at a higher level One can only presume that cord compression does not occur in Dr Belton's practice since he has always found the effects of jugular compression to be identical with those produced by straining In that case he could well afford to dispense altogether with the Queckenstedt manœuvre, but in the interests of good practical neurology he would be better advised to carry out the full orthodox routine of recording the comparative effects of right, left, and bilateral jugular compression, together with those of coughing and straining

Department of Neurology,
University of Manchester

L A LIVERSEDGE

DEATH OF PATIENT WITH ARTIFICIAL PNEUMOTHORAX

Dr PATRICK O'ROONEY writes "In last week's issue you mention (p 110) the death of a patient with artificial pneumothorax Readers are referred to a report in the *Southend Standard* As I carry out most of the refills in the Southend area, I would be very much obliged if you would allow me to explain that this death did not take place in the Southend area"

Medicine and the Law

Payment for Drugs

THE Worcestershire Executive Council has taken action in the case of a doctor who, it was alleged, failed to collect the shilling prescription charge from patients to whom he dispensed drugs [1] The case is of special interest because it raises questions as to the responsibilities of practitioners in regard to the collection of these charges

The doctor told the council's investigating committee that the drugs in question were free samples which he had received from drug houses, and he did not feel justified in charging for them He did not consider that the stocking of his dispensary with free samples was a satisfactory method, but "it saved a lot of time and they are sometimes easier to give"

He had, he said, a small stock of ordinary medicines, but having dispensed these for patients, he was often presented with the difficulty of changing a £1 note Sometimes the patients offered to bring the charge on the next visit In such circumstances he found it difficult ever to collect the charge He had paid over all the charges he had received

The investigating committee reported that it did not object to the use of free samples but deprecated their use as a source of supply The council decided that the doctor had "abjectly failed" to collect the charges It was agreed that £10—"a reasonably accurate estimate of the amount involved"—should be withheld from his remuneration

The press report does not disclose the circumstances in which the doctor dispensed these drugs, but there are three possibilities

(*a*) The drugs may have been dispensed (under paragraph 7 (9) (a) of the Terms of Service) for immediate application or administration or for use before a supply could be obtained in the ordinary way

(*b*) The doctor may have been acting as a "dispensing doctor" in accordance with arrangements made by the executive council for patients living in a rural area or who have other difficulties in obtaining drugs

(*c*) The drugs may have been supplied by the doctor apart from any obligation under head (*a*) or (*b*)

The liabilities of the patient and the practitioner with regard to the shilling prescription charge vary accordingly If the drug is supplied under either head (*a*) or (*b*), the patient is liable to pay to the doctor the shilling prescription charge (N H S [General Medical and Pharmaceutical] Regulations, 1954, reg 30 [1]) The doctor is under no obligation to supply the drug except upon such payment (reg 30 [2]), alternatively, he may dispense the drug and, if he has difficulty in recovering the charge at a later date, he may sue for it as a civil debt (reg 34) In these circumstances, the patient's liability would appear a purely civil one to the practitioner, the patient is not under any direct obligation, civil or criminal, to the State

The question then arises as to whether the practitioner is under a duty to enforce his right to the shilling Here the position varies

As to head (*a*) in respect of his duty under paragraph 7 (9) (a) of the Terms of Service, every practitioner receives a payment of 2*s* 6*d* per annum for every 100 patients on his list, the automatic receipt of that payment imposes a clear obligation on the practitioner to demand and account for the shilling charge

As to head (*b*) the practitioner may claim payment for drugs supplied either on a flat-rate basis for each patient (with additional payments for especially expensive items) or on the basis of the *Drug Tariff* for every item supplied If the practitioner claims payment on either basis, then clearly he ought to recover the shilling charge, but if he does not claim, there appears to be no obligation upon him to recover the charge and no good reason why the executive council should expect him to do so This view of the matter appears to be confirmed by the statement in the official *Handbook for General Medical Practitioners* (para 74) that the Minister has determined that the payment of a dispensing doctor for the supply of drugs and appliances is subject to the condition that the charges be collected and paid over

In the case of head (*c*) the patient appears to be under no liability to pay the shilling charge, so there can be no question of the practitioner being obliged to collect it

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Obituary

HUGH SPEAR PEMBERTON

M B Lpool, F R C P

Dr H S Pemberton, senior physician to the David Lewis Northern Hospital, Liverpool, died at his home at Neston, Wirral, on Jan 15 at the age of 65

He qualified in 1913 with first-class honours in medicine at Liverpool University, and joined the staff of the David Lewis Northern Hospital a year later as clinical pathologist During the 1914–18 war he served with the R A M C After demobilisation in 1919 he was appointed junior physician to the David Lewis Northern Hospital He took the M R C P in 1921 and was appointed a full physician in 1924 He also joined the staffs of the Liverpool Hospital for Women and of the Liverpool Radium Institute He was lecturer in clinical medicine at Liverpool University The whole of his active clinical life was thus associated with Merseyside, but his greatest devotion was given to the David Lewis Northern Hospital He was especially interested in dietetics, and his diabetic clinic, founded in 1922, was the largest in the district and kept outstanding records He followed closely the work of the dietitians and the diet kitchen, and he took the leading part in producing the *David Lewis Northern Hospital Diet Book*, first published in 1935 He was the first director of the hospital's biochemical laboratory He was elected F R C P in 1941. He retired from the hospital staff last year

A colleague writes "Pemberton was an outstanding teacher and there was always great competition among the undergraduates to be appointed to him as clinical clerks The meetings of all the members of the medical staff of the hospital over which he presided every week provided a very great stimulus to his colleagues and were a constant source of lively discussion His publications were chiefly concerned with diabetes and diseases of the peripheral vascular system, but he brought original and stimulating criticism to papers by his junior colleagues on a wide variety of subjects"

Dr Pemberton leaves a widow and a daughter

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[1] *Birmingham Post*, Dec 29 1955

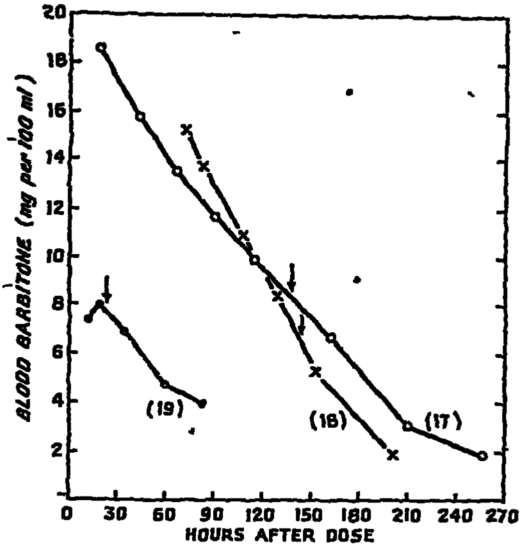

Fig 2—Fall in blood levels of 3 cases of barbitone poisoning The figures in parentheses indicate the case number, and the arrows the time at which consciousness was regained

Case-records

A Typical Case (no 20)

A man, aged 27, was found unconscious, having taken an overdose of butobarbitone the previous evening His progress in hospital is illustrated in fig 4 He was given a stomach washout on admission, but this yielded a negligible amount of barbiturate He passed no urine in the first 40 hours, but after intravenous therapy, including noradrenaline, he excreted 0 5 g butobarbitone in 15 hours At the end of the 2nd day he showed no sign of returning consciousness, and since his chest condition was causing anxiety he was given picrotoxin This produced no change in the rate of fall of the blood-butobarbitone level He recovered consciousness 90 hours after the dose, when the blood-level was 2 5 mg butobarbitone per 100 ml

An Exceptional Case (no 16)

A woman, aged 67, was found unconscious, having taken not less than 22 g barbitone 12 hours previously Respiration failed on the journey to hospital, and was re started by manual artificial respiration On admission to hospital all reflexes were absent, and the blood pressure was 90/50 mm Hg She was given nikethamide ('Coramine') and oxygen, and gastric lavage was performed Later respiration again failed, and, after tracheotomy, was maintained by an intermittent positive pressure apparatus The blood pressure was maintained by an intravenous infusion of noradrenaline Bemegr ('Megimide') in doses of 50 mg intravenously was given a total of 1 g, without apparent effect Tube feedin intermittent positive pressure, and noradrenaline infus were continued until the patient died, 96 hours after admissio Necropsy showed that death was due to pulmonary oeden and pneumonia

Barbiturate estimations of this patient are given in table

PATIENTS FOUND DEAD

Barbiturate levels of specimens taken from the patients found dead are shown in table v In only cases (58 and 59) were the blood barbiturate level

TABLE III—BLOOD-BARBITURATE LEVELS AT RETURN OF CONSCIOUSNESS

Barbiturate	Case no	Picrotoxin I V (mg)	Blood barbiturate at return of consciousness (mg per 100 ml)	Mean blood barbiturate (mg per 100 ml)
Phenobarbitone	1	Nil	7 9	
	2	Nil	7 8	
	3	18	8 9	6 8
	5	Nil	6 0	
	6	Nil	5 6	
	7	Nil	5 0	
Barbitone	17	++	7 8	
	18	++	6 9	7 5
	19	1 5	7 7	
Butobarbitone	20	120	2 6	
	21	Nil	2 6	2 3
	22	Nil	1 7	
Amylobarbitone	24	++	4 2	
	25	447	3 5	
	26	12	3 3	
	27	Nil	2 3	2 9
	28	Nil	2 4	
	29	Nil	2 5	
	30	Nil	2 4	
Tuinal	32	Nil	1 7	
Cyclobarbitone	33	Nil	1 7	
Pentobarbitone	34	260	1 4	1 3
	35	24	1 3	

significantly higher than those of *surviving patients* who had taken the same drug (table II) The C S F levels were lower than those of blood, and, in general, only small amounts of barbiturate were found in urine, liver, and kidney *Stomach and intestinal contents usually con*tained large amounts of barbiturate, contrasting strongly with the amount recovered by stomach washout from the surviving patients

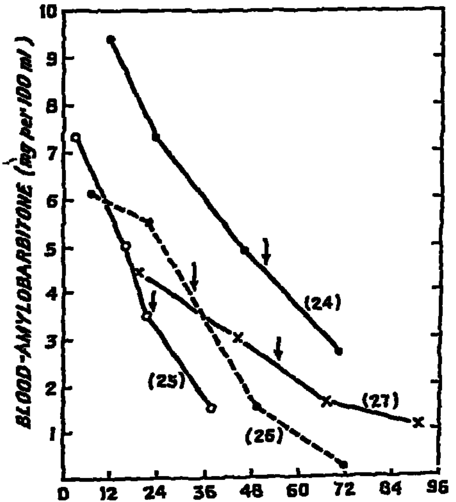

Fig 3—Fall in blood-levels of 4 cases of amylobarbitone poisoning The figures in parentheses indicate the case number, and the arrows the time at which consciousness was regained

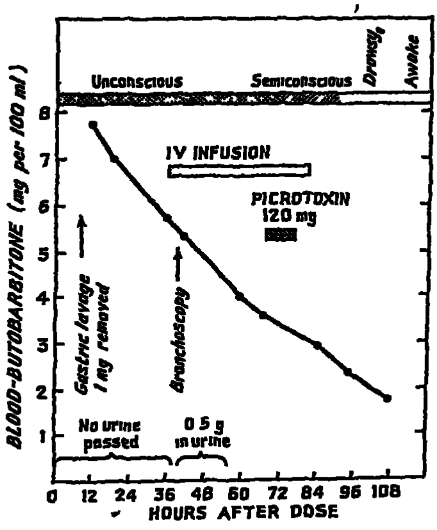

Fig 4—Progress of a typical case of barbiturate poisoning (case 20, butobarbitone)

Discussion

The reaction of barbiturates with cobaltous salts (Koppanyi et al 1934) is widely used as a qualitative test in cases of suspected poisoning, but it is relatively insensitive and may not be specific (Riley et al 1940) The test is usually applied to urine or gastric contents These specimens may be unreliable guides to the presence of barbiturate in the body and to the severity of the poisoning and, *furthermore*, are not always available from unconscious patients

Notes and News

HAROLD HILL HEALTH CENTRE

BETWEEN 1948 and 1954 a community of thirty thousand people was created at Harold Hill in Essex as part of the dispersal plan for the population of Greater London This new population brought with it a need for medical care, and a report by the professional committee of the Harold Hill Health Centre describes steps taken to meet it

In the early stages new practices were declared by the executive council and special doctors' houses with attached surgeries were built, but during early 1954 a health centre was completed This centre was originally intended to accommodate four practitioners, either singly or in partnership, as well as the personal health services and dental services provided by the local authority with certain clinics run by the North East Metropolitan Regional Hospital Board

After preliminary discussion with all the doctors who had care of patients on the estate, nine doctors (two in partnership) accepted invitations to lease the general practitioner accommodation, and a rota system was devised whereby each had the use of a suite—waiting room, consulting room, and examination room—for five sessions a week These practitioners share the services of a trained nurse and of the secretarial staff of the centre, and the report notes that, despite acknowledged differences of temperament between the doctors, coöperation has been perfect and no disagreements of importance have arisen during the first year s work

The doctors attending the centre retain their own surgery premises, but are provided with filing cabinets for the medical records of those patients who attend regularly at the centre Attendances at the centre have hitherto been smaller than those at the doctors' own surgeries but greater familiarity with the centre may reverse this. The centre will certainly play an increasing part in health education in the locality, for it is designed for a waiting room and an adjacent clinic room to be thrown together as a lecture hall Patients attending the centre will see their own doctor working side by side with clinic medical officers, while contact between the doctors and nursing staff is encouraged by a shared staff room This direct contact must surely improve the standard of health care in the community and it should encourage direct case work by the practitioner/health-visitor team In this respect it is an advantage that more practices than the four originally intended are brought into close touch with the local health authority

A SURGICAL CAUTERY

Mr J E Richardson, of the London Hospital, informs us that he has had good results with a variety of cautery originally made to the specifications of Mr W Calvert, M R C O G, and now manufactured in this country, with blades of various shapes and weights He has used it to cut stomach and small and large intestine, and finds that with practice the heat can be adjusted to cut down to the blood-vessels, which can then be dealt with individually It operates on approximately 12 volts (A C or D C) by means of a miniature element situated at the end of the shaft As the heating element is totally enclosed there is no risk of fire or accidental burning

The Oryx-Calvert' cautery is made by Oryx Electrical Laboratories at Brighton and is distributed by Antex, 3 Tower Hill London E C 3

University of Manchester

On March 23, at 5 P M , Lady Violet Bonham Carter, D B.E , will give the Lloyd Roberts lecture Her subject will be Of Human Greatness

University of Glasgow

On Jan 14 the following degrees were conferred .

M D—Thomas Jack A C Kennedy (with high commendation) J A Ritchie P M Shepherd (with commendation) D M Kissen (with honours), A J M Campbell * James Carswell

Ch.M—L S Scott (with commendation)

Ph D—J S Gillespie Ann B McNaught

M B Ch B—Ian Airlie W D Balfour T J Coady, B H G Collie Charles Diamond Emmanuel Doc Doosey H P Doig G R Dow Nathaniel Fell Max Gold R D Gray, W S Livingston J E Lunn A W McCracken C D McCusker J W McIntosh, N D MacRor e J M Martin, J P Mellon Margaret Montgomery, J L Morrison Jean B Owens Christine Pattie A J Peters, A R Robertson D S Ross J H Smith J H Stewart R M Todd J C Waugh

* In absentia

University of Bristol

The dissertation of Dr Suzanne Clarke for the degree of M D has been approved

Royal College of Surgeons of England

A meeting of the council held on Jan 12, with Sir Harry Platt, the president in the chair The fellowship was granted to Vasudevrao Govindrao Diwanker and the membership to J D Atwell Diplomas were also awarded jointly with the Royal College of Physicians, to the following

D L O—I A F Bouloux Philip Cole E I P Ebosie Kamalakar Chintaman Gadre Israr Hasan Jafri David Lyen C L T McClintock Achyutananda Sinha Patricia Tellesson T J Thwaite G C W M Wallis Percy Winston

D Path—E G Gordon C K Heffernan J G Hoult R C Jennings H W MacIntyre S O Waller H J Woodliff

D P M—R M Bowman R F Caddell Daphne C Collins P J Crowley T F Grant W O Heffernan J M Hughes F D Kelsey W M M Lyon B F MacCarthy Austin McCawley John McConnell Balbir Singh Manocha Margaret F Morgan Jagatbandhu Mukerjee Dayanand Naidoo, H M Park H S Paull J D Pollitt A B Samaraweera Tisse Appuhamilage Chandrapala Siriwardena J M A C Stewart J D Sullivan P G Woolf

D T M & H—Abul Khayer Muhammad Nawab Ali J M Bolton W F Clifford H S Moore Kersasp Rustomji Patel A M Robertson Mohammad Shafi Mansoor Moulabukhsh Soomro Somrouy Tongsopit

D M R D—Ajit Kumar Bhattacharyya J H G Brodribb T W Cowie Sumant Gaurishanker Daftary Bimal Kumar Dey R F Eban Kathleen A Elliott K T Evans L A Gillanders John Hamill I A B Harrison R G Hirons P J Hurley James Kalokerinos Fun Yong Khoo H E Knowles R F C McDowell B D McKee F A F Mackenzie W F, Magnus J P Murray P N Newsam W J Payne S W Shellshear J N Sidhva Sybil S Stein H I J Van Heerden L R Whittaker M J Wright

D A—D H Alltree Frances J Baker John Barker Bhagwan D Belani M H Berk P H Beves G J Bigley Cecil Bishop C G Blakeley D E Borg I M Brown Margaret E Burns C M Campbell Mary D Campbell Antonio Canellas Maurice Chait Paritosh Chaudhuri D I Chisholm G E Chorley A J Cilliers Gordon Clarke Mary J Clifford W H Cochrane, P A Coldrey Patrick Coleman Barbara P Coppen Elizabeth P Cracroft T J Crowley Ouida M S d Abreu S H Dallas T D W Davies E J Delaney M J Diamond J C Dick Mary A Elsdale Ellie Eting N H Eve Nancy L Ferguson Isabel M Forster Denise I Foulkes, Henry Frank Katharine M R Franklin A S Gardiner Jean O Gerrard Rustum Yusuf Gool J L Hadley, M H Heyns J M Hiddleston K B Holloway Agnes C Howie Ruth R Irvine, Mervyn Jeffries Christina M Jones J D Kelly J H Kerr Louis Khan Pamela D Kilner R S Lamble Laurence Langdon Herring Veronica R E Lethbridge Mendel Levitt I A Levy R B Lewis D T Lovell D F Lunn T M McAneny Rhoda G McCall John MacDermott I R McDonald Shirley M McLean D A H McNaught W M Martin W D Meldrum J F Meynell Marguerite Midgley Peter Milne, T N Munro A L Nathan Joan M Newton Anne Nunan, J G O Mahony Pamela M Ordish Sidney Owitz Olive J Paine G R C Palmer Frida M E Parker Odile M E P Plantevin Venugopal Ramachandra K W Robinson R A Rollison G M Ross Gwyn Rowlands Isobel B A Shivas, Louis Shubitz Bijoy Kumar Sil J L Simcock Radha Sitaram, P C Smart S E Smith Vivian Stanhill W G Staples C J Stephens Helen L S Tennent Jack Walker, R S Walsh R A J Williams F R H Wrigley N L Wulfsohn W G Wurth M B Yorston

Medical Research Council

The council invite applications for the following fellowships for 1956–57

Rockefeller Travelling Fellowships—These fellowships are intended for graduates resident in this country who have had some training in research work in clinical medicine or surgery or in some other branch of medical science and who are likely to profit by a period of work at a centre in the United States or elsewhere abroad before taking up positions for higher teaching or research in the United Kingdom Fellowships tenable in the United States will normally carry a maintenance allowance at the rate of $2700 per annum for a single fellow and $3900 per annum for a married fellow Provision will also be made for travelling and other approved expenses

Eli Lilly and Lederle Travelling Fellowships—These fellowships tenable in the United States are offered on terms and conditions similar to those attaching to the Rockefeller fellowships

Dorothy Temple Cross Fellowships in Tuberculosis—These fellowships offer special opportunities for study or research to British doctors who intend ' to devote themselves to the advancement by teaching or research of curative or preventive treatment of tuberculosis The Fellowships will as a rule be awarded to candidates who wish to make their studies or inquiries elsewhere than in the United Kingdom They provide for the payment of a maintenance allowance at the rate of £650 per annum for a single fellow and £900 per annum for a married fellow An allowance will be made for travelling and other approved expenses

Alexander Pigott Wernher Fellowships in Ophthalmology and Otology—These fellowships are intended for doctors who are likely to profit by a period of work in ophthalmology or otology at a centre abroad before taking up positions for higher teaching and research in these branches of medical science The awards will normally be tenable for one year The fellowships provide for the payment of a maintenance allowance at the rate of £650 per annum for a single fellow or £900 per annum for a married fellow An allowance will be made for travelling and other approved expenses

Forms of application may be had from the secretary of the council, 38, Old Queen Street, London, S W 1, with whom applications must be lodged by March 15 (March 31 for the Pigott Wernher fellowships)

Determinations of barbiturate in tissues reported by other workers (Andrew and Neubauer 1947, Goldbaum 1948, Copeman 1954, Wright 1954) and in this paper are poor indications of the severity of the poisoning It is noteworthy, however, that the stomach and intestines of fatal cases often contain large amounts of barbiturate, and that this may indicate a rapidly rising blood-level at the time of death

Summary

The value of the determination of blood-barbiturate levels in cases of acute poisoning has been shown Qualitative tests for barbiturate in urine and gastric contents may be misleading

The levels of barbiturate in blood and other materials have been determined in 36 cases of acute poisoning Patients returned to consciousness with blood-levels of 5–9 mg per 100 ml of long acting, 1 7–4 2 mg per 100 ml of intermediate, and 1–2 mg per 100 ml of short-acting barbiturates Useful predictions of the time of return to consciousness can often be made

Picrotoxin therapy appeared to result in an earlier return to consciousness in some patients

The difference in blood-levels of patients on medicinal doses of barbiturates, and of those with acute poisoning, is discussed

Analyses of necropsy material from 10 persons found dead after ingestion of barbiturates are reported, and fatal blood-levels are discussed

We thank Dr A M Cooke, Dr F G Hobson, Dr P C Mallam, and Prof L J Witts for permission to study their patients and for access to case notes

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"People have known for a long time that food sometimes goes bad, and that *children sometimes go wrong*, but, whereas they found out long ago that the way to keep the food sweet is to keep it in a cool place, they still entertain the most varied and often unsuccessful *ideas about how to* keep the children straight Bacteriology can now explain fairly exactly what happens when food goes bad, while psychology can tell us only a little about some of the things which can happen to make children go wrong, but that little is of immense value, because it is much harder to guess or find out what to do about the children than what to do about the food, and psychology has in fact disclosed errors in the care of children far more gross than anyone was making in the care of food But this knowledge is much harder to apply Engineers can make us a machine which will dispense coolness in the larder but no one will ever make us a machine which will dispense love and security in the home We have to do that for ourselves"—SIR GEOFFREY VICKERS, V C, *Listener*, *Jan 12, 1956, p 44*

ADRENALECTOMY AND THE METABOL RESPONSE TO INJURY

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THE normal complex metabolic response to injury modified by removal of the adrenal glands, but t administration of cortisone enables the totally adrenale tomised or hypophysectomised patient to react to inju with a metabolic response which in some respe resembles that of a healthy person with intact adren and hypophysis

In a patient maintained on a constant daily dose cortisone 200 mg after removal of the second adren gland Robson et al (1955) found increased urina excretion of nitrogen and potassium and decreas urinary excretion of sodium, as in postoperative patien with intact adrenal glands (Wilkinson et al 1949, 195 and concluded that this response was not due to increas secretion by the adrenal cortex

Mason (1955) found that patients undergoing tot hypophysectomy or adrenalectomy and maintained wi a constant daily dose of 80 mg of either corticotroph or cortisone also exhibited a similar metabolic respon to that found in postoperative patients with inta adrenals He concluded that the postoperative metabol changes do not depend solely on adrenal cortical activit

Neither of these reports includes a study of anoth operation preceding that of total adrenalectomy in th same patient Therefore I report here, in a patient wi recurrent carcinoma, the metabolic response followi bilateral ovariotomy and removal of one adrenal glan and, later, the removal of the remaining adrenal glan

Methods

Urine was collected in six hour specimens, urinar sodium and potassium levels were measured with a flam photometer, and nitrogen by the micro kjeldahl metho No attempt was made to maintain a constant intake o sodium or of potassium, the free consumption by th *patient of food* and *drink* was *recorded*, and the sodium potassium, and nitrogen contents were then calculate from the tables of McCance and Widdowson (1946) Fæces were not analysed The data for sodium potassium, and nitrogen are shown in the accompanyin *figure according to the method of* Reifenstein et al (1945) Intake is plotted down from the base line and output is then plotted up from the intake line Th area above the base line represents excess of output ove intake (negative balance), a clear area below the base line indicates an excess of intake over output (positive balance)

Case-report

In 1946 a married woman, aged 53, developed a left mam mary carcinoma, which was treated by radical mastectomy Her chest wall and axilla were subsequently treated wit X rays in February, 1947, and again in July, 1947, after nodule had appeared in the operation site She remained wel until 1952, when she noticed in the operation site anothe swelling, which in June, 1953, was treated by further radio therapy and with testosterone In March, 1954, the skin in *the treated area became* ulcerated and infected

On admission on Sept 6, 1954, her general condition was good, and the ulcer on her chest wall was 3 inches in diamete *and involved the ribs and intercostal* muscles There were no bony or glandular metastases

Operations—Laparotomy, bilateral ovariotomy, and lef adrenalectomy were *done on Sept 10, 1954, and* righ adrenalectomy on Sept 29, 1954

Postoperative course—During and after the first operation there was much fluctuation in *blood pressure*, but after the second operation the blood pressure was much less disturbed Noradrenaline was administered by slow intravenous infusion

THE RESULTS OF VALVOTOMY FOR AORTIC STENOSIS

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THE successful treatment of mitral and pulmonary stenosis inevitably raised the question of valvotomy for aortic stenosis Though the object is the same—to relieve the heart muscle from the strain of working against an obstruction—it presents a more difficult problem to both surgeon and physician

In all three conditions minor degrees of stenosis, though they give clear diagnostic signs, are well tolerated, and functional impairment of the heart and circulation is long in arriving, and may never appear In mitral stenosis, the effect on the pulmonary circulation gives some warning and often a liberal span of time before a critical degree of stenosis threatens the patient's life In uncomplicated pulmonary stenosis and in aortic stenosis, failure of the right and left ventricle respectively may be the first sign of danger and by then the optimum time for surgery has past In pulmonary stenosis the electrocardiogram generally helps to decide the best time for operation (Campbell and Brock 1955), and the pressure gradient across the valve can be measured by cardiac catheterisation

In aortic stenosis, the pressure gradient across the aortic valve is more difficult to obtain We do not yet know the stage at which symptoms justify the risk of operation, nor the significance that should be attached to left ventricular strains as demonstrated by the electrocardiogram Further the valve itself is likely to be calcified, and this makes operation difficult and increases the risk of valvular incompetence after operation Incompetence is not only more likely but also more serious with aortic valve than with the pulmonary valve, because it is subjected to higher pressure Nor can one welcome the approach through the wall of the left ventricle, which at present seems necessary

Our purpose in reporting the results of aortic valvotomy in the first 16 of our patients who were operated on up to December, 1954, is to try to solve some of these problems and to emphasise the difficulty the surgeon faces in treating advanced aortic stenosis Though good results can be obtained the risk of operation and the risk of producing aortic incompetence are both high

Condition of Patients Before Operation

We are here discussing patients with predominant aortic stenosis and not those with mitral stenosis as well In most patients who have had operations for both conditions, the mitral stenosis has been predominant the gradient across the aortic valve (measured at operation) has been less than in the present group with isolated aortic lesions, and the improvement after double valvotomy has been mainly due to relief of the mitral lesion Our predominantly aortic cases presented quite a different problem

As will be seen from table I, 12 of our 16 patients showed a similar clinical picture though the following 4 differ in some features

In case 8 there was more incompetence, with a blood-pressure of 120 70 mm Hg For this reason great hesitation was felt about operation, though it was strongly indicated by the patient's frequent anginal and syncopal attacks and was, in fact, successful for a time

Case 7 had a very large heart and gross congestive failure

Cases 11 and 15 were children with congenital aortic stenosis Operation was advised because of their increasing disability and anginal pain

Most of our patients were men between 40 and 50 years old, and the average age was 46 The onset of symptoms was less than five years before operation in all but 4 cases On the other hand the cardiac murmur had nearly always been noted much earlier, at an average age of 22 None of the patients, except case 8, had any evidence of rheumatic fever or of other valvular disease We need not discuss here whether the stenosis was congenital with secondary atherosclerosis and calcification, or whether these had developed on a valve that was normal in either case they can be distinguished from the obvious rheumatic condition where there is nearly always mitral stenosis and aortic incompetence

All the patients were in normal rhythm All had a high grade of stenosis with little or no incompetence Those with more incompetence were excluded because this indicates that the valve is less completely stenosed and that regurgitation would probably increase if the valve were opened more widely 8 of the 16 had a soft aortic diastolic murmur, but except in case 8 the degree of incompetence was insignificant All had classical signs of aortic stenosis, with a rough systolic murmur and thrill in the aortic area, a strong apical thrust, and a pulse that was slow-rising and generally small It is, however, sometimes difficult to take the

TABLE I—FINDINGS IN PATIENTS WITH AORTIC STENOSIS BEFORE VALVOTOMY

Case no	Sex	Age (yr)			Syncopal attacks	Angina	Heart-failure	Cardiothoracic ratio (%)	Aortic 2nd sound	Aortic diastolic murmur	Degree of calcification of aortic valve (radioscopy)	Blood pressure (mm Hg)	Leads in which T waves were inverted
		When murmur first heard	Onset of serious symptoms	At time of operation									
1	M	27*	57	61	Many	– –	LV	50	Absent	–	– –	105/80	I–III V4–V6
2	M	17*	49	51	Few	–	LV	48	Normal	–	– –	102 67	I II V5 V6
3	M	10	42	48	Some	– –	RV	54	Diminished	–	– –	105/85	I V5 V6
4	M	11	48	50	None	–	RV	53		–	–	102/85	I V5 V6
5	M	32*	38	40	None	– – –	LV	52		–	– –	98/68	I, II, V4–V6
6	M	19	41	43	None	– – – –		53	Absent	–	–	95/70	I II V3–V6
7	M	?	38	46	None	–	RV	66	Diminished	–	– –	100 85	
8	F	20	38	40	Many	– –	LV	45		–	–	120/70	I II V4–V6
9	F	21	40	48	Few	– –	LV	61		–	– –	122/100	I–III V4–V6
10	M	25*	36	38	Few	– –		49	Normal	–	– –	102/77	I II V5 V6
11	M	2	4	6	None	– –		59	Diminished	–	–	95 85	I II, V4–V6
12	M	33	35	40	Few	– –		47	Normal	–	– –	110 80	I–III V5 V6
13	F	1	29	40	Many	– – –		50		–	+	115 90	I–III V3–V6
14	M	23	33	37	Many	– –		51		–	– –	140/100	I–III V5 V6
15	F	4	7	10	Once	– –		55	Diminished	+	–	95 70	I–III V3–V6
16	M	49	49	51	Few	–	LV	50		–	– –	115 85	I V3–V6

* These murmurs were noted while they were in the Army LV = Left ventricular RV = Right ventricular

cortical extract and did not occur in rats maintained with 1% saline solution only

Campbell et al (1953), who also used the urinary excretion of nitrogen as an index of the metabolic response to injury in rats, found that a similar increase in urinary nitrogen followed both fracture of a femur and implantation of cortisone acetate 25 mg, and that a further and similar increase followed both the implantation of cortisone acetate 50 mg and the combination of fracture of a femur with the implantation of cortisone acetate 25 mg In the present patient the second surgical trauma was less severe than the first, but it was expected that this would be amply compensated by the large dosage of cortisone, it is very surprising that after the second operation the nitrogen and potassium in the urine were respectively only half and a quarter as much as after the first operation

Since this patient was very ill with recurrent malignant disease, an important factor in reducing the urinary excretion of nitrogen after the second operation may have been the previous loss of nitrogen due to tissue katabolism after the first operation In addition, the daily intake of dietary protein was low for at least three weeks before the second operation, and it is well recognised that many of these patients are in negative nitrogen balance and depleted of protein, 4 of the 5 patients reported by Mason (1955) were in negative nitrogen balance before operation The reduced potassium loss after the second operation can be related in part to the smaller tissue katabolism indicated by the reduced urinary nitrogen loss

Comparing the metabolic effects of bilateral splanchnicectomy Moore et al (1955) found a smaller urinary nitrogen loss with increased sodium conservation after the second operation than after the first, their patient, however, did not suffer a large loss of sodium after the first operation I made a similar observation after the resuture of a disrupted laparotomy wound Moore et al suggested that the difference in response after the second operation might be a continuing effect of the first operation, and they discounted any likelihood that it might be due to adrenal "exhaustion" or insufficiency In the present patient the apparently abnormal response to the second operation may be the normal result of a second operation *after a short interval* and thus evidence of the success of cortisone as a substitute for the whole adrenal

After the second operation water loading by the intravenous infusion of 5% glucose solution was followed by diuresis Gaunt et al (1949) found that there was an increased reabsorption of water by the renal tubules after adrenalectomy and a diminished diuretic response to a water load Mirsky et al (1954) showed, however, that the increased antidiuretic activity of the plasma in adrenalectomised rats, maintained on 1% sodium-chloride solution, was abolished by the administration of cortisone The antidiuretic effect of adrenalectomy seems to have been similarly diminished in the present patient by the administration of large doses of cortisone Later, after the second operation, when the dose of cortisone was reduced there was a tendency to retain water, and it seems more likely that this was due to increased antidiuretic activity than to sodium conservation, since, because of the low daily intake of sodium, only a little sodium was retained in the body

Llaurado (1954) concluded that a "sodium retaining" and "potassium excreting" factor is excreted in the urine immediately after operation, concomitantly with a large loss of potassium and inversion of the urinary sodium potassium ratio Although he did not isolate aldosterone from urine after operation he suggests that aldosterone is the electrolyte controlling substance, and that an increased production of aldosterone is part of the normal endocrinological response to injury Evidence from only one patient must be viewed with the greate caution, yet the intense conservation of sodium afte adrenalectomy with large maintenance doses of cortisone suggests that either large doses of cortisone may have powerful sodium retaining activity or aldosterone may be produced elsewhere than in the adrenals Further comparison between the two stages of bilateral ovariotomy and bilateral adrenalectomy, with varied dosage of cortisone after the removal of the second adrenal, and with similar doses of cortisone after both operations, i clearly desirable and is being undertaken

Summary

The metabolic responses of a woman with recurrent carcinoma of the breast to bilateral ovariotomy and removal of one adrenal and to the removal of the remaining adrenal, although basically similar, showed large differences in degree

The urinary nitrogen and potassium were respectively only half and a quarter as great after the second as after the first operation, but sodium conservation was more complete and prolonged after the second operation

After adrenalectomy cortisone restores the ability to respond by diuresis to a large water load

These results indicate a need for caution in the interpretation of metabolic studies after adrenalectomy

I am indebted to Sister Duguid and her staff for the collection of the urine and measurement of food and fluid intakes, and to Miss Edna Simpson and Mr Gordon Shewan for their assistance in the analysis of the urines

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ACUTE TUBULAR NECROSIS OF THE KIDNEY FOLLOWING ABORTION

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Abortion procured by intra uterine douching with soapy water is one of the common causes of acute tubular necrosis of the kidney The factors bringing this about may be severe shock, infection (particularly with *Clostridium welchii*), and the circulation and renal excretion of heme pigments formed by hæmolysis The following 13 cases of abortion anuria were seen at the Hammersmith Hospital between 1947 and 1952, when we were studying anuria (Bull et al 1949, 1950)

7 of the patients admitted that intra uterine douching had been carried out either by themselves or by other persons 1 patient had had a therapeutic abortion in a nursing home by

she has been free from cardiac asthma and syncopal attacks for eighteen months, but she now has a significant degree of aortic incompetence

Case 10 —This man, aged 38, had led an active life and played tennis until two years previously, when, after running 200 yards for a bus, he collapsed and became unconscious He began having angina on hurrying and unless he stopped he soon lost consciousness during the next year the attacks of angina became more severe and frequent

At aortic valvotomy, the valve was split freely, and the pressure gradient was reduced from 94 to 59 mm Hg A year later he was able to do as much as before his collapse three years previously, he had no anginal pain or any suspicion of loss of consciousness He still showed inversion of the T wave in leads V5 and V6, as before operation

Case 11 —A boy, aged 6, with congenital aortic stenosis, had always been short of breath, but from the age of 4, when he could walk a mile easily, he became worse and developed anginal pain which was severe if he ran for 20 yards His heart was getting larger the cardiothoracic ratio in 1950 was 52%, but in 1953 it was 59%

At aortic valvotomy, the valve was felt to split widely with the expanding dilator and the pressure gradient fell from 128 to 12 mm Hg A year later he was able to run about with other boys There was less left ventricular preponderance and the T wave inversion had disappeared from leads I, II, and V4 and was much less in leads V5 and V6 There was now a soft aortic diastolic murmur, his blood pressure was 110/65, and his heart was no smaller

PATIENTS WHO WERE IMPROVED

5 patients gained some relief from the operation, but less than those classed as good results Case 1 has been described Case 6 had led a very active life including whaling in the Antarctic, but for two years he had been disabled by anginal pain He was somewhat better for the year after operation, but he died suddenly after severe anginal pain and a sharp fall of blood pressure Case 2 still has angina and dyspnœa on exertion, but he has had no syncope since operation three years ago and has been able to work which was not possible before None of the 3 patients showed any great change in the pressure gradient across their aortic valves after operation

Cases 13 and 16, on the other hand had moderate reductions in their systolic gradients the first has not improved as much as was hoped, probably because aortic incompetence has developed, while the second, though he is relieved of symptoms and is back at work, has an aneurysm of his left ventricle

PATIENTS WHO HAVE DIED

3 patients died at or soon after operation, and 3 some weeks or months later without much improvement The first 3 (cases 3, 4, and 5) were all men, aged 40–50, with the usual picture that has been described In case 4 the pressure gradient was reduced from 102 to 60 mm Hg but in the other 2 there was little change Cases 3 and 4 have been reported by Campbell and Kauntze (1953) as their cases 32 and 37 in the former the valve was bicuspid but in the latter it was tricuspid, and in both there was heavy calcification, there was no evidence of rheumatic disease of the other valves Case 5 had gross calcification of his aortic valve

The other 3 developed free aortic incompetence and this seemed the main reason for their deaths All 3 showed a good drop in the pressure gradient across the aortic valve at operation (table II)

Case 12 died four months after operation with left ventricular failure, there was a fracture across the calcified part of the aortic valve and the fibrous element was split, the mitral ring was dilated but there was no rheumatic disease

Case 14 developed free aortic incompetence and died four months after operation with right and left ventricular failure At necropsy the right posterior aortic cusp was found to be split obliquely, the mitral valve was healthy

Case 15 —This girl with congenital aortic stenosis had a large heart (cardiothoracic ratio 55%) and a slight incompetence when she was 7 years old Three years later she became more breathless and had anginal pain on walking uphill or into the wind, and two more alarming attacks led to all her activity at school being stopped At aortic valvotomy, the pressure gradient across the valve was almost abolished, but severe aortic incompetence and cardiac asthma developed and she died suddenly two weeks later

DISCUSSION

Some of the problems of valvotomy for aortic stenosis were first discussed by Smithy and Parker (1947) and by Brock (1950) Bailey et al (1952) emphasised the danger of regurgitation after incision of the valve and Larzelere and Bailey (1953) thought that good results were more likely in rheumatic than in congenital and atherosclerotic stenosis Later Bailey et al (1954) reported valvotomy in 62 patients, of whom 27 had aortic valve disease only In this group the operative mortality was 22%, and though many of the survivors were said to be better, it is not easy to know how much they were improved or how advanced the condition was before operation

Muller et al (1954), reporting the results in 16 cases of pure aortic stenosis (13 with calcification), thought that only half the patients were improved there were 2 deaths Logan and Turner (1954) held that surgical treatment should be advised before symptoms became severe their 9 rheumatic cases were somewhat similar to ours but 4 had coexisting mitral stenosis only 1 of these patients died and the others were said to be improved

Marquis and Logan (1955) reported the results of operation in 6 patients with congenital aortic valvular stenosis None died and most of them were improved, but 4 developed aortic incompetence In retrospect, Marquis and Logan thought it would have been wiser to postpone surgery in 3 of the 6 cases, but the immediate prognosis in the other 3 was bad enough to justify the risk of even severe aortic incompetence They concluded that progressive left ventricular strain or increasing heart size in growing children were indications for valvotomy

Many of these papers report a mortality rate that is not unduly high but they emphasise the risk of producing aortic incompetence In our experience, neither of these risks is serious with combined mitral and aortic stenosis but both are serious in older patients with pure aortic disease—whether they have trivial incompetence or not—probably because of calcification If one decides that this risk cannot justifiably be taken until a late stage, the surgeon is given a difficult problem and one must expect a high mortality

The decision is hard to make, because most patients do well for so many years that any great risk does not seem justified When deterioration starts, the time before death is often short, and the patient is gravely ill For example, 3 of our patients died (1 suddenly and 2 with heart failure) after a decision to operate had been reached

The poor prognosis and short duration of life after the onset of severe symptoms are well recognised (Kumpe and Bean 1948, Lewes 1951, Bergeron et al 1954, Mitchell et al 1954) Matthews et al (1955) estimate the period between the onset of severe symptoms and death at only one or two years compared with five to ten years in mitral stenosis

Our results after valvotomy for pure aortic stenosis are much less satisfactory than those for mitral stenosis and for pulmonary stenosis The 5 good results show that success can be achieved and emphasise the importance of the mechanical obstruction, but the 6 deaths (3 at the time of operation and 3 later) show the difficulties, even among those patients who were improved, 3 died within two years

One difficulty is that the deformity of the valve by calcification makes it hard to avoid producing aortic cortical extract and did not occur in rats maintained with 1% saline solution only

Campbell et al (1953), who also used the urinary excretion of nitrogen as an index of the metabolic response to injury in rats, found that a similar increase in urinary nitrogen followed both fracture of a femur and implantation of cortisone acetate 25 mg, and that a further and similar increase followed both the implantation of cortisone acetate 50 mg and the combination of fracture of a femur with the implantation of cortisone acetate 25 mg In the present patient the second surgical trauma was less severe than the first, but it was expected that this would be amply compensated by the large dosage of cortisone, it is very surprising that after the second operation the nitrogen and potassium in the urine were respectively only half and a quarter as much as after the first operation

Since this patient was very ill with recurrent malignant disease, an important factor in reducing the urinary excretion of nitrogen after the second operation may have been the previous loss of nitrogen due to tissue katabolism after the first operation In addition, the daily intake of dietary protein was low for at least three weeks before the second operation, and it is well recognised that many of these patients are in negative nitrogen balance and depleted of protein, 4 of the 5 patients reported by Mason (1955) were in negative nitrogen balance before operation The reduced potassium loss after the second operation can be related in part to the smaller tissue katabolism indicated by the reduced urinary nitrogen loss

Comparing the metabolic effects of bilateral splanchnicectomy Moore et al (1955) found a smaller urinary nitrogen loss with increased sodium conservation after the second operation than after the first, their patient, however, did not suffer a large loss of sodium after the first operation I made a similar observation after the resuture of a disrupted laparotomy wound Moore et al suggested that the difference in response after the second operation might be a continuing effect of the first operation, and they discounted any likelihood that it might be due to adrenal "exhaustion" or insufficiency In the present patient the apparently abnormal response to the second operation may be the normal result of a second operation after a short interval and thus evidence of the success of cortisone as a substitute for the whole adrenal

After the second operation water loading by the intravenous infusion of 5% glucose solution was followed by diuresis Gaunt et al (1949) found that there was an increased reabsorption of water by the renal tubules after adrenalectomy and a diminished diuretic response to a water load Mirsky et al (1954) showed, however, that the increased antidiuretic activity of the plasma in adrenalectomised rats, maintained on 1% sodium chloride solution, was abolished by the administration of cortisone The antidiuretic effect of adrenalectomy seems to have been similarly diminished in the present patient by the administration of large doses of cortisone Later, after the second operation, when the dose of cortisone was reduced there was a tendency to retain water, and it seems more likely that this was due to increased antidiuretic activity than to sodium conservation, since, because of the low daily intake of sodium, only a little sodium was retained in the body

Llaurado (1954) concluded that a "sodium-retaining" and "potassium excreting" factor is excreted in the urine immediately after operation, concomitantly with a large loss of potassium and inversion of the urinary sodium potassium ratio Although he did not isolate aldosterone from urine after operation he suggests that aldosterone is the electrolyte controlling substance, and that an increased production of aldosterone is part of the normal endocrinological response to injury Evidence from only one patient must be viewed with the greate caution, yet the intense conservation of sodium after adrenalectomy with large maintenance doses of cortisone suggests that either large doses of cortisone may have powerful sodium retaining activity or aldosterone may be produced elsewhere than in the adrenals Further comparison between the two stages of bilateral ovariotomy and bilateral adrenalectomy, with varied dosage of cortisone after the removal of the second adrenal, and with similar doses of cortisone after both operations, i clearly desirable and is being undertaken

Summary

The metabolic responses of a woman with recurrent carcinoma of the breast to bilateral ovariotomy and removal of one adrenal and to the removal of the remaining adrenal, although basically similar, showed large differences in degree

The urinary nitrogen and potassium were respectively only half and a quarter as great after the second as after the first operation, but sodium conservation was more complete and prolonged after the second operation

After adrenalectomy cortisone restores the ability to respond by diuresis to a large water load

These results indicate a need for caution in the interpretation of metabolic studies after adrenalectomy

I am indebted to Sister Duguid and her staff for the collection of the urine and measurement of food and fluid intakes, and to Miss Edna Simpson and Mr Gordon Shewan for their assistance in the analysis of the urines

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ACUTE TUBULAR NECROSIS OF THE KIDNEY FOLLOWING ABORTION

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Abortion procured by intra uterine douching with soapy water is one of the common causes of acute tubular necrosis of the kidney The factors bringing this about may be severe shock, infection (particularly with *Clostridium welchii*), and the circulation and renal excretion of heme pigments formed by hæmolysis The following 13 cases of abortion anuria were seen at the Hammersmith Hospital between 1947 and 1952, when we were studying anuria (Bull et al 1949, 1950)

7 of the patients admitted that intra uterine douching had been carried out either by themselves or by other persons 1 patient had had a therapeutic abortion in a nursing home by

In children with congenital aortic stenosis, valvotomy should be considered when they have anginal pain or syncope on exertion, when left ventricular strain is increasing, or when the heart is enlarging

In adults with isolated aortic stenosis, increasingly severe symptoms are indications for valvotomy before there is heart failure or irreversible fibrosis of the heart muscle The chance of success is greater if the valve is not calcified, but this is unusual

We are greatly indebted to Sir Russell Brock, without whose help this paper would not have been possible We should like to thank Dr R J Shephard, Dr P R Fleming, and Dr L Brotmacher for the measurements of ventricular and aortic pressures during operations

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ACUTE MASTITIS

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Two kinds of acute mastitis associated with pregnancy and lactation are well recognised, the superficial and the intramammary (Waller 1938, Romanis and Mitchiner 1952), but their essential differences are often not appreciated

Superficial mastitis is here viewed as either a staphylococcal infection of the skin or a Montgomery tubercle which penetrates into the breast Intramammary mastitis, even when declared by an accompanying rigor, is believed to be non-infective at first, although staphylococcal infection may soon supervene Both kinds of mastitis are common, painful, and largely preventable

Incidence

The incidence of mastitis has been as high as 8 91% in the mothers giving birth in an area where the condition was notifiable (Fulton 1945), 7 0% in mothers delivered in hospital among a representative sample of Britain (Douglas 1950), and 2 6% in Newcastle upon Tyne (Spence et al 1954)

Ætiology

Two main views are held about their cause Waller (1938) emphasised the importance of sore nipple, and Macpherson (1943), Walsh (1949), and Czermac (1952) drew attention to the prime importance of stagnation and retention of milk The figures published by Blaikley et al (1953), though small, confirm the belief that the incidence can be reduced by antenatal and puerperal care

Present Investigation

The courses of the two diseases and the conditions associated with them in 129 cases seen in the two years from September, 1951, to September, 1953, were analysed and contrasted All the cases were in women delivered by the staff of University College Hospital and include all those which we treated, or of which we heard, in pregnancy or during or after lactation

The term mastitis is used here to describe not only frank cases but also the very least conditions which, for reasons given below, are held to be incipient mastitis There were 25 cases of superficial mastitis and 109 of intramammary, 5 patients had both types at some time In the two years there were 2701 deliveries under the care of the hospital Although the patients seen were not necessarily delivered in this period, the rates of incidence may be taken as 4 2% for intramammary mastitis and 1 0% for superficial mastitis, and the incidence of intramammary abscess was 1 1% In six months in 1955 the rates were superficial mastitis 1 0% and intramammary mastitis 0 9%, and there have been 1 intramammary abscess in pregnancy and 1 in lactation in 717 cases (2 1%)

SUPERFICIAL MASTITIS

Superficial mastitis could be seen to have begun, in all the patients coming early for treatment, either as an infected Montgomery tubercle or else as a spot on the areola or on the skin close to it As it progressed, a lump formed which was found to consist of pus, however early it was incised

The early course of the mastitis was slow, and those patients who came later for treatment could seldom say definitely when the inflammation had begun This slow early pace suggests that the causes should be sought in the preceding days rather than in the days of onset No patient in this series was seen to have superficial mastitis in the first ten days after delivery, but the frequency with which it arose in the next ten days after leaving hospital suggested that the cause lay in the earlier period

Those patients who came when the mastitis was established complained either of pain or of a lump Only 1 had pyrexia in the course of the illness, and her temperature only rose as she developed a superimposed intramammary mastitis (fig 1) Except in 4 patients whose lesion was seen before the indurated lump was as large as a pea, improvement did not last if the pus was not discharged either spontaneously or through an incision Unopened abscesses tended to track behind the nipple, and pus escaped out of the nipple of 1 patient Apart from this case, where mechanical difficulty prevented suckling and there was the risk that the baby might

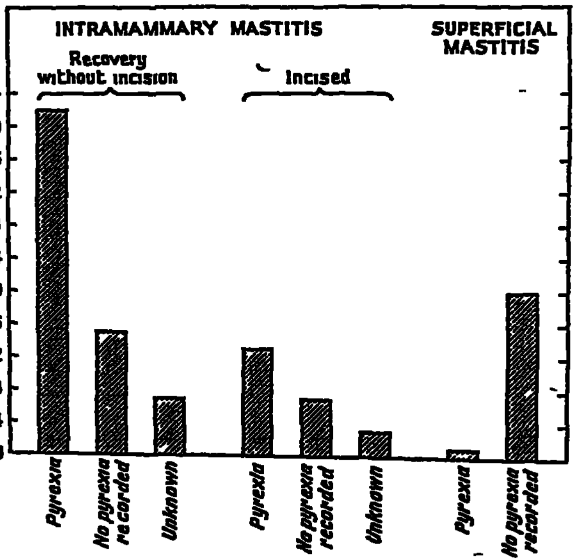


Fig 1—Pyrexia in intramammary mastitis does not mean pus, pyæmia, or poor prognosis

DURATION OF OLIGURIA AND DAY OF ONSET OF DIURESIS

Case no	Oliguria * (days)	Diuresis † (day)	Blood urea		Outcome
			Highest level (mg per 100 ml)	Day of illness	
1	?	?	514	14	Recovered
2	12	14	400	12	Died
3	12	15	299	10	Recovered
4	13	18	482	18	
5	10		520	10	Died
6	20	24	508	22	Recovered
7	13	15	364	14	
8	?	9	396	8	Died
9	?		672	26	
10	9	12	340	14	Recovered
11	11	15	384	18	
12	10	12	?		
13	15		560	17	Died

* Urinary output of less than 300 ml per day
† Urinary output of 1 litre or more per day

out by the insertion into the cervix of a commercial preparation containing medicated soap Severe abdominal pain and shock developed, and subsequently oliguria and signs of pelvic peritonitis The *intragastric drip feeding régime was instituted* No laboratory data were obtained The pelvic peritonitis was controlled by large doses of antibiotics, and she made a good recovery During convalescence mild right sided uveitis developed which responded to cortisone

Case 13 —A woman, aged 26, gave herself an intra-uterine douche of soapy water on Dec 3, 1948 This was followed by vaginal bleeding, vomiting, and oliguria She was admitted to hospital on Dec 12, and her uterus was evacuated the next day

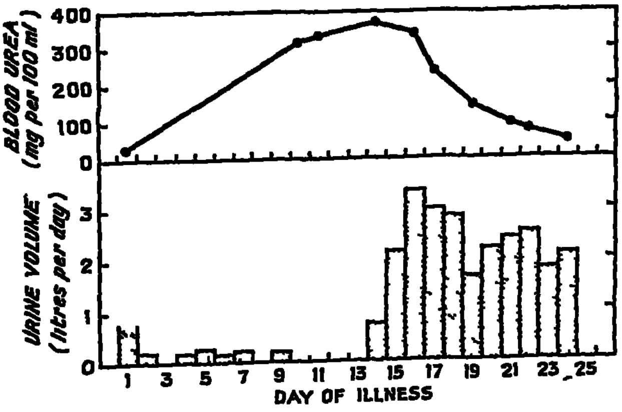
Treatment and progress —Initially she was treated by large amounts of intravenous fluids and by lumbar splanchnic blocks She then showed signs of fluid overloading and uræmia, and intragastric drip feeding was begun on Dec 14 We saw her on Dec 16 when diuresis was starting, the urinary output on Dec 18 was 500 ml Pulmonary œdema supervened, and she died on Dec 19

Necropsy showed acute tubular necrosis

Discussion

Early Treatment

The patient should be admitted to hospital as soon as possible and emergency treatment of shock instituted We saw no patient at the onset of her illness, there were delays varying from a few hours to as much as 14 days before admission to hospital, and there were further delays before the patients were seen by us 4 patients had blood-transfusions on admission for shock, but none had signs of a hæmolytic transfusion reaction Only 1 patient, who did not have a transfusion, had "bloody" urine at the onset of renal failure Several patients were thought to be jaundiced on admission but no supporting laboratory evidence is available In some patients (for example, case 7) shock was severe and prolonged, but in others (cases 1 and 6) renal failure developed insidiously, and there were delays of several days before their admission to hospital



Blood urea level and urine volume in case 7

Infection

Infection of the genital tract, peritonitis, and septicæmia are considerable hazards and may require careful treatment, particularly with antibiotics 2 patients had severe infections, these possibly influenced the development of renal failure

Case 5 had septicæmia due to *Cl welchii* which was controlled by penicillin and sulphathiazole When seen by us on the 10th day of her illness she showed signs of gross overloading with fluid, she was in coma and died before dialysis could be performed

Case 8 died from a flare up of peritonitis after she had had a diuresis and a fall in her blood-urea level from 396 mg to 80 mg per 100 ml High blood-levels of antibiotics are readily obtained during anuria, because of lack of renal excretion A fall in blood antibiotic level, due to diuresis, may have been responsible for death in this case

Oliguria and Anuria

All patients had anuria or severe oliguria for periods varying from 9 to 20 days and maximal blood-urea levels varying from 299 mg to 672 mg per 100 ml (see accompanying table)

In 5 cases there was necropsy confirmation of acute tubular necrosis, and in the 8 surviving patients the clinical course of the illness and the pattern of renal dysfunction were typical (Bull et al 1950) The accompanying figure shows the fall in the blood urea level after the start of diuresis in a 16 year old girl (case 7) who recovered Some of the other cases have been described previously (Bull et al 1949, 1950)

Until 1949 the emphasis in treatment in our unit was on the removal of waste products from the blood and the correction of electrolyte balance by dialysis with an artificial kidney Cases 2 and 3 had successful dialyses, but case 2 died of pyæmia probably caused by staphylococci introduced during dialysis, these organisms were resistant to the antibiotics then available

Renal Failure

Criminal abortion is a common cause of acute renal failure according to most workers Hamburger (1954), reviewing 100 cases of acute tubular nephropathy, noted that 39 were postabortive Elsewhere abortion seems to have accounted for a smaller proportion of cases of acute renal failure (Swann and Merrill 1953, Brun 1954), but in our experience abortion is as important a cause of renal failure as concealed accidental hæmorrhage of pregnancy, postoperative or traumatic shock, mismatched blood transfusion, or poisoning by mercury, &c

The lesion is probably caused by renal ischæmia brought about by blood loss or the severe pain following uterine douching In addition, the soap solution probably causes intravascular hæmolysis at the placental site, the resulting heme pigments circulate and form casts in the kidney Moreover phenol or another nephrotoxic agent may be incorporated in the douche and make the tubular necrosis worse Quinine used as an abortifacient, and infection with *Cl welchii*, both cause intravascular hæmolysis and shock and possibly renal failure subsequently, but both these causes are rare in our experience

Renal failure should be recognised early by the daily volume, specific gravity, and composition of urine, and the blood chemistry If rational treatment is applied (Bull 1955), renal failure should rarely cause death

2 patients died from water and electrolyte imbalance Case 13 was grossly overloaded with fluid early in the

If the first cause of intramammary mastitis is infection, what is the lump made of? In these cases removal of the secretion rather than the usual defences against bacteria brought cure. In all the cases under observation the secretion obtained by emptying the affected breast, even when the lump disappeared in the process, was milk, not pus. No baby was made ill by continuing to feed from the breast, and this was allowed for the first two days of illness and afterwards, if improvement was steady. There is no doubt that the lump consists of secretion and its containing breast tissue and is so much a part of the mammary gland that it is best palpated by the finger tips rather than the surgical flat of the hand. Although no patient in this series was operated on in what was literally the first flush of mastitis, cases have been seen in which a free incision through the lump has revealed apparently normal tissue.

The records of these cases of mastitis provide two other pieces of information which are obstacles to accepting infection as the cause. The concurrent apparently staphylococcal infection rate of 18%—4 patients with preceding superficial mastitis and 15 others (table I)—is little greater than the average for mother and child in the wards, whereas the rate among the patients with superficial mastitis was 60%. Then there is the remarkable fact that, although in every instance where the mastitis led to an abscess and this was incised the organism was *Staph. pyogenes*, there was not one pyæmic abscess, even though at the outset of the mastitis the patient's temperature had risen sharply to 104°F with a rigor. Either a second organism, never seen, causes the mastitis and, carried round the body, also causes a transient septicæmia, or else the cause of the pyrexia is non-infective. Attempts to find an organism have failed on the five occasions when blood was taken for culture as the temperature rose. The hypothesis of the independence of the pyrexia and infection is supported by the fact that prognosis is unaffected by pyrexia (fig. 1).

The subjective account given by patients during the pyrexia of mastitis is conspicuously like that of one suffering from an incompatible transfusion or from an intravenous dose of pyrogen. Typically the mother considers herself to be well or may already have noticed a slight headache or a tenderness in her breast and then, after emptying her breast by feeding or by artificial means, she suddenly collapses with pyrexia and a rigor. In the present series this happened in 5 patients, all of whom recovered entirely without abscess formation. A subjective account was that the patient "ached all over, down her legs and up her neck, and she felt as if she had been sleeping on boards." This reminds one of the days before the rhesus factor and pyrogens were known, when reactions to transfusions were common and every bottle of blood or of saline solution causing pyrexia was searched, usually in vain, for infection. The concept of bacteria causing pyrexia hindered doctors from thinking of other causes.

I suggest that, in intramammary mastitis, the sequence of events is as follows: retention of milk in a lobule of the gland either from failure to empty or from excess secretion, increased viscosity, or blockage of the duct; high pressure within the captive secretion; attempt at contraction of the myo-epithelial cells when the draught reflex comes into action; and leakage or even rupture of the alveoli or duct, with extravasation of the pent-up secretion. Since the breast is very vascular, the secretion may enter the blood-stream and have a pyrogenic effect comparable to that of cow's milk in humans. As Walsh (1949) has suggested, bacterial infection of extravasated milk and the surrounding tissue may then readily ensue and may also arise in merely pent-up secretion. There is some experimental backing for this hypothesis, for Selye et al. (1934) found that, in rats and mice, if the milk ducts were ligated and suckling maintained, milk was extravasated into the gland. In man the rigor or milder pyrexia usually comes on while the breasts are full or immediately after a feed and not in the two or three hours while the breasts are relatively empty. These are the times most likely to have been preceded by a draught reflex with its transient high intra-alveolar pressure.

Intravenous injection of a patient's own milk was not tried, because of the obvious difficulties not only of distress but of preparing an aseptic unaltered sample of milk. Milk 0.1 ml. given intramuscularly caused no pyrexia. To produce pyrexia where there is retention of milk previous sensitisation is apparently unnecessary, since such reactions were observed, and cured by emptying only, in 5 primiparæ in the first week after delivery. On the other hand, frank mastitis with a painful lump and a flush was seen in 7 cases without any detectable rise in temperature.

One argument in favour of a bacterial origin of mastitis is its common association with sore nipple. This is not convincing, for soreness usually develops when the breast is not taken properly, owing to its poor shape or to faulty posture of either the mother or the baby; these same factors, as Cruickshank (1942) has pointed out, also cause faulty emptying. In addition, soreness may make adequate emptying difficult, and trauma caused by emptying may be followed by mastitis. Furthermore, mastitis is seen where there has been no lesion of the nipple (Macpherson 1943), in pregnancy (2 cases in the present series), and where the baby has not been put to the breast at all. It can arise most unhappily in the breast of a woman given inadequate œstrogens to suppress lactation after a stillbirth.

Reasons have been given for rejecting the hypothesis of bacterial invasion as the first cause of intramammary mastitis. The histories of the patients support the hypothesis of retention. In common with Isbister's (1952) cases, factors or events conducive to faulty emptying were unduly common among the 109 women in whom this form of mastitis developed. There were 130 attacks after delivery. The 30 which developed during the ten-day lying-in period (and therefore under observation) were all associated with one or more of the following conditions: excess secretion with engorgement and much manual expression; sore nipples in breasts with poor protractility; an ill or small baby; physical obstruction to removal of milk (e.g., an adenoma and a scar); fear of giving the breast (in patients with healed pulmonary tuberculosis or with close relations who had had breast abscesses); and puerperal psychosis (2 cases).

Similar causes were found where mastitis arose later in lactation. 8 attacks followed resting sore nipples; 4 arose from physical obstruction; 5 from acute anxiety in the mother; and in 17 patients mastitis developed on twenty-two occasions after interruptions due to family emergencies or cutting down the number or duration of feeds or giving supplementary feeds without regard to the breast secretion. Most of these interruptions were made on medical advice. One patient provided an example of a condition which has been seen outside this series: when the area of retention yielded its milk to the 'Humalactor,' small pearly objects were seen which proved to be agglutinates of colostrum bodies and may have caused obstruction. Their origin is unknown, but in vitro colostrum bodies agglutinate on cooling.

Failure to keep the breasts emptied during weaning preceded fourteen attacks of mastitis: 4 patients did not attempt to empty the breast at all after starting a course of œstrogens; 5 were given inadequate doses of œstrogens; and 5 just ceased to put the baby to the breast and sought no help, for fear of having to continue feeding. This reckoning of precipitating causes leaves 29 cases with no clear cause; included in their number are some patients who seem either to have a predisposition or

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2	12	14	400	12	Died
3	11	15	299	19	Recovered
4	13	18	482	18	
5	10		520	10	Died
6	20	24	508	22	Recovered
7	13	15	364	14	
8	?	9	396	8	Died
9	?		672	26	
10	9	12	340	14	Recovered
11	11	15	384	18	
12	10	12	?		
13	15		500	17	Died

* Urinary output of less than 300 ml per day
† Urinary output of 1 litre or more per day

out by the insertion into the cervix of a commercial preparation containing medicated soap Severe abdominal pain and shock developed; and subsequently oliguria and signs of pelvic peritonitis The intragastric drip feeding regime was instituted No laboratory data were obtained The pelvic peritonitis was controlled by large doses of antibiotics, and she made a good recovery During convalescence mild right sided uveitis developed which responded to cortisone

Case 13 —A woman, aged 26, gave herself an intra-uterine douche of soapy water on Dec 3, 1948 This was followed by vaginal bleeding, vomiting, and oliguria She was admitted to hospital on Dec 12, and her uterus was evacuated the next day

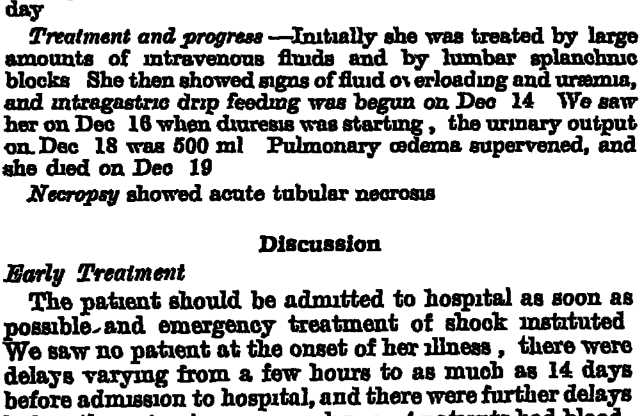
Treatment and progress —Initially she was treated by large amounts of intravenous fluids and by lumbar splanchnic blocks She then showed signs of fluid overloading and uræmia, and intragastric drip feeding was begun on Dec 14 We saw her on Dec 16 when diuresis was starting, the urinary output on Dec 18 was 500 ml Pulmonary œdema supervened, and she died on Dec 19

Necropsy showed acute tubular necrosis

Discussion

Early Treatment

The patient should be admitted to hospital as soon as possible, and emergency treatment of shock instituted We saw no patient at the onset of her illness, there were delays varying from a few hours to as much as 14 days before admission to hospital, and there were further delays before the patients were seen by us 4 patients had blood-transfusions on admission for shock, but none had signs of a hæmolytic transfusion reaction Only 1 patient, who did not have a transfusion, had "bloody" urine at the onset of renal failure Several patients were thought to be jaundiced on admission but no supporting laboratory evidence is available In some patients (for example, case 7) shock was severe and prolonged, but in others (cases 1 and 6) renal failure developed insidiously, and there were delays of several days before their admission to hospital



Blood urea level and urine volume in case 7

Infection

Infection of the genital tract, peritonitis, and septicæmia are considerable hazards and may require careful treatment, particularly with antibiotics 2 patients had severe infections, these possibly influenced the development of renal failure

Case 5 had septicæmia due to *Cl welchii* which was controlled by penicillin and sulphathiazole When seen by us on the 10th day of her illness she showed signs of gross overloading with fluid, she was in coma and died before dialysis could be performed

Case 8 died from a flare-up of peritonitis after she had had a diuresis and a fall in her blood urea level from 396 mg to 80 mg per 100 ml High blood-levels of antibiotics are readily obtained during anuria, because of lack of renal excretion A fall in blood antibiotic level due to diuresis, may have been responsible for death in this case

Oliguria and Anuria

All patients had anuria or severe oliguria for periods varying from 9 to 20 days and maximal blood urea levels varying from 299 mg to 672 mg per 100 ml (see accompanying table)

In 5 cases there was necropsy confirmation of acute tubular necrosis, and in the 8 surviving patients the clinical course of the illness and the pattern of renal dysfunction were typical (Bull et al 1950) The accompanying figure shows the fall in the blood urea level after the start of diuresis in a 16-year-old girl (case 7) who recovered Some of the other cases have been described previously (Bull et al 1949, 1950)

Until 1949 the emphasis in treatment in our unit was on the removal of waste products from the blood and the correction of electrolyte balance by dialysis with an artificial kidney Cases 2 and 3 had successful dialyses, but case 2 died of pyæmia probably caused by staphylococci introduced during dialysis, these organisms were resistant to the antibiotics then available

Renal Failure

Criminal abortion is a common cause of acute renal failure according to most workers Hamburger (1954), reviewing 100 cases of acute tubular nephropathy, noted that 39 were postabortive Elsewhere abortion seems to have accounted for a smaller proportion of cases of acute renal failure (Swann and Merrill 1953, Brun 1954), but in our experience abortion is as important a cause of renal failure as concealed accidental hæmorrhage of pregnancy, postoperative or traumatic shock, mismatched blood transfusion, or poisoning by mercury, &c

The lesion is probably caused by renal ischæmia brought about by blood-loss or the severe pain following uterine douching In addition, the soap solution probably causes intravascular hæmolysis at the placental site, the resulting heme pigments circulate and form casts in the kidney Moreover phenol or another nephrotoxic agent may be incorporated in the douche and make the tubular necrosis worse Quinine used as an abortifacient, and infection with *Cl welchii*, both cause intravascular hæmolysis and shock and possibly renal failure subsequently, but both these causes are rare in our experience

Renal failure should be recognised early by the daily volume, specific gravity, and composition of urine, and the blood chemistry If rational treatment is applied (Bull 1955), renal failure should rarely cause death

2 patients died from water and electrolyte imbalance Case 13 was grossly overloaded with fluid early in the

TABLE III—RESULTS OF ANTIBIOTIC TREATMENT OF INTRAMAMMARY MASTITIS

Antibiotic	No resolved	No incised		
		Organism resistant	Organism sensitive	Unknown
Penicillin	61	7	2	4
Other	12		1	2
Penicillin and other	7	5	2	2
None	18		2	
Unknown	3			7
Total	101	12	7	15

incised if pus is found Like Saner (1950) we have been impressed by the benefits of a small radial skin incision, which rarely needs to be as long as 1 inch If the breast is still secreting milk, emptying should have been maintained and done not more than an hour before operation By this means the outline of the lump is delineated, and the surgeon can be certain of the extent of the abscess and avoid opening up loculi Aspiration without incision, where tried, has had to be followed by incision, and local penicillin injections have produced lasting indurated lumps in the breast without curing

A method introduced by Miss Aileen Dickins of dressing abscess wounds was adopted in which ribbon gauze, newly dipped in sterile penicillin cream base, is led into the cavity and left untouched for forty-eight hours The discharge of pus, provided the gauze constitutes a wick and not a pack, is very satisfactory, and the dressing causes the minimum of pain to the patient All patients needing incision were admitted to hospital

The antibiotic of first choice for preventing infection has remained penicillin (table III) In contradistinction to superficial abscesses, intramammary mastitis appears still to be protected from infection by aqueous penicillin 1 0 mega unit daily or 0 5 mega unit twice daily from infection Once penicillin is deemed necessary, the dosage should be maintained for at least four days When infection has probably taken place already, aureomycin is used

Course of Infection

The infecting organism in all abscesses which were incised was *Staph pyogenes* and, except for secondary infection after incision, it was the only organism found in all the cases I have seen in fifteen years This conforms with the experience of Macpherson (1943), Walsh (1949), Saner (1950), and Isbister (1952) Duncan and Walker (1942) and Cunliffe (1949) have shown that *Staph pyogenes* is also found in the noses and throats of babies very soon after birth, and discussion has often arisen about the source of infection—does the breast give it to the baby, or the baby to the breast ?

Staphylococci, even virulent pathogens, appear to be protean, and from the infected person's point of view the size of the infecting dose of organisms appears important In terms of the organism the heavy dose derives from where the organism can multiply If it is conceded that staphylococci abound wherever there is stale breast milk or colostrum—in the pent up secretion of the breast, in the neonate's nasopharynx, and on the finger-tips and in the eyes, where colostrum and milk may easily get, and even in witch's milk—it seems reasonable to postulate that breast secretion is a vehicle of a growth promoting system (either a combination of factors or, like bifidus factor, a single substance) which affects *Staph pyogenes* The remarkable fact is that where breast secretion is pent up, even without the aid of a skin lesion or trauma, in regions remote from airborne organisms, even at the periphery of the gland in pregnancy, staphylococci establish themselves and may cause an abscess If indeed stale secretion contains an almost specific means of promoting the growth of staphylococci, the sepsis rate of neonatal skin may be expected to rise where the expression of colostrum is not followed by adequate washing of the hands The determining factor of clinical infection would then be the provision for the organisms' multiplication, which is less common, rather than the arrival of the organism, which is almost inescapable The inhibitory qualities against bacteria which fresh colostrum possesses do not rule out the possibility that fresh or altered secretion contains growth promoting substances Auclair (1954) has suggested that bovine colostrum may contain specific growth promoting substances for *Streptococcus agalactiae*

Prophylaxis

Prevention of intramammary mastitis consists in the *avoidance of retained secretion* In point of time antenatal treatment for poor protractility of the nipple comes first This enables the baby to take the breast vigorously and effectively from within a few hours of birth Antenatal expression of colostrum puts control of excess secretion into the mother's hands during lactation After delivery engorgement should be avoided, for it is often at this stage that an unemptied lobule becomes unemptiable

Since this investigation ended, a routine has been introduced which almost completely avoids engorgement Each woman, except those aged more than 35 and those who have been shocked or who have been delivered by cæsarean section, receives two tablets of stilbœstrol 0 25 mg within two hours of delivery and one tablet twenty-four hours later By this method and the occasional use of the humalactor, handling of the breasts before the fifth day by either the mother or the nurse has been largely eliminated These methods are defeated if care is not taken to see that the baby takes the breast properly, and this duty of the midwife is increased where pain from episiotomy or following obstetric interference immobilises the mother

The proper protractility of the nipple and the proper position of the baby at the breast are also safeguards against sore nipple and its sequelæ Demand feeding in the early days and night feeding from the breast also help, and anyone who sees the distension of the mother's breasts in the puerperium after eight hours at night in which the baby has not been breast fed must wish that hospital routine, where demand feeding may have drawbacks, should provide for the mother to feed her baby at 3 or 4 A M and then sleep until 7 A M

Milk retention and mastitis during lactation would often be avoided if those advising on infant feeding would recognise that the rate of secretion usually remains approximately constant day in day out Any event which reduces the amount of milk withdrawn—the dropping of a feed, or the giving of supplementary feeds—may be followed by mastitis, unless the mother has the knowledge and skill to avoid retention The time of weaning was shown in this series to be one of vulnerability There appear to be three requirements adequate œstrogens, judgment in keeping the breasts empty while the œstrogens take effect, and the need to accept the mother's intention to discontinue feeding Are there those who almost view mastitis as a punishment on the mother ?

Œstrogens given to suppress established lactation do not take much effect in the first twenty-four hours Although there is much individual variation, the mother should breast-feed her baby as usual on the day of starting treatment, about three times on the next day and twice on the next If the course of œstrogens is not tapered or is short, lactation may return at the time of œstrogen-withdrawal bleeding Since our practice over four years has been to give the following course, no patients have had mastitis with this method of

SULPHÆMOGLOBINURIA DURING ADMINISTRATION OF STIBOPHEN

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The accidents which sometimes happen during the treatment of bilharziasis with antimonial compounds, especially stibophen ('Fouadin,' 'Repodral,' 'Fantorin'), cause much concern to those engaged daily in treating the infected population The sudden collapse, which is nearly always fatal in a few hours, has often been ascribed to sudden heart-failure We, however, suspected that there must be another factor to explain the sudden onset and the symptoms of shock

During the past few years we have investigated blood-antimony levels without being able to correlate them with the sudden death, the patients who died had normal amounts of antimony in their organs Recently the case reported here was associated with hæmoglobinuria and sulphæmoglobinuria Subsequently we found two more cases of hæmoglobinuria developing during treatment with stibophen

Case-report

A man, aged 32, and weighing 8 st $2^1/_2$ lb, with painful micturition and terminal hæmaturia, had had a course of intravenous tartar emetic five years ago and a course of intramuscular stibophen a year before admission for antibilharzial treatment

On examination he had nothing abnormal in his heart, chest, or abdomen His Hb was 65% (Sahli) before treatment Ova of *Schistosoma hæmatobium* were present in his urine

Treatment and Collapse—He was given 3 75 ml of a 6% solution of stibophen intramuscularly daily for eight days On the eighth day, at 10 30 A M (half an hour after the last injection) he collapsed, with pulse rate 120 and blood pressure 130/90 mm. Hg, and soon passed into coma with pulse almost imperceptible He was deeply cyanosed and had blotchy reddish areas all over his body His heart was dilated, and a weak systolic murmur was heard over the apex Coarse crepitations in both bases, with signs of consolidation, were detected Liver and spleen were palpable Oxygen inhalation was administered After an hour the patient regained consciousness and his pulse became palpable Although his general condition improved, he had convulsions occasionally At 2 P.M he was somewhat irritable and wished to urinate but could not do so Catheterisation produced 150 ml of port-wine coloured urine, which contained few red blood cells and numerous granular casts Spectroscopy of the urine revealed sulphæmoglobin and oxyhæmoglobin The patient's pulse rate was 110 and his temperature 101 3°F At 3 P M he was quiet but felt chilly He was therefore placed in an electric cradle intermittently He passed unaided 250 ml of port-wine coloured urine, whose condition was unchanged Next morning he passed 400 ml of urine, still port-wine coloured but of a lighter tint During the day the urine became gradually clearer, approaching the normal amber colour but still containing a brownish sediment of granular casts and traces of sulphæmoglobin and oxyhæmoglobin

Laboratory Findings—Hb 40%, red cells 2,820,000 per c mm, white cells 21,400 per c mm (neutrophils 93%, lymphocytes 7%), cephalin cholesterol flocculation test positive, thymol turbidity 10 units, blood-urea level 80 mg per 100 ml, blood bilirubin level 0 9 mg per 100 ml No malaria parasites were found in the blood

Progress—On the fourth day the urine still contained albumin and numerous granular casts, it was of low specific gravity (1 008) and sterile on culture. The icterus index was 8 units, and the blood-bilirubin level 0 5 mg per 100 ml On the ninth day the urine contained granular casts but no sulphæmoglobin, and the blood contained no malaria parasites and gave a negative Wassermann reaction, and the fragility of the red cells was within normal limits Radiographically the lungs proved normal except for slight increase in vascular and lymphatic markings From the fourth day onwards the patient's temperature declined gradually to normal level on the tenth day After a month his urine contained no casts or urobilinogen, and there was no evidence of sulphæmoglobin or of oxyhæmoglobin, blood urea level 38 mg per 100 ml, cephalin cholesterol flocculation test negative, thymol turbidity 4 units, Hb 80%, red cells 4,216,000 per c mm, white cells 8800 per c mm (eosinophils 25%, neutrophils 54%, lymphocytes 20%, monocytes 0%, basophils 1%)

Discussion

Although this condition is rare, it is necessary to draw attention to it It is noteworthy that the patient did not complain of any side effects until he received the eighth injection The clinical picture was of severe shock with acute intravascular hæmolysis, in addition a patch of pneumonic consolidation was present—a condition which is known to develop occasionally during antibilharzial treatment and has been ascribed to disintegration of the worms The urine was characteristic of acute hæmoglobinuria, and on spectroscopy proved to contain sulphæmoglobin and oxyhæmoglobin

The patient said that for a long time before the injections he had not taken any medicine which could cause this acute sulphæmoglobinuria The only explanation for this hæmolysis is the possible action of the sulphonic group in the stibophen on a susceptible person There was also no relation to any of the known hæmoglobinurias, as shown by the laboratory findings We have also found that stibophen stored for a long time is apt to undergo molecular dissociation and become toxic

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New Inventions

AN INSTRUMENT RACK FOR CASUALTY SURGERY

To accelerate the preparations for casualty suturing and other minor surgical operations, a rack has been designed which will hold the few instruments commonly needed (figs 1 and 2) If kept filled in the casualty department it can be placed bodily in the steriliser when required for use, and can be lifted out by the handle, this is fixed at the point of balance and is made to fit the end of Cheatle's forceps

Construction is of one piece of 22 S W G polished stainless-steel sheet, with a handle of $^1/_8$ in stainless steel wire, bent and riveted in position Slots are cut to hold the instruments, those at each side of the rack have spring retainers (part of the single steel sheet) to hold scalpels firmly so that the blades cannot come into contact with other instruments in sterilisation (a too common cause of blunting)

One end of the rack has slots to hold 2 scalpels, 1 needle-holder, and 2 pairs of dissecting or toothed forceps, while the other has four slots to hold Spencer Wells's or Lane's forceps or scissors, as required The over-all dimensions of the rack are 10 in by $4^3/_4$ in

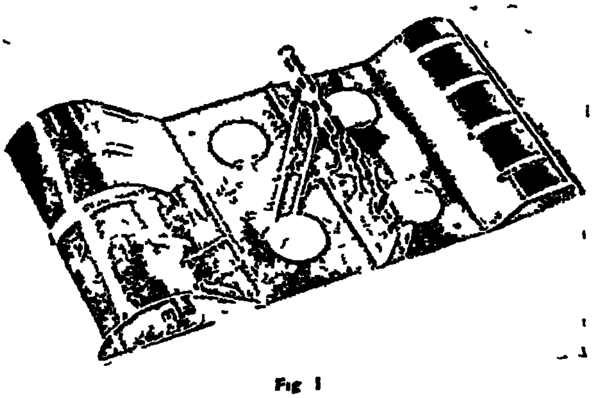

Fig 1

(where known) and their state of consciousness, are shown in table II For each barbiturate the blood-level appeared to be related to the degree of consciousness of the patient Analyses were made at different times after the dose, and it is therefore difficult to detect any absolute correlation between dose and blood-level However, long acting barbiturates produced higher blood-levels than similar doses of the short-acting ones For example, cases 1 and 34 had taken comparable amounts of phenobarbitone and pentobarbitone, yet their blood-levels at similar times after the dose were 10 2 and 6 1 mg per 100 ml respectively

The fall in blood-levels in 4 patients who had ingested different barbiturates is illustrated in fig 1 Blood-levels of the long acting drugs were higher, and the rates of fall slower, than those of the short acting ones

Thus in case 17 the blood level was 18 5 mg barbitone per 100 ml 19 hours after the dose, and 1 9 mg per 100 ml 10 days later when the patient had recovered

Case 3 was admitted to hospital within 2 hours of ingesting phenobarbitone, and the blood level continued to rise for about 12 hours 7 days after taking the drug the patient was awake, but the blood still contained 4 0 mg phenobarbitone per 100 ml.

Patients who had taken short acting barbiturates usually recovered more rapidly, for example, in case 34 only 0 7 mg pentobarbitone per 100 ml blood remained 3½ days after the dose

The rates of fall of blood-levels in patients who had taken the same barbiturate were similar but showed some individual variations, depending on the dose and the treatment given Results for 3 patients who had ingested barbitone are given in fig 2, the rates of fall are similar, although the peak blood-levels (18 5, 15 1, and 8 0 mg per 100 ml) differed considerably 2 of these patients (cases 17 and 18) remained unconscious for 6 days Fig 3 shows similar results, obtained from 4 patients after ingestion of amylobarbitone, in whom the peak blood-levels were 9 4, 7 3, 6 1, and 4 4 mg per 100 ml; these patients all regained consciousness within 2½ days

TABLE II—HIGHEST BLOOD BARBITURATE LEVELS FOUND IN LIVING PATIENTS

Barbiturate	Case no	Age (yr)	Dose (g)	Hr after dose	State of consciousness	Blood-barbiturate (mg per 100 ml)
Phenobarbitone	1	25	4 5	13	U	10 2
	2	35		15	U	9 9
	3	31		31	U	9 0
	4			17	U	8 5
	5	41	2 9	12	U	6 6
	6	4		18	S	6 1
	7	61	0 6	5	S	5 3
	8	57		31	D	4 2
	9	50	1 2	6	D	3 3
	10	37	0 4	7	D	2 8
	11	44		14	D	2 8
	12	22	1 0	17	A	2 2
	13	21	1 5	14	A	1 8
	14				A	1 6
	15	42	1 5	82	A	1 3
Barbitone	16	67	22 —	35	U	53 0
	17	69		19	U	18 5
	18	67		72	U	15 1
	19	46		19	D	8 0
Butobarbitone	20	27		12	U	7 7
	21	31		9	S	2 9
	22	40		3	U	2 6
	23	47	1 0	7	D	1 6
Amylobarbitone	24	65		12	U	9 4
	25	33	4 1	3	U	7 3
	26	30	7 0	7	U	6 1
	27	63		19	U	4 4
	28	70		15	U	3 1
	29	50	6 2	36	U	3 0
	30	36		4	S	2 4
	31	30		15	A	1 8
Tuinal	32	48		21	U	3 0
Cyclobarbitone	33	63		12	U	4 5
Pentobarbitone	34	24	5 3	15	U	6 1
	35	63		3	U	2 9
	36	39		3	S	2 1

U = unconscious S = semiconscious D = drowsy A = awake

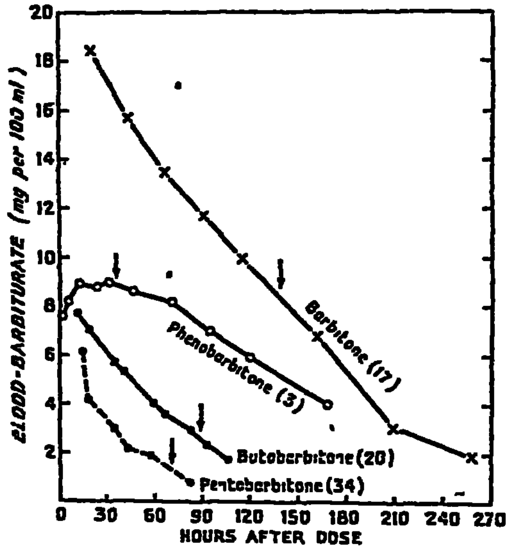

Fig 1—Fall in blood levels of different barbiturates. The figures in parentheses indicate the case number, and the arrows the time at which consciousness was regained

The blood-barbiturate levels of 23 patients at their return to consciousness are given in table III The mean levels are 7 mg (±2 mg) per 100 ml for the long-acting, 3 mg. (±1 mg) per 100 ml for the intermediate, and 1–2 mg per 100 ml for the short-acting barbiturates These conclusions are also illustrated by fig 1 and table II

Effect of Picrotoxin

Treatment of these patients varied considerably Picrotoxin was the analeptic most commonly used, but this did not appear to influence the rate of fall of blood-barbiturate levels Table III suggests that patients who were treated with picrotoxin regained consciousness at blood-levels slightly higher than those of other patients who had taken the same drug, but the data are insufficient for statistical analysis In 2 cases of phenobarbitone poisoning (nos 2 and 3) the blood-levels, and their rates of fall, were similar, case 2 was unconscious for 82 hours and his blood level was 7 3 mg per 100 ml when he regained consciousness, but case 3 was treated with picrotoxin, was unconscious for only 36 hours, and his blood-level was 8 9 mg per 100 ml when he regained consciousness

Gastric Contents

Quantitative analyses of gastric contents and washings were made in 21 patients The volumes of these contents were variable and the barbiturate levels ranged from 1 to 1500 mg per 100 ml The total amount of barbiturate removed by gastric lavage was 0 1–119 mg, and it was the equivalent of less than 4% of the dose in the 6 cases in which data were complete When this treatment was given more than 12 hours after the dose the total amount of barbiturate removed was insignificant, irrespective of the dose

Urine

Single specimens of urine from many of these cases were also analysed Except in 1 case (no 16—see below), the highest barbiturate level found was 42 mg barbitone per 100 ml 71 hours after the dose (case 18) In most cases of phenobarbitone poisoning the level in urine was less than 10 mg per 100 ml, but no correlation between urine levels and the degree of unconsciousness could be detected.

Many English books still advise that the breasts should be palpated with the flat of the hand, though this advice stems from a wrong translation of Velpeau's French

The book can be read as a whole, and not just as an encyclopædia It may not give the reader a very original point of view, but it achieves its object of summarising the main facts and the important questions about breast cancer, as an experienced surgeon sees them

The Boke of Chyldren

THOMAS PHAIRE Edited by Prof A V NEALE, F R C P, and H R E WALLIS, M D Edinburgh E & S Livingstone 1955 Pp 76 7s 6d

PUBLISHED in 1545, this was the first book on pædiatrics ever written by an Englishman and one of the earliest medical books to be published in the English language At that time the world was beginning to emerge from the darkness of the Middle Ages printing had been invented a hundred years before, and Vesalius's *Fabrica* had just appeared, but books written by Avicenna and Galen were still in everyday use

Phaire was born about 1510 probably in Norwich He went to Oxford to study medicine and to Lincoln's Inn to study law He started to practise medicine about 1540 and took his M B and doctorate at Oxford twenty years later He was also a solicitor and Member of Parliament He lived in Kilgerran in Pembrokeshire and died there in 1560

This is an exact copy of the first edition with the original spelling

"The gut called of the latines rectum intestinum, falleth out at the foundament, and cannot be gotten in agayne without peine and labour" "Of smal pockes & measilles The best and most sure helpe in this case is not to meddle with anye kynde of medicines, but to let nature work her operacion" Phaire says that the cause of ulceration of the head is from sides of bacon or salt beef falling from the hooks in the ceiling (Then, as now, accidents at work and in the home were important) The author's credo is "Here to doo them good that haue most nede, that is to saye children"

The editors and publishers have earned our thanks by reprinting this book of quaintness and charm

Somme de médecine contemporaine

Vol III *La thérapeutique* Editors Prof ANDRÉ LEMAIRE, Prof GREGORIO MARAÑÓN Prof JEAN LA BARRE, Prof ARVID WALLGREN Nice Les Éditions Médicales 1955 Pp 390

THIS is the third volume of the Contemporary Medicine series, prepared under the direction of the late Rene Leriche, which will be completed by a fourth volume on Medicine in Modern Life In a foreword, Prof André Lemaire puts the case for more international "pooling" of methods of treatment, but he condemns those periods of "inflation" which he thinks all active treatments pass through

The early chapters on general subjects include a short but interesting history of therapeutics by Prof Jean La Barre The rest of the book is divided according to the different systems of the body or different forms of treatment, ranging from phytotherapy to stomatology Curiously enough there is little mention of radiotherapy or radioactive isotopes There is no index except for a list of authors with a short "bio bibliography" of each and a list of names quoted in the text

Social Casework in Marital Problems

The Development of a Psycho dynamic Approach A Study by a Group of Caseworkers London Tavistock Publications 1955 Pp 199 15s

THIS is an account by six caseworkers of the origins, development, and working of the Family Discussion Bureau, which is a child of the Family Welfare Organisation Society and the Tavistock Clinic

The Bureau is rather like the Marriage Guidance Council —but with a difference Its caseworkers are not counsellors or advisers but have had some training in the school of analytic psychology, and have analytically trained psychiatrists immediately available for consultation They endeavour to work out with marriage partners in difficulties the nature, psychological content, and origins of their emotional disharmonies If both partners are willing, each has his or her own caseworker, and the situation revealed is discussed by the caseworkers and a psychiatrist in conference The expectation is that many interviews will be needed in a given case, though occasionally much good springs from a few or even a single interview when the troubled partner has been able to clear his own mind by talking to a receptive but uninvolved listener, who neither adjudicates nor takes sides

Cases, both short and long, are used to illustrate the various problems, their working out, and the measure of success achieved Some attempt is made to assess statistically the results of five years' development and work

The material is presented with modesty and candour and makes interesting and instructive reading

Operative Dental Surgery

7th ed J B PARFITT, M R C S, F D S R C S, consulting dental surgeon, Guy's Hospital, W E HERBERT, M R C S, F D S R C S, professor of dental surgery in the University of London at the hospital London Edward Arnold 1955 Pp 524 45s

BASED on lectures delivered at Guy's Hospital by Mr Parfitt, this book first appeared just over thirty years ago Its scope, which was to give a concise account of the technical procedures of dental surgery with enough theoretical background to explain the underlying principles, has remained unaltered, and there is no other English book which covers precisely the same range of subjects

The chapters on filling materials and cavity preparation are good, but that on the uses of gutta percha seems redundant in the present day, and a fuller account of the auto polymerising acrylic resins would be welcome Crown and bridgework are dealt with adequately for all but the specialist An excellent discussion of the pulpless tooth and "focal sepsis" will interest both doctors and dentists called upon to decide whether or not dead teeth should be retained The ætiology of dental caries is oversimplified and there is no account of some of the more recent work on this controversial and perplexing subject

The chapter on local anæsthesia is somewhat disappointing, considerable space is devoted to obtundents, which are recognised to be of limited value, and the detailed account of the preparation of procaine solutions in the surgery could well give place to further information about lignocaine More space, too, could have been given to discussing the advantages and disadvantages of the now almost ubiquitous "cartridge" syringe, especially since it is in regular use by the students at the authors' own hospital Mercurochrome is advocated as an oral antiseptic, but the general opinion is that aqueous solutions are useless, and solutions in alcohol or in acetone are no more nor less effective than the solvents alone

Most of the many illustrations really help to clarify points in the text, and the radiographs are reasonably well reproduced, with the exception of that showing the normal mouth

Another edition of this valuable book will undoubtedly be called for fairly soon, and the opportunity could perhaps be taken to remove those parts of the text that are becoming of less immediate interest to students and dental surgeons today

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Diseases of the Nervous System (5th ed London Oxford University Press 1955 Pp 996 55s)—To the students' chagrin, successive editions of textbooks tend to get bigger, but, despite the addition of much fresh material, the new edition of Sir Russell Brain's book is a few pages shorter than its predecessors There is new material on cervical spondylosis, the Coxsackie viruses, inclusion body encephalitis, acute hæmorrhagic leucoencephalitis, toxoplasmosis, polymyositis, and neuropathy and myopathy associated with carcinoma, and Sir Russell has added a section on consciousness and unconsciousness to the chapter on the psychological aspects of neurology The treatment of meningitis has been brought up to date with the latest advances in chemotherapy, and recent developments in the treatment of poliomyelitis and lead poisoning are discussed Comprehensiveness and clarity have made Sir Russell's book a firm favourite alike with students, with practitioners, and with neurologists

TABLE IV—BARBITURATE ESTIMATIONS IN BARBITONE POISONING (CASE 16)

Hr after dose	Blood-barbitone (mg per 100 ml)	Urine		
		Volume (ml)	Barbitone content (mg per 100 ml)	Barbitone excretion (mg)
13	41 1			
16½	45 3			
22	49 5			
27		700	73	510
35	53 0	110	137	151
43		140	108	151
52		550	66	362
60	45 6	360	74	266
67		350	74	259
75		240	90	216
83	35 0	360	83	298
91		560	96	537
99		270	129	348
107	27 9	290	117	339
108	Died			
			Total	3 43 g

Ultraviolet spectrophotometric analysis of blood is a rapid and reliable test for the presence of barbiturate, but the significance of a blood estimation depends on the type of barbiturate ingested The long-acting barbiturates are mostly excreted in the urine unchanged (Lous 1954a), and this is reflected in the relatively slow rate of fall of blood-levels The short acting barbiturates are metabolised more rapidly and undergo not only oxidation of their alkyl side chains, but also fission of the pyrimidine ring (Maynert 1952a, b, and c) This is reflected in the more rapid fall of blood-barbiturate levels Those metabolites with an intact pyrimidine ring give positive results with cobalt salts and with most ultraviolet spectrophotometric tests (Maynert 1952c)

When the barbiturate has been identified, or at least classified, the blood-level is a good index of the severity of the poisoning, and may be used to distinguish between medicinal and toxic doses

Lous (1954b) reported that patients given phenobarbitone in doses of up to 400 mg per day had blood levels of up to 6 mg per 100 ml Other workers (Fisher et al. 1948, Goldbaum 1948, Lauritzen 1952, Lous 1954a) have reported blood-barbiturate levels of 0 4–4 mg per 100 ml after medicinal doses, the long acting drugs producing higher blood-levels than the short-acting ones

In acute barbiturate poisoning blood-levels are usually much higher than those found after medicinal doses Several workers (Fisher et al 1948, Goldbaum 1948, Helldorf et al 1949, Nillson 1951, Kyle et al 1953, Wright and Johns 1953, Lous 1954c, Sunshine and Hackett 1954, Wright 1955) have reported blood-levels after acute poisoning, but since different analytical methods were used, and results were often expressed as the unnamed barbiturate or as the acid or sodium salt, such figures may not be comparable From the results given in the present paper it is concluded that blood-levels of 9 mg per 100 ml of long acting, 6 mg per 100 ml of intermediate, and 4 mg per 100 ml of short acting barbiturates indicate severe poisoning These figures, and those at which patients return to consciousness, accord with those of other workers, and are of practical value in that it is now possible to assess the prognosis of an unconscious patient, to have some objective measure of the depth of unconsciousness and to observe the effect of treatment on the blood-level With the data given in this paper useful predictions of the time of return of consciousness can often be made, but it must be remembered that patients may show individual variations or develop tolerance to the drug after prolonged dosage

Blood barbiturate levels previously reported by other workers in fatal cases vary widely (table VI) In some instances this may be due to the presence of other drugs Fisher (1949) suggested that alcohol may exert a synergistic effect and from our results (cases 55 and 59) it is possible that salicylate and paraldehyde have a similar action When assessing fatal blood barbiturate levels it is essential to distinguish between patients found dead, and those who died later in hospital, when complications, such as pneumonia or uremia, may have developed Published reports suggest that the majority of patients who had ingested fatal doses of the long-acting barbiturates died in hospital, whereas those who had taken short-acting ones were more often found dead It will be observed from table VI that blood-barbiturate levels of some patients who recovered were higher than those of patients who died For example, our case 16 remained alive for 4 days with a blood-level higher than that previously recorded for any living patient It is therefore apparent that the fatal blood-level of a given barbiturate cannot be stated, but we may conclude that the following blood-levels are compatible with death from barbiturate poisoning

Long acting barbiturates more than 10 mg per 100 ml
Intermediate-acting barbiturates more than 7 mg per 100 ml
Short-acting barbiturates more than 3 mg per 100 ml

We agree, however, with Fisher (1949) that the finding of these blood-levels does not constitute prima facie evidence of death from barbiturate poisoning

TABLE VI—REPORTED BLOOD BARBITURATE LEVELS

Barbiturate	Blood-barbiturate (mg per 100 ml)		
	Found dead	Died in hospital	Recovered (highest figures)
Phenobarbitone	8	9–40	21 (Lous 1954c)
Barbitone		10–53	20 6 (Fisher et al 1948)
Butobarbitone	1–7		7 7 (this investigation)
Amylobarbitone	3–17	1–2 5	8 6 (Sunshine and Hackett 1954)
Tuinal		4	5 0 (this investigation)
Cyclobarbitone	12		4 5 (this investigation)
Quinalbarbitone	2–7		5 0 (Sunshine and Hackett 1954)
Pentobarbitone	1–58		6 1 (this investigation)

TABLE V—BARBITURATE LEVELS IN NECROPSY MATERIAL

Case no	Age (yr)	Ingested	Blood	C S.F	Urine	Kidney	Liver	Stomach contents	Intestinal contents	Notes
			mg per 100 ml			mg per 100 g		Total (g)		
51	64	Phenobarbitone			Tr *			6 1*	Tr *	Found dead
52		Butobarbitone			22*	Tr *	Tr *	Nil*	0 02*	Found dead
53	50	Amylobarbitone	6 8	~1	4	—	16	3 1	0 57	Found dead
54	45	Amylobarbitone	7 8					0 88*	0 16*	Found dead
55	65	Amylobarbitone – salicylate	>2 5		20	—	5 2	1*	Nil*	Stomach washout 1 hr before death Salicylate present in urine post mortem
56	42	Tuinal	4 9	2 8	5 6	10 1	12 2	0 07	0 37	Found dead
57	45	Quinalbarbitone				21*	2*	0 13*	0 04*	Found dead
58	54	Pentobarbitone	9 0	~5	9 7		98	←17 5→		Died 4 hr after dose
59	39	Pentobarbitone	24 1	3 3	2 2			0 34	0 71	Found dead
60	60	1 8 g pentobarbitone – 340 ml paraldehyde	0 9	0 3	Nil	Nil	Nil	0 43		Found dead Blood-paraldehyde 36 mg per 100 ml

*Figures obtained by weighing after Stas Otto extraction, and barbiturate detected by the reaction with cobalt salts
The remaining results were obtained by spectrophotometric methods

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*Lancet, 1954, i, 1011

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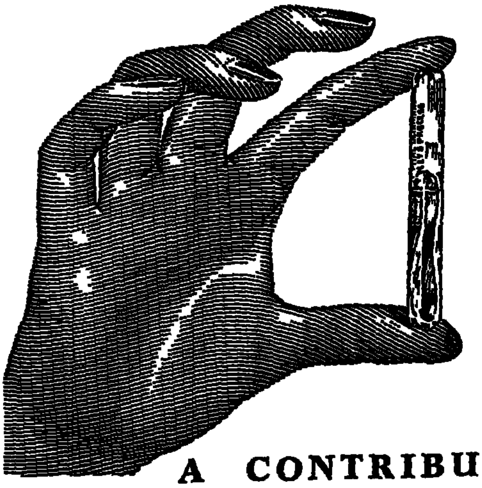

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from nineteen to seventy hours after the second operation The administration of cortisone was started three days before the second operation (the dosage is shown in the figure) The right adrenal gland weighed 4 5 g and the left 3 5 g , on histological examination both appeared normal, and malignant tissue was not found in either gland At first the patient made satisfactory progress, the mammary ulcer began to diminish, and within three weeks of the second operation she was getting out of bed

Terminal course—Pressure necrosis in both buttocks and necrosis of the skin of the left calf over the internal saphenous vein subsequently led to sloughing of the skin and infection The ulcer on the chest wall began to increase in size and depth, and the patient died of bacterial *toxæmia* six weeks after the second operation

Necropsy findings—The carcinoma was confined to the chest wall, and the histological appearance of this tumour still closely resembled that of the original specimen—an anaplastic adenocarcinoma with much necrosis

Intake of Food and Fluid

The patient was encouraged to consume as much food and fluid as she could but was not given a constant intake of either food or minerals , the intakes of protein and calories were deficient throughout the period of study, the daily nitrogen intake seldom exceeding 4 g The intake of potassium was consistently larger than that of sodium, but both were less than the normal minimum The intravenous administration of fluid was limited after the first operation to a short infusion of 5% glucose solution as long as there was anxiety about maintaining the blood pressure After the second operation an infusion of 5% glucose solution was maintained for ninety hours to allow of the administration of noradrenaline and was supplemented by 900 ml of 0 9% saline solution

Findings in Urine

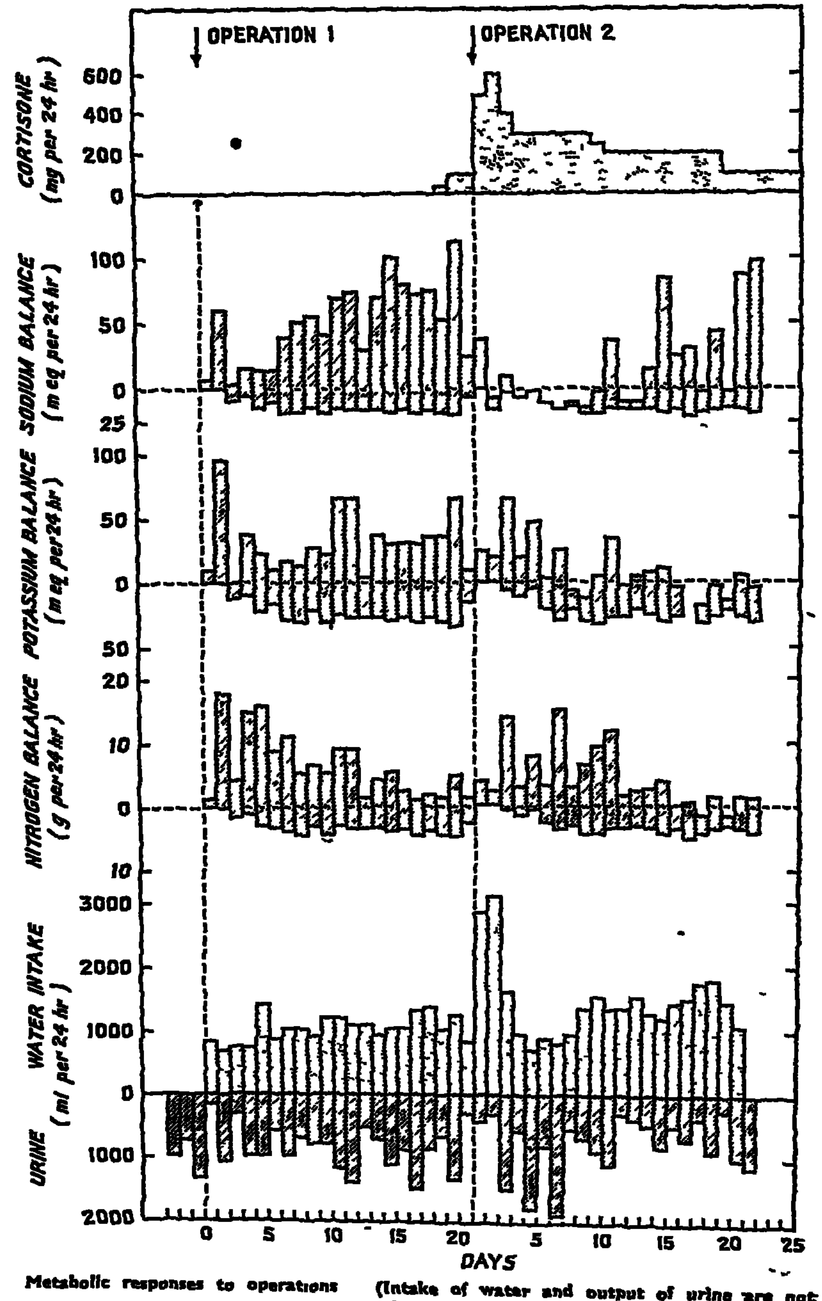
Volume—During the first ten days after the first operation the water intake was equal to the volume of urine, but in the second ten days exceeded the volume of urine by 2 0 litres , after the second operation the water intake exceeded the volume of urine by 5 litres in the first ten days and by 9 2 litres in the second ten days During the first two days after the second operation the water intake was 5 4 litres but the volume of urine only 760 ml Over the next five days the water intake was 4 96 litres and the volume of urine 6 41 litres Thus, after a delay of forty eight hours, there was a large maintained diuresis while the daily dosage of cortisone was 300 mg or more

Specific gravity—After the first operation the specific gravity of the urine remained steadily above 1 018 for three days and thereafter fell below this in only a few six-hour periods—a response which was similar to, but less severe than, that which is usual after operations such as partial gastrectomy (my unpublished observations) After the second operation the specific gravity of the urine fell below 1 012 on the third day and remained below this level for six days and then rose and remained at or above 1 016 from the ninth to the sixteenth day, when it again fell below 1 012

Composition—The changes in composition of the urine (see figure) indicate that, although the metabolic responses to the two operations were in some respects similar, there were also striking differences The total loss of nitrogen was only about half as great after the second operation, and of potassium only a quarter as great, as after the first operation The large negative balance of sodium during the first ten days after the first operation gave place to a small positive balance over the same period after the second operation Sodium conservation after the first operation was within the range to be expected after such an operation, but the later urinary loss of sodium was unexpectedly large After the second operation the sodium conservation was almost complete for thirteen days The potassium sodium ratio of the urine was inverted after both operations , but, whereas it reached a peak of only 1 6 on the second day and was inverted for six days after the first operation, so complete was sodium conservation after the second operation that there was a peak of 50 on the fifth day and the ratio was inverted for thirteen days

Discussion

After total adrenalectomy in animals a normal response to injury appears to depend on the administration of a sufficient quantity of adrenal cortical hormone Ingle et al (1947) showed that, in adrenalectomised rats, after fracture of a tibia the increased urinary excretion of nitrogen, indicating increased katabolism of tissue protein depended on the administration of adrenal



Metabolic responses to operations (Intake of water and output of urine are not expressed as a balance) derivatives was then undertaken.[3-5] Non-sulphonamide thiodiazoles have no hypoglycæmic action, but several compounds of the *p-amino-benzene-sulphonamido-thiodiazole* group lower the blood-sugar in animals. The tertiary butyl and isobutyl derivatives are the most active; then, in decreasing order of activity, follow the butyl, amyl, isoamyl, propyl, and isopropyl derivatives. The ethyl and methyl derivatives are inactive in this respect. Recently another sulphonamide compound, sulphanilyl-*n*-butylurea, has been found to have a similar effect on the blood-sugar level.[6 7] This compound has been more fully investigated in man. After a dose of 2 g. a maximum concentration of free sulphonamide of about 7.5 mg. per 100 ml. of blood is reached in three hours, and there is a considerable fall in the blood-sugar level, which returns to normal in about six hours. The hypoglycæmia can be corrected by giving glucose. With this background information, it was a natural step to ascertain the effect of this substance in diabetic patients.

In one clinical trial[8] sulphanilyl-*n*-butylurea was given to 82 patients with diabetes mellitus of varying duration and severity. The sulphonamide was given after a preliminary period of observation, usually 2.5 g. on the first day, 1.5 g. on the second, and thereafter 1 g. daily. The best results were seen in elderly diabetics. In one group of 28 patients, aged 49 to 77, who had received inadequate or no previous treatment, all but 3 responded well to the drug without the addition of insulin. The glycosuria, by which about 100 g. of sugar had been lost daily, disappeared within a few days and at the same time the blood-sugar fell from fasting values of above 300 mg. to less than 150 mg. per 100 ml. and remained below 200 mg. throughout the day. The renal threshold for glucose did not change. Treatment with sulphonamide was substituted in a second group of 38 patients, aged 41 to 77, who had been previously stabilised on insulin. In 28 it was possible to continue treatment without any insulin. The most favourable results were seen in those with diabetes of recent onset; the response was less satisfactory if previous treatment with insulin had been given for more than a year or two. Further observations in the older patients show that the drug acts gradually and has a long-lasting effect. It is suggested that either intermittent massive therapy or long-continued treatment with small maintenance doses should be given. There is no evidence of the development of tolerance. Fewer observations have been reported in younger diabetics,[6 8] and the results have not been so successful, even where higher doses were given. In most of the younger patients the drug had little effect on blood-sugar levels, but in a few it enabled the dose of insulin to be reduced. In the presence of acidosis there was a poor response, and the substance is clearly unsuitable for use in emergencies. Apart from occasional skin rashes few undesirable side-effects have been reported. As the sulphonamide in its acetylated form is relatively soluble in an acid pH range, there is little danger of crystalluria.

The way in which these compounds work arouses much interest. LOUBATIÈRES[3 5] originally suggested that the β-cells of the islets of Langerhans are stimulated to secrete insulin—a view compatible with the complete lack of action after total pancreatectomy. More recently, evidence has been produced that the primary action is on the α-cells, which are thought to be the site of production of the hyperglycæmic polypeptide known as glucagon.[9] Histological studies in the dog, rat, and rabbit have shown that the α-cells are damaged or destroyed after administration of these sulphonamides[10]; and in one diabetic patient who had received this treatment and who died in uræmic coma, no α-cells were found in the pancreas examined immediately after death.[6] Glucagon is considered by some to play a part in the normal regulation of the blood-sugar level and to act in some respects as an antagonist of insulin. In alloxan diabetes the β-cells are damaged but the hyperglycæmia can be controlled by administration of either *p*-amino-benzene-sulphonamido-thiodiazole or sulphanilyl-*n*-butylurea,[5 7] which destroys the α-cells and presumably thus restores the equilibrium. LOUBATIÈRES and his colleagues[11] now suggest that the sulphonamide not only damages the α-cells but also stimulates the formation of new β-cells. But CHEN et al.,[12] investigating the action of a closely allied compound, sulphanilamido-cyclopropylthiazole, found that in normal rabbits it consistently caused hypoglycæmia, although in alloxan-diabetic rabbits it produced a conspicuous rise in blood-sugar. With the other compounds, a transient hyperglycæmia has sometimes been noted before the fall in blood-sugar. In human diabetes it has been suggested that insulin sensitivity or resistance may be associated with the activity of the α-cells, but this has not yet been fully established.

So far the evidence is insufficient for any definite conclusion about the pharmacological action of these compounds. They clearly open up a new approach to the study of carbohydrate metabolism and diabetes mellitus. The preliminary reports suggest that they may be useful in the oral treatment of elderly diabetics but not of young or acidotic patients. Further carefully planned clinical trials may determine the place of these sulphonamide compounds in the management of diabetes, and we hope that the trials will be completed before these powerful substances become widely available.

Precocious Immunity

IN the classical sense immunity to an infection or toxin depends upon the presence of circulating antibodies. There are, however, circumstances in which some protection is conferred when the presence of antibodies can be excluded. Interference phenomena of this kind are seen in certain virus diseases. Of course, in the case of some viruses the presence of circulating antibodies can be detected and passive immunity can be transferred by serum from convalescent patients; but in other virus diseases the immunity appears to be due to exclusion effects, and after an initial acute infection a permanent symbiosis

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[3] Loubatières, A. *Ibid*, p. 830.
[4] Bovet, D., Dubost, P. *Ibid*, p. 764.
[5] Loubatières, A. *Arch. int. Physiol.* 1946, 54, 174.
[6] Franke, H., Fuchs, J. *Dtsch. med. Wschr.* 1955, 80, 1449.
[7] Achelis, J. D., Hardebeck, K. *Ibid*, p. 1452.
[8] Bertram, F., Bendfeldt, E., Otto, H. *Ibid*, p. 1455.
[9] de Duve, C. *Lancet*, 1953, ii, 99. Constam, G. R. *Schweiz. med. Wschr.* 1955, 85, 92.
[10] von Holt, C., von Holt, L., Kröner, B., Kühnau, J. *Arch. exp. Path. Pharmakol.* 1955, 224, 66, 78.
[11] Loubatières, A., Bouyard, P., de Lados, C. I. *C.R. Acad. Sci., Paris*, 1955, 241, 515.
[12] Chen, K. K., Anderson, R. C., Maze, N. *Proc. Soc. exp. Biol., N.Y.* 1946, 63, 183.

the insertion of a soap paste into the cervix; and another patient, a trained nurse, had passed an instrument into her uterus. The other 4 patients refused to disclose details of their abortions.

Case-reports

Case 1.—A woman, aged 38, gave herself a vaginal douche in the 4th month of pregnancy, 14 days before admission to Hammersmith Hospital on Oct. 15, 1947. Vaginal bleeding, vomiting, and oliguria developed, but she had no medical attention until admission, when the products of conception were passed spontaneously. She had passed a very small quantity of dark urine for several days after the onset of vaginal bleeding.

On admission she was pale and drowsy and was vomiting. She was already in the early diuretic phase of acute tubular necrosis, passing large quantities of dilute urine.

Treatment and progress.—She was given an oral Borst diet and her water and salt balances were maintained. She made a satisfactory recovery and was in good health 2 years later, although she had diminished renal function and mild hypertension.

Case 2.—A widow, a trained nurse aged 27, passed an instrument into her uterus on March 25, 1948, and aborted that day. She was admitted to hospital next day because of anuria and jaundice. She was given penicillin on account of fever, and intravenous feeding. She was transferred to Hammersmith Hospital on April 1.

On admission she was pale but not jaundiced; she had facial œdema and epistaxis and she was vomiting. She had a raised venous pressure and a collapsing pulse. There were basal crepitations in both lungs.

Treatment and progress.—The patient was given a protein-free diet, water and salt balance, and blood-transfusion. She was treated twice by dialysis with an artificial kidney, but she died from pyæmia on April 9.

Necropsy showed acute tubular necrosis of both proximal and distal tubules with eosinophil casts in the distal tubules. Acute endometritis and multiple pulmonary abscesses were also present.

Case 3.—A woman aged 27, aborted on April 12, 1948, when 22 weeks pregnant; details of the abortion were not disclosed. She had been anuric from the time of the abortion, and had been admitted to hospital, where she was treated with forced fluids, potassium citrate, and intravenous sodium sulphate. On April 16 she was given a high spinal anæsthetic, and the next day her right kidney was decapsulated. On April 18 she was transferred to Hammersmith Hospital.

On admission she was pale and drowsy, and had a high venous pressure in her neck and œdema of her legs. She was treated with an oral Borst diet, water and salt balance, and dialysis (artificial kidney) on the 5th and 13th days of illness. She made a good recovery.

Case 4.—A woman, aged 24, gave herself an intra-uterine douche of soapy water on Aug. 28, 1948, with the immediate onset of shock, vomiting, and abdominal pain. She was admitted to hospital that day and delivered of an immature fœtus. She was given intravenous fluids and penicillin, and on Aug. 30 high spinal anæsthesia was induced.

She was transferred to Hammersmith Hospital on Aug. 31 and an intragastric drip-feeding régime (Bull et al. 1949) was instituted. She was severely ill in the early diuretic phase, but she eventually made a good recovery.

Case 5.—A woman, aged 20, had a criminal abortion on Oct. 20, 1948, and was subsequently admitted to hospital with uterine sepsis, peritonitis, and anuria. She had blood-transfusion, intravenous fluids, and gastric suction. Uræmic fits developed on Oct. 26, and she was transferred to Hammersmith Hospital three days later.

On admission she was comatose, acidotic, grossly œdematous, and moribund. She died that day before dialysis could be performed.

Necropsy showed acute tubular necrosis of the kidneys.

Case 6.—A woman, aged 27, gave herself a douche of soapy water on Nov. 23, 1948. Within 24 hours she aborted and became oliguric and began vomiting, but she was not admitted to hospital until Dec. 1, when she was given a blood-transfusion for anæmia and kept in salt and water balance. She was transferred to Hammersmith Hospital three days later, when the intragastric drip-feeding régime was started; this was continued for 19 days. Although she was severely ill on admission, she made a good recovery.

Case 7.—A girl aged 16 gave herself an intra-uterine douche of soapy water on Nov. 30, 1948. She was admitted to hospital that day, and her uterus was evacuated and penicillin given. Blood-transfusion for anæmia was started after several days of anuria, and she was given forced fluids and mercurial diuretics without effect. She was transferred to Hammersmith Hospital on Dec. 9, when intragastric drip feeding was started; this was continued for 13 days. She made a satisfactory recovery.

Case 8.—A girl aged 17 had an intra-uterine douche of soapy water and was admitted to hospital the following day with pelvic peritonitis and anuria. There was spontaneous delivery of the fœtus and the placenta was removed digitally. Blood-transfusion was given, and the intragastric drip-feeding régime started. She had a spontaneous diuresis with fall of blood-urea level to 80 mg. per 100 ml. and evidence of recovery of tubular function, but on the 12th day of her illness she showed signs of generalised peritonitis, and she died on the 15th day.

Necropsy showed acute tubular necrosis of the kidneys.

Case 9.—A married woman, aged 37, pregnant for the 5th time, gave herself an intra-uterine douche with soapy water and 'Dettol' on June 18, 1950. This was followed by vaginal bleeding, backache, headache, and vomiting. She was admitted to hospital on June 27 as a case of incomplete septic abortion. On July 3 she underwent dilatation and curettage, and blood-transfusion was given for anæmia (Hb 48%). On July 7 she became drowsy and began having epileptic fits; she had passed urine only about once daily for the previous few days. Her blood-pressure was 176/112 mm. Hg and blood-urea 515 mg. per 100 ml. During the next few days she received intragastric drip-feeding with sugar, fat, and water only; no allowance was made for electrolyte loss in the urine, although her diuresis was steadily increasing. She entered a second phase of oliguria and finally became anuric [illegible] another rise in the blood-urea level, and a fall in blood-pressure due to sodium depletion. She was transferred to Hammersmith Hospital on July 1[illegible].

On admission she was pale and had [illegible] and a dry tongue. Pulse-rate 1[illegible] per minute; [illegible] 80/65 mm. Hg; [illegible] Chvostek's sign; [illegible] muscular weakness and was [illegible] irrational. The plasma [illegible] fell to normal (1·027) when she was given [illegible] chloride and sodium lactate with glucose. [illegible] depletion had been corrected her blood-pressure [illegible] and her blood-urea to fall and she began to pass [illegible]. After this temporary improvement [illegible] developed on July 2[illegible], and [illegible] finally coma, serum-potassium level [illegible] per litre, and the characteristic electrocardiographic [illegible] were present. Despite intravenous [illegible] she died on July 21.

Necropsy showed acute tubular necrosis.

Case 10.—A woman aged 2[illegible], had an abortion induced on [illegible], 1950, but she did not disclose the method used. She was admitted to hospital that day and spontaneous delivery of the fœtus followed with manual removal of the placenta. Blood-transfusion was given for shock. She was oliguric from the time of the abortion. She was transferred to Hammersmith Hospital in the late oliguric phase, and the intragastric drip-feeding régime was continued. She made a good recovery.

Case 11.—A woman, aged 21, aborted on Oct. 20, 1951, by a method not disclosed. She was admitted to hospital, but because of anuria was transferred to Hammersmith Hospital next day. Intragastric drip-feeding was started, but owing to continued vomiting this was changed to intravenous infusion of 2[illegible]% glucose given by 'Polythene' tubing into the superior vena cava. She made a good recovery.

Case 12.—A woman of unknown age was first seen in a nursing-home where a therapeutic abortion had been carried derivatives was then undertaken.[3–5] Non-sulphonamide thiodiazoles have no hypoglycæmic action, but several compounds of the *p*-amino-benzene-sulphonamido-thiodiazole group lower the blood-sugar in animals. The tertiary butyl and *iso*butyl derivatives are the most active; then, in decreasing order of activity, follow the butyl, amyl, isoamyl, propyl, and isopropyl derivatives. The ethyl and methyl derivatives are inactive in this respect. Recently another sulphonamide compound, sulphanilyl-*n*-butylurea, has been found to have a similar effect on the blood-sugar level.[6 7] This compound has been more fully investigated in man. After a dose of 2 g. a maximum concentration of free sulphonamide of about 7.5 mg. per 100 ml. of blood is reached in three hours, and there is a considerable fall in the blood-sugar level, which returns to normal in about six hours. The hypoglycæmia can be corrected by giving glucose. With this background information, it was a natural step to ascertain the effect of this substance in diabetic patients.

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So far the evidence is insufficient for any definite conclusion about the pharmacological action of these compounds. They clearly open up a new approach to the study of carbohydrate metabolism and diabetes mellitus. The preliminary reports suggest that they may be useful in the oral treatment of elderly diabetics but not of young or acidotic patients. Further carefully planned clinical trials may determine the place of these sulphonamide compounds in the management of diabetes, and we hope that the trials will be completed before these powerful substances become widely available.

Precocious Immunity

IN the classical sense immunity to an infection or toxin depends upon the presence of circulating antibodies. There are, however, circumstances in which some protection is conferred when the presence of antibodies can be excluded. Interference phenomena of this kind are seen in certain virus diseases. Of course, in the case of some viruses the presence of circulating antibodies can be detected and passive immunity can be transferred by serum from convalescent patients; but in other virus diseases the immunity appears to be due to exclusion effects, and after an initial acute infection a permanent symbiosis

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the insertion of a soap paste into the cervix, and another patient, a trained nurse, had passed an instrument into her uterus The other 4 patients refused to disclose details of their abortions

Case-reports

Case 1 —A woman, aged 38, gave herself a vaginal douche in the 4th month of pregnancy, 14 days before *admission* to Hammersmith Hospital on Oct 15, 1947 Vaginal bleeding, vomiting, and oliguria developed, but she had no medical attention until admission, when the products of conception were passed spontaneously She had passed a very small quantity of dark urine for several days after the onset of vaginal bleeding

On admission she was pale and drowsy and was vomiting She was already in the early diuretic phase of acute tubular necrosis, passing large quantities of dilute urine

Treatment and progress—She was given an oral Borst diet and her water and salt balances were maintained She made a satisfactory recovery and was in good health 2 years later, although she had diminished renal function and mild hypertension

Case 2 —A widow, a trained nurse aged 27, passed an instrument into her uterus on March 25, 1948, and aborted that day She was admitted to hospital next day because of anuria and jaundice She was given penicillin on account of fever, and intravenous feeding She was transferred to Hammersmith Hospital on April 1

On admission she was pale but not jaundiced, she had facial œdema and epistaxis and she was vomiting She had a raised venous pressure and a collapsing pulse There were basal crepitations in both lungs

Treatment and progress—The patient was given a protein-free diet, water and salt balance, and blood transfusion She was treated twice by dialysis with an artificial kidney, but she died from pyæmia on April 9

Necropsy showed acute tubular necrosis of both proximal and distal tubules with eosinophil casts in the distal tubules Acute endometritis and multiple pulmonary abscesses were also present

Case 3 —A woman, aged 27, aborted on April 12, 1948, when 22 weeks pregnant, details of the abortion were not disclosed She had been anuric from the time of the abortion, and had been admitted to hospital, where she was treated with forced fluids, potassium citrate, and intravenous sodium sulphate On April 16 she was given a high spinal anæsthetic, and the next day her right kidney was decapsulated On April 18 she was transferred to Hammersmith Hospital

On admission she was pale and drowsy, and had a high venous pressure in her neck and œdema of her legs She was treated with an oral Borst diet, water and salt balance, and dialysis (artificial kidney) on the 8th and 13th days of illness She made a good recovery

Case 4 —A woman, aged 24, gave herself an intra uterine douche of soapy water on Aug 28, 1948, with the immediate onset of shock, vomiting, and abdominal pain She was admitted to hospital that day and delivered of an immature fœtus She was given intravenous fluids and penicillin, and on Aug 30 high spinal anæsthesia was induced

She was transferred to Hammersmith Hospital on Aug 31 and an intragastric drip feeding regime (Bull et al 1949) was instituted She was severely ill in the early diuretic phase, but she eventually made a good recovery

Case 5 —A woman, aged 20, had a criminal abortion on Oct 20, 1948, and was subsequently admitted to hospital with uterine sepsis, peritonitis, and anuria She had blood-transfusion, intravenous fluids, and gastric suction Uræmic fits developed on Oct 26, and she was transferred to Hammersmith Hospital three days later

On admission she was comatose, acidotic, grossly œdematous, and moribund She died that day before dialysis could be performed.

Necropsy showed acute tubular necrosis of the kidneys

Case 6 —A woman, aged 27, gave herself a douche of soapy water on Nov 23, 1948 Within 24 hours she aborted and became oliguric and began vomiting, but she was not admitted to hospital until Dec 1, when she was given a blood transfusion for anæmia and kept in salt and water balance She was transferred to Hammersmith Hospital three days later, when the intragastric drip feeding regime was started, this was continued for 19 days Although she was severely ill on admission, she made a good recovery

Case 7 —A girl, aged 16, gave herself an intra uterine douche of soapy water on Nov 30, 1948 She was admitted to hospital that day, and her uterus was evacuated and penicillin given Blood-transfusion for anæmia was started after several days of anuria, and she was treated with forced fluids and mercurial diuretics without effect She was transferred to Hammersmith Hospital on Dec 9, when intragastric drip feeding was started, this was continued for 13 days She made a satisfactory recovery

Case 8 —A girl, aged 17, had an intra uterine douche of soapy water, and was admitted to hospital the following day with pelvic peritonitis and anuria There was spontaneous delivery of the fœtus, and the placenta was removed digitally Blood transfusion was given, and the intragastric drip feeding regime started She had a spontaneous diuresis with fall of blood urea level to 80 mg per 100 ml and evidence of recovery of tubular function, but on the 12th day of her illness she showed signs of generalised peritonitis, and she died on the 15th day

Necropsy showed acute tubular necrosis of the kidneys

Case 9 —A married woman, aged 37, pregnant for the 5th time, gave herself an intra uterine douche with soapy water and 'Dettol' on June 18, 1950 This was followed by vaginal bleeding, backache, headache, and vomiting She was admitted to hospital on June 27 as a case of incomplete septic abortion On July 3 she underwent dilatation and curettage, and blood-transfusion was given for anæmia (Hb 48%) On July 7 she became drowsy and began having epileptic fits, she had passed urine only about once daily for the previous few days Her blood pressure was 176/112 mm Hg and blood-urea 515 mg per 100 ml During the next few days she received intragastric drip feeding with sugar, fat, and water only, no allowance was made for electrolyte loss in the urine although her diuresis was steadily increasing She entered a second phase of oliguria and finally became anuric, there was another rise in the blood urea level, and a fall in blood-pressure due to sodium depletion She was transferred to Hammersmith Hospital on July 15

On examination she was pale and had dry, inelastic skin and a dry tongue Pulse rate 120 per min, blood pressure 80/63 mm Hg, jugular venous pressure not raised, positive Chvostek's sign, right septic parotitis She had general muscular weakness and was slow in thought and action but rational The plasma specific gravity was high (1 035), but it fell to normal (1 027) when she was given intravenous sodium chloride and sodium lactate with glucose When the sodium depletion had been corrected, her blood pressure began to rise and her blood urea to fall, and she began to pass more urine After this temporary improvement potassium depletion developed on July 20, with tremor, muscular weakness and finally coma, serum potassium level fell from 5 1 to 2 8 m eq per litre, and the characteristic electrocardiographic changes were present Despite intravenous potassium therapy she died on July 21

Necropsy showed acute tubular necrosis

Case 10 —A woman, aged 32, had an abortion on Aug 18, 1950, but she did not disclose the method used She was admitted to hospital that day and spontaneous delivery of the fœtus followed with manual removal of the placenta Blood-transfusion was given for shock She was oliguric from the time of the abortion. She was transferred to Hammersmith Hospital in the late diuretic phase, and the intragastric drip-feeding regime was instituted She made a good recovery

Case 11 —A woman, aged 21, aborted on Oct 20, 1951, by a method not disclosed She was admitted to hospital, but because of anuria was transferred to Hammersmith Hospital next day Intragastric drip feeding was started, but owing to continued vomiting this was changed to intravenous infusion of 20% glucose solution by 'Polythene' tubing into the superior vena cava She made a good recovery

Case 12 —A woman of unknown age was first seen in a nursing home where a therapeutic abortion had been carried sac itself are *not very helpful* But the fœtal mucosæ, especially apparently that of the vagina, provide sufficient suitable cells

There have *lately* been claims for endocrinological methods of antenatal sexing, but none of them seems to have provided an acceptable degree of accuracy Examination of the amniotic fluid seems to be the answer, and, if the first findings are confirmed, it remains *only* to decide what scientific use the method has It could be a *great satisfier of curiosity, and a social* convenience, but it is very seldom *strictly necessary to the health of* either mother or child to know the baby's sex in advance Indeed, it is easy to picture disastrous results, especially when the examination shows that the *child is of an* unwanted sex The discovery is of great interest, but its thoughtless use could be very harmful The same could be *said of pregnancy tests*, which have *sometimes* been abused, but no-one would deny the value of these tests, or of the number of new and unexpected observations in *related fields to which they have led*

Twins are a complication which is not discussed by Dr James or by Serr et al [6] Perhaps the chances of *confusion are not great*, but the occasional occurrence (not so rare apparently as is generally supposed [10]) of dissimilar twins in one amniotic cavity is a possible trap The frequency of multiple pregnancies in most animals of economic importance will probably reduce the interest of the method to veterinarians

Further interesting news of nuclear sexing by non-histological methods is the confirmation from two sources [11] [12] of Davidson and Smith's [13] method of sexing blood-films by examination of the polymorphs

POLYPOSIS OF THE COLON WITH ADDITIONAL FEATURES

MULTIPLE polyposis of the colon has long been known to be due to a dominant mutant gene with nearly 100% penetrance It has been clearly distinguished from Peutz's syndrome, in which other parts of the gastro-intestinal tract (stomach and small intestine) are involved Dukes [14] has lately given a good account of English families with multiple polyposis

A distinct and true breeding variation of the condition, also probably due to a dominant gene, was described in 1954 by Oldfield,[15] in which the polyposis of the colon was associated with multiple sebaceous cysts But, though only one small family was involved, it is possible, but unlikely, that two separate dominant genes, one for the polyps and one for the cysts, were present and that their association in the same individuals was *fortuitous* Another variant was recorded in the United States by Gardner [16] in which in addition to multiple polyposis there were widely distributed epidermoid cysts, fibromas, and osteomas Here a single dominant gene was clearly responsible Precisely the same condition has now been found in another family [17] It is certain, therefore, that here the association is not fortuitous and that a single pleiotropic gene mutation is responsible or, less probable, two or more closely linked gene mutations

Thus, one condition appears in some families by itself, and apparently the same condition, *with further features* constantly added, crops up in other families This situation has a number of parallels for example, pachyonychia congenita in some *families* is accompanied by follicular keratosis and xerodermia, in some families by teeth erupted at birth, but no skin changes, and in one family by follicular keratosis, xerodermia, erupted teeth, and sebaceous cysts Any explanation of the phenomenon must be speculative It seems unlikely that the resemblance within families and differences between families are due to gene modifiers, since they would not be constant within families Research in lower organisms has shown that much the same pheno-*typic character* may be due to a number of mutations of distinct genes which are nevertheless linked It has been suggested that the genes concerned bring about a *chain reaction* and that mutation of any of these may result in the same main biochemical dysfunction But the side effects of these mutations may well differ and *so add different features to the main condition* In other instances mutations having apparently the same main effect may take place on distinct chromosomes and under such circumstances the side effects might be expected to be even more variable

EPIDEMIC KERATO-CONJUNCTIVITIS

THE suggestion that epidemic kerato conjunctivitis was a virus infection was first made by Wright,[1, 2] who, in his study of an outbreak in Madras, was able to demonstrate what he called inclusions in corneal epithelial scrapings, and this material could be used to transfer the disease from man to man Attempts to isolate any infective agent in culture or by transmission experiments in animals were unsuccessful

In 1941 an epidemic of great economic importance broke out in the shipyard workers of the west coast of the United States and gradually spread through most of the country Working with the scrapings from one of these patients, Sanders [3] claimed to have isolated a virus by intracerebral passage in mice This virus could produce the disease in a human volunteer and was neutralised by convalescent serum from patients with the disease After two or three years the major epidemic wave died down and only sporadic outbreaks were reported, from these the Sanders virus was rarely isolated It is interesting to note that in many of these sporadic outbreaks the common connection between those infected was a visit to an ophthalmologist for some other condition, and on occasion it seemed that an instrument may have been the means of transfer—for example, all patients infected may *have had tonography* performed

During 1951 and 1952 work on the Sanders virus [4, 5] made it clear that it was a variant of the St Louis encephalitis virus, and it was *also shown* that sera from the local epidemics then occurring no longer neutralised the virus [6] In contrast to the experiences in the United States, claims to have *isolated* a virus *similar to the* Sanders virus have been made in Turkey [7] and Japan [8] In both cases the virus caused an encephalitis in mice, and Sezer was able to *adapt his virus to produce* lesions on the chorio allantoic membrane of the chick embryo

Despite the isolation of virus by Sanders and others, *there* was considerable *doubt about the importance* of these agents in the disease Recently the condition has been reinvestigated by two groups of workers—Fowle [9] *and her colleagues* in Canada and Jawetz [10] and his associates in California Both these groups have succeeded in isolating viruses of the A P C *group from their patients* In Canada the virus appeared to be an atypical form of course of illness Despite the institution of intragastric drip-feeding on the 11th day of her illness and the onset of diuresis on the 16th day, she died from pulmonary œdema In case 9, renal failure was recognised too late for effective treatment to be applied

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Summary

13 patients had acute renal failure after abortion, procured in most cases by intra-uterine douching with soapy water

In all patients the clinical features and laboratory data, and in the 5 fatal cases the necropsy findings, were those of acute tubular necrosis

Of the 5 deaths 3 were due to infection and 2 to water and electrolyte imbalance Some of these deaths could possibly have been avoided by rational treatment in the early stages

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MEDIASTINAL SURGICAL EMPHYSEMA
DUE TO PERFORATED DUODENAL ULCER

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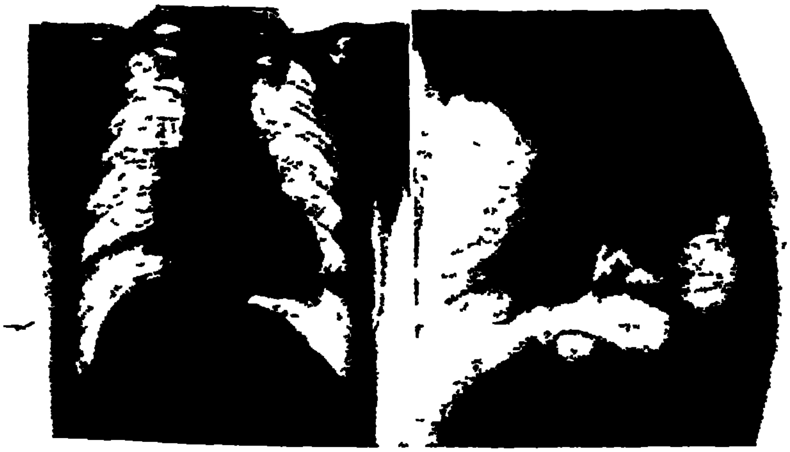
THE unusual case described here presented an interesting problem in diagnosis

Case-report

A man aged 72, was admitted to hospital seven hours after the sudden onset of severe upper abdominal pain Six hours previously he had noticed in the region of the right shoulder pain which rapidly became severe and persisted He had not vomited. He had long had "digestive troubles" without pain or dysphagia

On examination the patient was dyspnœic, immobile, and ill looking, with cyanosed extremities There was a diffuse surgical emphysema extending from the upper half of the chest-wall over the clavicles and suprasternal notch into the neck as far as the angles of the mandible The pulse was regular and of good volume, blood-pressure 200/100 mm Hg Respiration was rapid and shallow, and the upper abdomen was rigid, intensely distended, and grossly tympanitic



Anteroposterior and lateral radiographs.

Radiography—Anteroposterior and lateral radiographs of the chest and upper abdomen showed wide separation of liver from diaphragm, and mediastinal emphysema extending into the tissues of the neck (see figure)

Operation and Progress—Through a Ryle's tube a large quantity of air was aspirated from the stomach At laparotomy there was severe distension of the peritoneal cavity, which contained a large quantity of free gastric content On the anterior surface of the first part of the duodenum was a small perforation about the size of a pin-head Para-œsophageal herniation of the peritoneum, with intact wall was present The perforation was closed and the peritoneal cavity cleared by suction The wound was closed without drainage Postoperatively the bowel sounds returned on the second day, the emphysema had appreciably diminished by the third day, and finally disappeared on the twelfth day During convalescence there was no suggestion of a "post-operative chest" or of mediastinitis When the patient was seen at follow up six months later his general condition was good, and he was symptom-free

Discussion

Sudden spontaneous epigastric pain with abdominal rigidity, respiratory distress, and subcutaneous emphysema of the neck in an elderly patient is reasonably regarded as pathognomonic of spontaneous rupture of the œsophagus Yet this is uncommon, especially where there has been no previous evidence of an œsophageal lesion In the present case there was little reason to assume the presence of a predisposing œsophageal lesion such as injury, nor was there sudden overdistension by the ingestion of an over-bulky bolus or volume of fluid A trivial and unsuspected injury, however, may sometimes cause a breach in the mucosa producing a "dissecting" lesion (Nanson and Milnes Walker 1953) The patient was not shocked Clinically the likeliest diagnosis was spontaneous rupture of a healthy œsophagus—a disorder diagnosed preoperatively and successfully treated on only a score or so of occasions (most recently in three cases reported by Borrie (1955))

The clinical findings therefore indicated spontaneous œsophageal rupture, but this was not supported by the history There were however adequate grounds for diagnosing perforated peptic ulcer, and this diagnosis was later substantiated by the radiographic findings

The association of perforated duodenal ulcer with mediastinal surgical emphysema must be very rare Mediastinal emphysema is a recognised complication of artificial pneumoperitoneum, but the mechanism is not clear

In the present case air may have escaped into the mediastinum through a small breach in the thin peritoneum of the hiatus pouch, but this was not evident on cursory palpation At all events the radiographs demonstrate continuity of the abdominal and thoracic air. The important factor in this case was the extreme tension within the peritoneal cavity and stomach Gastric contents must have been forced into the lower mediastinum but this gave rise to no untoward reactions during convalescence

There is a good case for routine radiographic examination of the chest and upper abdomen in cases of clinically "obvious" perforated peptic ulcer

I thank Mr N E Stidolph, senior surgeon, Whittington Hospital, under whose care this patient was admitted, for the opportunity of treating and reporting the case

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Special Articles

PRESENT AND FUTURE COSTS OF THE HEALTH SERVICE

The Economic Evidence to the Guillebaud Committee

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IT is hard to recapture nearly three years later the mood of public opinion at the time the Guillebaud Committee was appointed There were many who believed that the National Health Service, adventurously launched in *1948*, would founder on the problem of finance The big supplementary estimates required for the service in the early years came as a shock to public opinion There was a widespread impression that the service was "*out of control*" Some ascribed the sharp increase in cost that was believed to have occurred to the boundless potentialities of medical science Others were under the impression that the demands of the aged were *very much greater than those* of younger people and feared the consequences of an ageing population on the bill for medical care Propelled by these and other forces, the cost was expected to soar relentlessly upward

These *apprehensions*, which were *expressed* in Parliament and outside, received support from the writings of Dr Ffrangcon Roberts His book on *The Cost of Health* was widely read and widely quoted Much of it was based on the experience of one teaching hospital

It was in this atmosphere that the Guillebaud Committee was appointed "to review the present and prospective cost of the *National* Health Service, to suggest means, whether by modifications in organization or otherwise, of ensuring the most effective control and efficient use of such Exchequer funds as may be made *available*, *to advise how, in view of the burdens* on the Exchequer, a rising charge upon it can be avoided, while providing for the maintenance of an adequate service, and to make recommendations"

Soon after the committee was set up, Mr Guillebaud asked the National Institute of Economic and Social Research to sponsor the preparation of a memorandum presenting an economic analysis of the costs of the National Health Service This memorandum, which was published this week in a revised form,[1] is summarised below Inevitably, conclusions are stated here without all *the reservations to which they are subject* And many questions discussed in the book are omitted

The cost of the National Health Service that emerges from the Government accounts is *ambiguous* Costs of many *different kinds are added indiscriminately together* in these accounts, the purpose of which is to ensure accountability to Parliament rather than to provide a useful record for economic *purposes* For example, the accumulation of cash and the purchase of herrings by hospital authorities clearly need separate treatment And, for certain purposes, higher remuneration awarded in one year for services performed in earlier years should be allocated to the year when the work was done, rather than to the year when payment was made

The figures which *follow* are derived from a laborious rearrangement of the official records of expenditure (published and unpublished) by the central Government, hospital authorities, executive *committees*, and local authorities Our main concern is with the cost of the National Health Service in terms of current productive resources to public authorities as a group, distinguishing current from capital *costs* so far as the records permit Often exact information was not available and we had to rely on estimates which we made in conjunction with the Ministry of Health The many qualifications to which *our figures* are subject are set out in the book

Current Cost

The current *cost of the National Health* Service falling on public authorities was £371$^{1}/_{2}$ million in 1949-50 In the subsequent years it rose by roughly *£15 million* each year, reaching £430$^{1}/_{2}$ million in 1953-54 This rise of £59 million was the result of a larger increase (£77 million) in gross costs, offset by a saving of £18 million by new or increased charges to beneficiaries

The *proportion of total* national resources (the gross national product) paid for by public authorities *fell* from 3$^{3}/_{4}$% in *1949-50 to* 3$^{1}/_{4}$% in *1953-54* Had the proportion of resources devoted to the service in 1953-54 been *the same as in 1949-50 the* net cost *would have* been £67 million higher

During the period under review there was a considerable general rise in prices We have tried to estimate the effect of *price increases on the cost of the Service*, recalculating expenditures at constant (1948-49) prices The current net cost of the service expressed in "real" terms in this way, was only *£11* million greater in 1953-54 than in 1949-50 Thus, the net *diversion of resources* to the National Health Service since 1949-50 has been of relatively insignificant proportions There was a *rise of nearly 2% in population during the period* under review Allowing for this and for changes in the age structure of the population, the cost *per head* at constant prices was almost the same in 1953-54 as in 1949-50

Trends of *expenditure have been very different* in different parts of the service Between 1949-50 and 1953-54 net current expenditure on the hospital services rose by £71 million, and that on local authority services by £11 million, while expenditure on executive council services fell by £24 million The movement of total health service expenditure thus represented the combined *result of these divergent trends, a fact which needs to* be taken into account in considering future trends

A major part of the rise in hospital expenditure was attributable to rising prices (£41$^{1}/_{2}$ million of the £71 million increase *from 1949-50 to 1953-54)*, but the rise in the net volume of goods and services purchased (£29$^{1}/_{2}$ million at 1948-49 prices) was also substantial The increase in labour services as a whole accounts for three quarters of the increase in resources used in the hospital service at constant prices The categories of staff which increased most were nurses and domestic staff The transfer of consultants from whole time to part time service and the expansion of the domiciliary specialist service contributed to the higher cost of labour services The major part of the increase in goods purchased by the hospital service was "medical goods" (drugs, dressings, equipment, appliances, &c) "Non-medical" purchases increased by only *£4 million* (7%) This increase of 7% was about the same as the increase in average daily occupied beds over the same period

Against this increase in cost have to be set the quantitative facts that the hospitals did more work for a larger national population, more confinements took place in hospital, more services were rendered to general practitioners, more provision was *made for road and industrial* accidents, more people were trained and more research was undertaken All these are quantitative indices of activity, what cannot be assessed is the *changing* work of the hospital as an agent of humanity

The different executive council services show different trends in expenditure While the pharmaceutical service and the general medical service each increased between 1949-50 and 1953-54 by £6 million, expenditure on the dental service fell by £24 million, and that on the *ophthalmic service by £13 million* The rise in the cost of the general medical service was almost entirely due to the increased cost per patient year resulting from the Danckwerts award to general practitioners The rise

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[1] The Cost of the National Health Service in England and Wales By B ABEL-SMITH and R M TITMUSS London Cambridge University Press 27s 6d

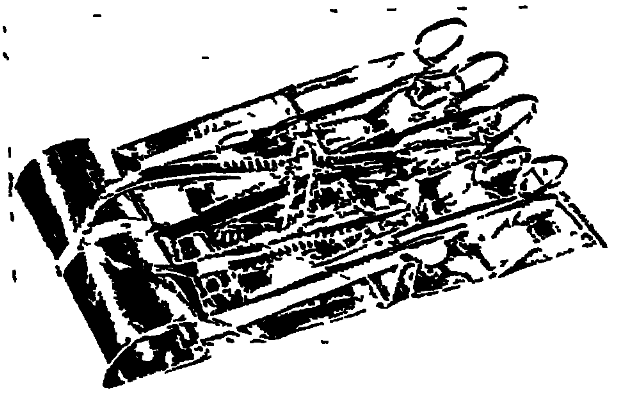


Fig 2.

In use, it has been found expedient to keep a threaded curved triangular needle fixed in the needle-holder

I am indebted to Mr R E W. Fisher, of Gillette Industries Ltd, for technical assistance

Gillette Industries Ltd
Isleworth Middx

GERALD OLLERENSHAW
M.A, B M. Oxfd

A HEADLIGHT FOR GENERAL SURGERY

It is necessary in many operations to see deep into narrow spaces At a certain degree of depth and narrowness this can only be done by means of a light which originates in front of the surgeon's eyes and coincides fairly closely with his line of sight This of course means a headlight and after many attempts I have designed one which satisfies me Its points are

1 Brilliancy sufficient to compete with the intensity of ordinary main operating-lights, so that there is no need to darken the theatre

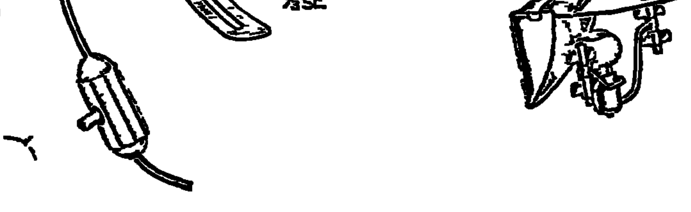
2 An area of illumination intense in the centre, gradually fading out towards the edges This corresponds to the visual consciousness of the surgeon, and is far better than the clear-cut levelly illuminated field I at first tried for Any slight irregularities in the field of light will be found quite unnoticeable when working

3 An approximately parallel beam, which remains without significant change in area or intensity on variations in working distance This can be attained only by a reflector system

4 A beam which coincides with the line of sight closely enough for all ordinary surgical work The slight increase in optical efficiency gained by looking through a hole in the mirror does not compensate for the loss of peripheral vision

5 A frame to hold the bulb which allows focusing accurately and firm fixation when this is arranged

6 An attachment to the head which is easily adjusted and which does not depend on that tight grip across the forehead which causes headache. The slight weight of the light is taken by an overhead band loosely held at either end by a circular one



7 An adjustment for different types of work by a friction joint allowing the only movement necessary—that of up and down in the sagittal plane (Most headlights have absurdly complicated and varied mountings) This can easily be adjusted by a non-sterile assistant

8 A bulb with an opaque-mirror backing over the front two-thirds of the lens This increases the light sent backwards into the mirror and in addition stops glare getting into assistants eyes

9 A shield round the lower part of the mirror to prevent glare into the surgeon's eyes It is possibly the lack of these last two devices which has caused the non-perforated reflector type of light to be little used

10 A battery, cheap and of large capacity, specially adapted to the bulb, it is worn on a belt round the waist with an ordinary commercial switch on the flex so that it can be put into action through the gown The light can, of course, be run off the main by those who do not object to being tethered by a flex

The light is made by Messrs Down Bros of 32, New Cavendish Street, London, W 1, to whom I am indebted for help in working out many details

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DENIS BROWNE
F.R C S

Reviews of Books

Breast Cancer and its Diagnosis and Treatment

EDWARD F LEWISON, M.D F.A C.S, assistant professor of surgery, Johns Hopkins University School of Medicine Baltimore Williams & Wilkins London Baillière, Tindall, & Cox. 1955 Pp 478 114s

In a foreword, Dr Grantley Taylor admirably sums up the importance of cancer of the breast to the whole problem of malignant disease As he points out, our ideas of malignant disease "derive largely from observations of breast cancer", and "breast cancer was the prototype for the development and perfection of the concept of the radical operation for cancer" The experimental study of heredity in cancer has been chiefly carried out on cancer of the breast in mice Again, cancer of the breast is one of the few forms of cancer which has so far responded to "therapeutic modifications of the hormonal environment" It is no wonder therefore that many people feel that, if the exceedingly tough shell of the cancer problem is broken at the clinical level, it is likely to be through cancer of the breast

This book assembles the known facts, with the emphasis on the tradition of surgery of the Johns Hopkins, and particularly of Halsted Thus, the first chapter gives an interesting account of the history of breast cancer the culmination of which is the development of the operation of radical mastectomy by Halsted And the greater part of the book represents the traditional surgical point of view, given by a surgeon who obviously has extensive knowledge and experience and has given much thought to the practical problems involved

Dr Lewison has taken the lion's share of the work, but he has been helped by eight distinguished colleagues The one British contributor, Mr R S Handley, has written an excellent chapter on the surgical anatomy of the breast, in which he cleverly manages to give a dynamic twist to the subject and to discuss the principles of breast surgery This is the only part of the book in which the question whether the pectoralis major should be sacrificed in radical mastectomy is discussed elsewhere this procedure, the main technical contribution of Halsted to breast-cancer surgery, is unquestioningly accepted The book makes no reference to the classical article by Gray on the lymphatics of the breast, which undermines the traditional pathological arguments in favour of routine removal of the pectoralis major

There is a very detailed account of "classical" radical mastectomy, but in the chapter on hormonal treatment only a bare mention (without any technical operative details) of adrenalectomy, and no discussion of the possible ways of destroying the pituitary influence Diagnostic manœuvres are fully described, and the importance of biopsy is properly stressed The author rightly notes that palpation of the breast should be carried out with the pulps of the fingers

In the case of capital expenditure, the central Government has proved a much sterner master than local authorities and those who directed the voluntary hospitals The population changes estimated for the next twenty-five years give no cause for concern

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Public Health

POLIOMYELITIS VACCINATION

At a press conference on Jan 19, Mr R H Turton, the Minister of Health, announced that a British variant of the Salk vaccine would be ready for local health authorities to use during May and June of this year Only a limited amount of vaccine would be available, and it would be given free under the National Health Service Mr Turton hoped that between 300,000 and 500,000 children would be vaccinated by the end of June Only children born in the years 1947–54 could be considered for vaccination at present, the scheme was entirely voluntary, and written permission for vaccination from parents or guardians was obligatory No vaccinations would be given between the end of June and November (the poliomyelitis "danger period"), and those children who could not be vaccinated before the end of June would receive priority when more vaccine had been prepared later in the year Each child would have two intramuscular injections of 1 ml of the vaccine with an interval of not less than three weeks between the injections For the time being, only local health authorities would be given supplies of the vaccine, but, when more became available, general practitioners would be given the opportunity of participating in the scheme

Mr Turton said that the British vaccine, which will be the only type used, had been subjected to the most stringent safety tests and was preferable to any made in other countries Asked whether parents might hesitate to have their children vaccinated because of the cases of poliomyelitis during early trials in the United States, he pointed out that, because of improved safety measures, at least 10 million children in the United States and over 1 million in Canada had since been vaccinated without a single mishap, and he was confident that this knowledge would remove any doubts as to the vaccine's safety

Prof S P Bedson, F R S, chairman of the Safety Committee of the Medical Research Council, said that the British vaccine was prepared from three strains of virus, but the highly virulent type I (Mahoney) strain of the Salk vaccine had been replaced by one of lesser virulence, it was planned eventually to replace types II and III with milder strains

Vaccine is being manufactured in the Glaxo and Burroughs Wellcome laboratories Both laboratories have substituted a less virulent strain for the type I used by Salk, and we understand that the Wellcome vaccine will contain attenuated strains of type II and III virus, as used by Sabin

A Ministry of Health circular to county councils and county-borough councils says that the councils should explain the proposals to all parents (or guardians) of children of eligible age in their area and ask them to express their willingness in writing to have their children vaccinated The circular goes on to say that "the selection of children to receive the vaccination from among those whose parents seek it will be made according to a centrally determined plan designed to maintain an even spread throughout the eligible age groups which will be based on the month of birth When the national picture can be studied local health authorities will be informed which months in each age group have been selected and the children whose birthdays are in those months should be vaccinated as and when the vaccine is received by the local health authority"

Influenza in Suffolk

As we briefly reported last week, there has been much influenza-like illness in recent weeks in Suffolk, and influenza-A virus has been identified from 2 cases in Ipswich A doctor in practice in the area has kindly sent us the following account of his experiences of the epidemic

"It began in mid December just as we were in the middle of an epidemic of measles The illness affected all ages and often involved several members of the household The incubation period was from 2 to 3 days The epidemic reached its height in the first week of January and has now practically disappeared

"The onset was acute with headache, generalised pains in the back and limbs, pyrexia, tachycardia, and, within 24 hours, a cough In younger patients the cough appeared to be a manifestation of a tracheitis, in the older people the disease often progressed to acute bronchitis and in the very old bronchopneumonia was fairly common My partners felt that for the bronchopneumonia aureomycin (chlortetracycline) or 'Achromycin' (tetracycline) was the most helpful, but I saw 4 cases in which the response was inadequate and penicillin was successful In the absence of antibiotic treatment the pyrexia lasted for 2 to 3 days, and by the 4th day most patients were much better, but the cough often persisted for a week or 10 days and longer in those who had bronchitis

"About 190 cases were seen among about 10,500 patients Only 1 death was attributable to influenza—in a man of 89 who died within 48 hours of bronchopneumonia In conjunction with the Public Health Laboratory Service we are trying to isolate the virus from garglings and to find antibodies in blood taken from the 10th to 21st day after the beginning of the illness

"On the whole we do not regard this as a big epidemic, and we were rather surprised to learn that the sickness-rate was so high compared with the rest of the country The epidemic is now tailing off and today (Jan 19) only 3 new cases were seen"

Before Our Time

A RELIC OF AN 18TH-CENTURY ISOLATION HOSPITAL

FRANCIS W STEER

F S A

COUNTY ARCHIVIST, EAST AND WEST SUSSEX

IN 1718, on her return from Constantinople, Lady Mary Wortley Montagu began to advocate the practice of inoculation against smallpox Seven condemned criminals were used as guineapigs in 1721, the success of the experiment led to two members of the royal family being inoculated in the following year But the idea of inoculation was to begin with "suspected as unnatural and even impious"[1] Bishops and clergy preached against it, though smallpox had been responsible for 1 out of every 14 deaths in London in 1723 From the journals of St Bartholomew's Hospital[2] we learn that in 1752 "it was resolved that patients taken ill with small-pox be immediately removed into other wards to be kept separate for that purpose", the wards named Job and Lazarus were aptly selected for these isolation blocks

Smallpox was common and devastating in the country as well as in towns, and it was a heavy burden on the poor rate because an outbreak meant expensive nursing charges After the early experiments with inoculation, the disease slackened, particularly in the country districts, but bills among the papers of the overseers of the poor

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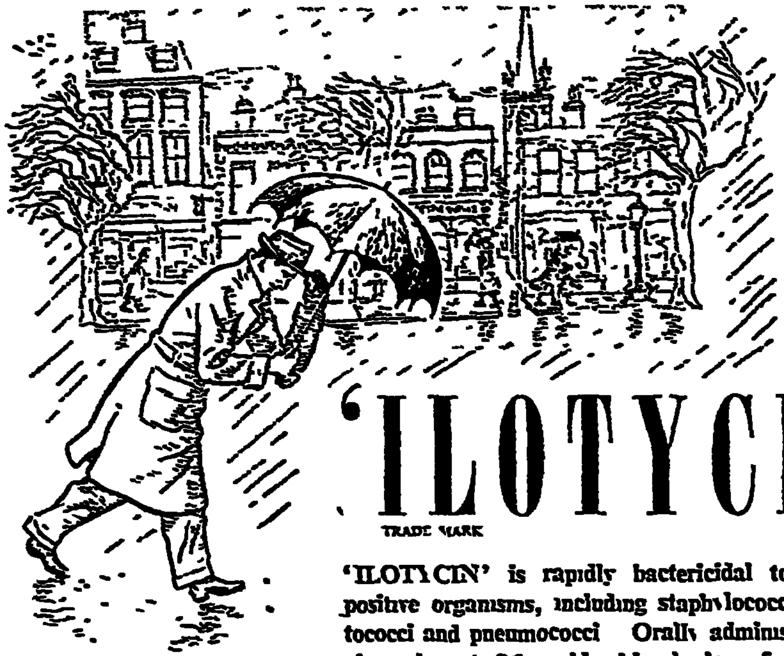
[1] Trevelyan, G M English Social History London, 1945 p 344

[2] Moore N History of St Bartholomew's Hospital London, 1918 vol 2, p 370



In common winter infections . . .

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'Eminently suitable for medicinal purposes'

'In view of these analytical and general evidences, this brandy may be described as particularly suitable for medicinal purposes'

See Lancet, July 22, 1899, p. 219

'The evidence both of analysis and taste indicates that the high standard of purity and quality has been maintained and that the brandy is eminently suitable for medicinal purposes'

See Lancet, May 7, 1932, p. 992

make friends with MARTELL

My visit may be the only live contact these remote folk have with the outside world within a week during the cold winter months I have learnt that a doctor's job may be varied On a night call I may find a patient with coronary thrombosis and give morphia But the house is cold and lonely for the old folk who have no outside help, and the kindling of a blazing fire in the hearth brings the patient almost as much comfort as the injection At another house an old lady is panting with asthmatic bronchitis I count out the antispasmodic tablets for her into a saucer, but far more important I supervise the removal of her bed from a bedroom up rickety stairs to the sitting-room on the ground floor It would be worth calculating the digitalis equivalent of this simple manœuvre to the over-burdened heart Yet another woman with involutional melancholia sits there immobile day after day I can do little for her She has had expert treatment But one thing she will let me do—cut her nails

* * *

G P s and M P s alike can hardly wait for the latest number of *Proscribers' Notes* with its detailed account of the recent brilliant investigation by Prof T Cobbleigh and his colleagues [1] at the Widdicombe Research Unit

These workers injected watery solutions of different antibiotics into a series of patients, and (owing to the near-sightedness of Professor Cobbleigh) also into a grey mare The mare hastily went A W O L, but all the patients recovered As water was the only ingredient common to all the injections, the logical inference is that the water was the curative agent

After the injection, the patients were asked, "How do you feel?"

25 % (Group A) replied, "Better"
25 % (Group B) replied, "Worse"
25 % (Group C) replied, "Don't know"
25 % (Group D) replied, "x — — — x x x you x x!"

He—i e, group D—was thereupon withdrawn from the series and sent for a Freudian analysis

When the survivors were confronted with further injections, even a glimpse of the solution in the syringe produced dramatic improvement For example, group B said that he had originally replied "Worse" only because the needle was getting a bit blunt when it was his turn, and group C acquired such an improvement of insight into the extent of his recovery that he reached the front door of the unit before recapture

The final percentage figures, confirmed by UNIVAC, random sampling, and extrapolation of skew-curve deviation—due to the bubbles in Professor Cobbleigh's syringe—prove that antibiotics are unnecessary

This discovery is as timely as it is revolutionary, for, as Professor Cobbleigh emphasised, there is a number of antabiotic addicts in these islands Indeed a suspected fourth one was reported yesterday, but it was found that he was only collecting the little bottles for his children to play with In contrast, there are no cases known of addiction to injections of water

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BALLAD OF SMITHFIELD

Twa butchers sat in Smithfield fair,
Bummaree, O Bummaree!
And there they made their moan so sair,
By the bonnie church of Bartholomew

There cam a buyer bold and brave,
Intent, it seems, on ways to save

"*Now sell me meat* of goodly brand,
And place it safely in my hand"

"O robber false, thy haste now stay,
Thou canst not carry it away

"Of trusty porters there's five score,
Ignore them and they'll raise a roar"

He's ta'en the meat in his right hand,
And flouted all the porter band

Foul fa' the hand that takes the meat,
Bummaree, O Bummaree!
And leaves the porters sair to greet,
By the bonnie church of Bartholomew

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[1] Pearse T, Brewer W Stewer J, Gurney P Davey P Whiddon D Awke A Cobbleigh T, et al (1955) *Widdicom lächerliche eingebildete Entdeckung and Advertiser* 123 45678

Letters to the Editor

DOMICILIARY CONSULTATION IN PSYCHIATRIC PRACTICE

SIR,—I am glad that Dr Hopkins now makes it cle (Jan 14) that admission to hospital was advised in 3 of the 5 schizophrenic patients in his series, though this was achieved in only 1

His very full reply to my inquiry emphasises two matters of considerable importance first, the need for agreed clinical criteria that should be fulfilled in order to establish a diagnosis of schizophrenia, and secondly the need for helping people with disabled personalities (whether due to partially remitted schizophrenia, inveterate neurosis, or anomalous deviation of the personality) who are incapable of benefiting by further active treatment, and are not ill enough to require prolonged hospital care but not well enough to stand on their own feet in the community In such cases the accent is often on social rather than strictly medical methods The day hospital that Dr Hopkins mentions is one practical step, certainly in large towns Another possibility is boarding out, which for many years was successful in Scotland and on the Continent but has never found much favour in England and Wales, perhaps because the propaganda which might have led to its effective adoption was in some ways imperfect when it was last propounded in the early 1930s

There is now a third possibility It is surprising how seldom one sees reference, in this context, to the powers of local authorities under Part III of the National Health Service Act A fair analogy would be to compare the kind of crippled personalities that we are discussing with ambulant tuberculous patients who can no longer benefit by inpatient treatment Progressive local authorities make no bones about their duties in respect of such patients, but few of them seem to have taken very active steps about the community care of mentally disabled persons other than ascertained mental defectives It is not easy to suggest exactly what local authorities might do, but at least it would be a beginning if one or two pilot surveys were made, in representative areas, in order to ascertain the numbers of such persons, the extent of their disabilities, their social circumstances, and the prospects of employing them gainfully under supervision, possibly as registered disabled persons Such surveys might justify the experimental establishment of one or two small hostels specifically for the use of patients within this group whose domestic circumstances were such that they could not suitably remain in their own homes, though they need not occupy beds in mental hospitals Such an experiment would be rather differently oriented from the "therapeutic community" type of venture, for it would aim to deal with those who, from the start, have little or no chance of complete rehabilitation

Dr C A H Watts's [1] survey, to which Dr Hopkins refers, is valuable and realistic in showing how this problem affects general practitioners as things are at present But there is more in this problem than clinical attention to individual patients, and I feel sure that general practitioners and psychiatrists together would welcome a more widely informative survey, and, if practicable, more comprehensive help, than any individual can provide

Warneford Hospital,
Oxford

IAN SKOTTOWE

SEXING FŒTUSES BY EXAMINATION OF AMNIOTIC FLUID

SIR,—Now that the sexing of nuclei has come into the field of exfoliative cytology,[2 3] its applications can be extended further The sediment of amniotic fluid

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[1] Watts, C A H *Lancet* 1954 ii 85
[2] Moore L K Barr M L *Ibid* 1955 ii 57
[3] Carpentier P J Stolte L A M, Visschers G P *Ibid*, p 874

THE LANCET
LONDON SATURDAY, JAN 28, 1956

Restriction of Antibiotics ?

AMONG antibiotics, erythromycin has the particular merit that it will often work when others have failed and from time to time we have urged our readers not to blunt this therapeutic weapon by using it for lesser purposes, but to keep it sheathed unless nothing else will save the patient's life The advantages of doing this are plain, but so also are the difficulties, and the New Zealand government have decided that on this subject advice to doctors must now be reinforced by restrictions Because a number of children have died from infections by organisms no longer vulnerable to any antibiotic, they have decreed that, from Feb 1, New Zealand doctors shall be able to get erythromycin only through hospitals and only for the treatment of diseases which do not respond to other remedies This announcement by the minister of health, Mr J R HANAN, will arouse interest in many other countries, for, like the ban on heroin, the action now being taken may be regarded as an interference, by a government, with the doctor's freedom to treat his patients in whatever way he chooses

Looking at it bacteriologically and epidemiologically, there seems everything to be said in favour of the New Zealand decision When penicillin was first made available to civilian hospitals in 1944, in desperately small quantities, its use as a life-saver was one of the spectacular advances of our time Those who had the hard task of allotting the scarce supplies will remember the many painful decisions they had to make, and the early days of penicillin were often darkened by the need to refuse, but they were also lightened by the remarkable efficacy of the drug when it was used in the right way in the right cases In those days of scarcity a few skilled hands achieved excellent results, and there were no mysterious and fatal forms of enteritis and no other complications due to sensitised patients and resistant organisms Now that antibiotics are plentiful, cannot the benefits of the lean years be restored, without their sufferings, by restricting the use of these substances, by common consent ? On purely scientific grounds, it is hard to see why such restriction should not have the desired effect, if it is wisely and firmly applied, for, when an antibiotic is used less widely, the number of bacteria resistant to it diminishes swiftly If the New Zealand plan is to do what is intended, the hospitals, of course, will have to be even more sparing than the general practitioners in their own use of erythromycin, for it is hospitals, not sickrooms in the home, that are the great sources of antibiotic-resistant organisms We hope, therefore, that Mr HANAN has told the hospitals to go very carefully in their own use of erythromycin Provided this vital point is covered, there are very good reasons for keeping one or more antibiotics in reserve for use in the last resort

But how exactly should the restriction be secured ? Some doctors are notably careful in their prescription of antibiotics, and it may be that the proportion who take thought about this has increased as more and more accounts have been published of the dangers of abusing these agents But it is still unfortunately true that the habit of giving antibiotics unwisely and even casually is the cause of much avoidable disability to patients and it would be over-optimistic to suppose that the mere publication of advice is enough to ensure that a drug such as erythromycin is used only when life is in imminent danger It would no doubt be easy to arrange for a suitably qualified group of doctors to meet from time to time to survey the antibiotics in use and to recommend that one or other should be "rested" long enough to restore its full power, but difficulty might well arise as soon as a move was made to give such recommendations the force of law It is possible that the kind of restriction now applied in New Zealand would be found acceptable here because its pattern resembles that already adopted for the distribution of important drugs while they are still scarce, and because it does not in fact embody anything like a complete ban On the other hand, recent happenings have made it seem likely that a regulation on the New Zealand pattern would be resented in this country Thus, paradoxically, it looks as though a course of action which most doctors would acknowledge to be sound scientifically, and necessary for the good of patients, may be neither voluntarily adopted nor tolerated if imposed It is evident that, as a profession, we must try to discover means of bringing to bear upon the interests of all patients, whether known to us by name or not, the kind of wise judgment and resolute action which a good doctor prides himself on giving the patient directly in his charge The New Zealand decision should make us think again about the way in which antibiotics are being used in our own country, and we should also consider from whom, if not from a Government, doctors would accept direction on such subjects

Sulphonamides and Hypoglycæmia

DURING a clinical trial of the chemotherapeutic action of *p*-amino benzene-sulphonamido-isopropyl-thiodiazole, JANBON and his associates[1] noted that this substance produces a fall in the blood sugar level which may be so profound as to lead to hypoglycæmic coma This clinical observation was confirmed by experimental studies in rabbits and dogs[2] Oral or subcutaneous administration to dogs results in hypoglycæmia, the blood-sugar falling to as low as 40 mg per 100 ml within five hours With continued administration, chronic hypoglycæmia develops and may cause irreversible neurological changes similar to those observed after prolonged insulin hypoglycæmia The decrease in blood-sugar is proportional to the concentration of this sulphonamide in the blood, and experimentally, hypoglycæmia is obtained with [illegible] lower doses if the sulphonamide is injected [illegible] into an artery supplying the neck of [illegible] After total removal of the pancreas [illegible] hypoglycæmic action, but it persists [illegible] of the gland is left A stud[illegible] its full complement of nurses of both sexes and a waiting-list

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[1] Janbon M, Chaptal J [illegible] *méd* 1942, 21 22

[2] Loubatières A [illegible]

None of us likes empirical treatments We are not enamoured of electroplexy, insulin, or neurosurgery Nevertheless, when employed with discrimination in every orthodox mental hospital, these methods produce remissions or recoveries They are not used for administrative purposes or as methods of restraint The ever *increasing* number of open wards, better atmosphere, and vastly increased freedom extant in such hospitals should be apparent to the meanest intelligence or most careless observer

Finally, no nurse of ours polishes floors Nurses of both sexes, if asked by Dr Hunter, will inform him in no *uncertain* terms that the last two decades have brought them increased dignity, stature, and standing rather than the reverse

We realise that we still have far to travel in the field of psychiatry, and we feel that its interests would best be *subserved* by balanced judgments and *fewer* sweeping assertions on the part of those practitioners in this sphere not immediately connected with mental hospitals

Dr Hunter would be well advised to pay a round of visits to representative mental hospitals wherein we are convinced he will find nursing personnel with erudition and *dignity* equal to his own

H C Beccle
Physician superintendent

Springfield Hospital,
London, S W 17

Morris Markowe
Deputy Physician superintendent

VENO-OCCLUSIVE DISEASE OF THE LIVER

Sir,—Your annotation on this condition [1] does not refer to our first article [2] in which the histology and pathogenesis—slightly misrepresented in your annotation—were fully described

Pathology Department,
University College of the West Indies
Mona St Andrew, Jamaica

G Bras

INTRAGASTRIC MILK DRIP IN TREATMENT OF UPPER GASTRO-INTESTINAL HÆMORRHAGE

Sir,—Dr Dawson, in his article on the continuous intragastric milk drip in the treatment of upper *gastro* intestinal hæmorrhage (Jan 14), makes critical reference to our observations [3] on the value of the indwelling tube in the management of hæmatemesis Our continued experience of the method, which now extends to 225 patients, has, if anything, increased our confidence in the procedure

The recognition of further gastric hæmorrhage formed *only a small part of the original study of* 105 patients, of equal value, and disregarded by Dr Dawson, has been the information provided as to the site of ulcer by the association of clear aspiration specimens with clinical evidence of continued bleeding, indicating a source of hæmorrhage beyond the pylorus These factors, in conjunction with the gastric secretory patterns observed during and after the acute stages of gastroduodenal hæmorrhage, led to the correct recognition of the pathological cause of the bleeding in a significant proportion of the patients studied We suggest that the complete application of the method might have improved the results obtained, our mortality of 4 8% in 225 unselected patients so investigated comparing favourably with Dr Dawson's series (8 in 100 patients)

We would agree with Dr Dawson that the reappearance or continuance of blood-staining of the gastric contents does not necessarily herald a further massive hæmorrhage, but its presence gives no grounds for complacency, and, with other criteria, will lead to the earlier recognition and treatment of this complication

We believe that a complete regard for all the points ma *in our paper* can do much to stimulate awareness of th diagnostic *problem and* to facilitate its earlier solutio *From our further* experience we see no reason to modif *our original* conclusion that early gastric aspiration a *materially in the management* of hæmatemesis

Department of Medicine,
University of Leeds

G N Chandler
G Watkinson

BREAD

Sir,—Professor McCance and Dr Widdowson concluded their article on Old Thoughts and New Work on *Breads* White and Brown [1] by saying "It is of course always quite possible that little attention will be paid to these experiments of ours " I have just re read their original report,[2] which confirms the conclusion I first came *to that the* experiments were vitiated by *the fact that* no *consideration* had been given to the *possibility that the* children suffered from hypothyroidism, and that iodine was the limiting factor in their inability to grow On seeing these undergrown children it is astonishing that any clinician could have *overlooked* this, apart from the fact that Duisburg is, I believe, in a goitrous area The effects of the secretion of the thyroid on protein *fat*, carbohydrate, and calcium metabolism, on nerve muscle function, on reproductive activity, and on resistance to infection are well known [3]

The *following* data *from* these experiments support this contention

At the start of the studies 5 children at Duisburg and 3 at Vohwinkel had thyroid enlargement, at the end 64 at Duisburg (66%) and 27 at Vohwinkel (50%) had enlarged thyroids The protein range at Duisburg was 61–73 g, at Vohwinkel 51–53 g, and in both groups the weight increase in the same time was the same, so that it can be seen that the lower Vohwinkel supply of protein was adequate for growth, the excess protein at Duisburg merely going to supply energy and accounting for the increased hypothyroidism in that group This is the reason why the addition of milk was ineffective owing to the exhaustion of the available iodine and the *comment* "cannot be improved by a milk supplement" is *meaningless*

The delay in epiphyseal ossification is typical of hypothyroidism, quite a different radiological picture to that of rickets The continued presence of skin infection supports this contention, as *does* the complete absence of puberty in boy *of* 14 *Amongst* British boys puberty may start at 10 or 11 years *Iodine* was given, and this in itself should have suggested the nature of the deficiency The *puzzling* œdema is due to the unbalanced vitamin supplement added to the 70% extraction flour and causing a conditioned vitamin B_1 deficiency It is said that the children were so ravenous that they cleared every scrap of food and yet gave scraps of food to the monkeys in the zoo This does not appear to have been allowed for in the tables One wonders what else the children *did ?*

It can be seen therefore that there are no grounds for Professor McCance's conclusions, as the question of iodine being the limiting factor in failure of growth was not considered, and the internal evidence in the experiments strongly *suggests* that it was

"Man cannot live by bread alone" It has never been claimed *that* man can subsist on wholemeal bread alone but with other foods it enhances their combined nutritional value It is astonishing that the claim should be made that the experimental diets were nutritionally adequate, when the subjects of the studies are shown at the end to have enlarged thyroids, skin sepsis, delayed puberty, bad teeth, and delayed epiphyseal ossification —and at an age well below that in which they will be called upon to sustain all the vicissitudes of life

Winnipeg, Manitoba
Canada

E P Evans

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[1] *Lancet* 1955, ii 1284
[2] *Arch Path* (*Lab Med*) 1954 57 285
Chandler G N, Watkinson G *Lancet*, 1953 ii 1170

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[1] McCance R A, Widdowson E M *Lancet* 1955 ii, 205
[2] Widdowson E M McCance R A *Spec Rep Ser med Res Coun Lond* no 287 H M Stationery Office 1954
[3] *Physiol Rev* 1951, 31, 205

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But how exactly should the restriction be secured ? Some doctors are notably careful in their prescription of antibiotics, and it may be that the proportion who take thought about this has increased as more and more accounts have been published of the dangers of abusing these agents But it is still unfortunately true that the habit of giving antibiotics unwisely and even casually is the cause of much avoidable disability to patients and it would be over-optimistic to suppose that the mere publication of advice is enough to ensure that a drug such as erythromycin is used only when life is in imminent danger It would no doubt be easy to arrange for a suitably qualified group of doctors to meet from time to time to survey the antibiotics in use and to recommend that one or other should be ' rested ' long enough to restore its full power, but difficulty might well arise as soon as a move was made to give such recommendations the force of law It is possible that the kind of restriction now applied in New Zealand would be found acceptable here because its pattern resembles that already adopted for the distribution of important drugs while they are still scarce, and because it does not in fact embody anything like a complete ban On the other hand, recent happenings have made it seem likely that a regulation on the New Zealand pattern would be resented in this country Thus, paradoxically, it looks as though a course of action which most doctors would acknowledge to be sound scientifically, and necessary for the good of patients may be neither voluntarily adopted nor tolerated if imposed It is evident that, as a profession, we must try to discover means of bringing to bear upon the interests of all patients whether known to us by name or not the kind of wise judgment and resolute action which a good doctor prides himself on giving the patient directly in his charge The New Zealand decision should make us think again about the way in which antibiotics are being used in our own country, and we should also consider from whom, if not from a Government, doctors would accept direction on such subjects

Sulphonamides and Hypoglycæmia

DURING a clinical trial of the chemotherapeutic action of *p*-amino benzene-sulphonamido-isopropyl-thiodiazole, JANBON and his associates[1] noted that this substance produces a fall in the blood-sugar level which may be so profound as to lead to hypoglycæmic coma This clinical observation was confirmed by experimental studies in rabbits and dogs[2] Oral or subcutaneous administration to dogs results in hypoglycæmia, the blood-sugar falling to as low as 40 mg. per 100 ml within five hours With continued administration, chronic hypoglycæmia develops and may cause irreversible neurological changes similar to those observed after prolonged insulin hypoglycæmia The decrease in blood-sugar is proportional to the concentration of this sulphonamide in the blood, and experimentally, hypoglycæmia is obtained with much lower doses if the sulphonamide is injected directly into an artery supplying the neck of the pancreas After total removal of the pancreas there is no hypoglycæmic action, but it persists if as little as a fifth of the gland is left A study of several thiodiazole area of the mamma, (2) the female sex hormones might take on local antigenic properties by passing through a similar denaturing process due to the radiation injury, or (3) in the mammary region, denatured cholesterol derivatives (the breakdown products of healing tissue cells, rich in cholesterol, and exposed to the heavy injury of irradiation with 6000r) might act as antigens and produce multivalent antibodies directed against a series of structurally related steroid hormones

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[1] Janbon M. Chaptal J Vedel A Schaap, J D *Montpellier méd* 1942 21–22 441

[2] Loubatières A. *C.R Soc Biol Paris* 1944, 138 766

Whatever the explanation, it seems that the primarily fixed antibodies, or those becoming sessile under the influence of the X-irradiation, manifested themselves by a pronounced allergic reaction Since general sensitivity to testosterone propionate (though in lesser degree) was demonstrated, and the Arthus like local necrosis suggested either an immediate or a delayed hypersensitivity,[2] antigenicity of the endogenous steroid hormones seems the most probable explanation

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OPPORTUNITIES IN AUSTRALIA

SIR,—I read with interest your correspondent's article last week I had a practice for several years in a small country town, such as is mentioned by your correspondent I should go further and say that to earn this figure of £A8000 per annum was exceptional and that £A5000, with one-third expenses, was much more general I do agree that most Australians welcome English graduates They also have a very high standard of all-round general practice, particularly surgery

I should finally like to add that it is a well-worthwhile adventure for anyone without family restrictions and that, as stated, three years would see him well established

Manchester R I JOHNS

INTERMITTENT CLAUDICATION AND SYMPATHECTOMY

SIR,—I have read with great interest the paper by Mr Mavor (Oct 15) in which he states that in the patients he has reviewed by questionnaire sympathectomy has had little or no alleviating effect on intermittent claudication due to atherosclerotic occlusion of large arteries Although he has cited the observations of previous workers who have maintained that benefit has been obtained in half or more of the patients treated, he has not mentioned any results similar to his own I should therefore like to draw attention to my own observations[3] which support Mr Mavor as to the ineffectiveness of sympathectomy in claudication It is of interest to consider the reasons for the differences between the reported observations

1 There is the patient's tendency to try to please the surgeon On looking over my records, I have observed that on the day when the surgeon noted that the patient was much better and could walk further, according to my notes his walking distance was unaltered I am rather surprised that Mr Mavor's results were not more "favourable" in view of his second question "Can you now walk further without leg pain ?" I tried to frame the question in a more neutral manner "Is the distance you can walk since operation more, the same, less ?"

2 After operation the patient can often walk further because he walks more slowly One patient was pleased because he could walk much further, but added "But of course I do not walk as fast" When asked what would happen if he walked at the same pace, he replied "Oh, then I could only walk the same distance as before, but I have now learned that it is better to walk slowly !"

3 As Mr Mavor has indicated, the relief of other ischæmic features may be taken into account by the patient when assessing the effect on the claudication In claudication, th muscle pain is often associated with paræsthesia of the f also occurring with exercise After sympathectomy, althou the former symptom may be unaffected, the latter may b alleviated

4 The symptom of claudication may be alleviated by placebo effect, even when assessed by a semi objective te such as noting the number of circuits a patient can walk a standard rate over standard steps[4]

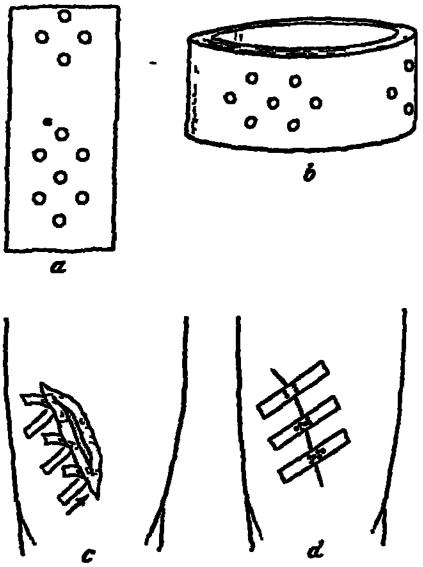
These comments are not offered as criticism of M Mavor's findings, which are entirely in line with my own but merely to mention my supportive evidence and t put forward an explanation of the differences betwee the findings of Mr Mavor and myself on the one han and those of most previous observers on the other

Baker Medical Research Institute,
Alfred Hospital,
Melbourne, Australia A J BARNETT

WOUND CLOSURE WITH PLASTIC TAPES

SIR,—For two years I have been investigating th closure of wounds with plastic tape The kind I now u is much like the 'Cellophane' tape that can be bough at any stationers, but it is made of polyester pla which stretches slightly in all directions and thus allow a little movement of the closed wound (figs *a* and *b*)

The tape is coated on one side with a special adhesi which is non toxic, and no skin reactions have been reporte from its use in over 1000 cases The adhesive is so compounde that it loosens on the sixth or seventh day after the tape applied, but the period of adherence can be varied b changing the proportion of certain ingredients The tape perforated at regular intervals by a pattern of small hole allowing drainage of wound secretions



To close a wound the edges are thoroughly dried an strips of tape are applied to the more mobile side of th wound (fig *c*) The tape will not stick when placed lightly on the skin surface, and consequently it can be moved to exactly the right place before pressure is applied to make it firmly adherent After the strips of tape have been attached to one side, they are used to pull the wound edges into exact apposition and then attached to the other side (fig *d*) An ordinary gauze dressing is then applied and left undisturbed for six days The tape will usually come away from the skin when the dressing is removed Rarely, healing may be so slow that another application of plastic tape is needed

One advantage of this method of wound closure is that it causes little pain, and it is therefore particularly useful in treating minor lacerations in children But in treating such lacerations additional advantages were observed

The average healing time was shortened by a day or more
The scar was less noticeable

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[2] Raffel S Immunity, Hypersensitivity, Serology New York, 1953

[3] Barnett A J *Aust Ann Med* 1954, 3, 295

[4] Newman, H C, Barnett, A. J *Ibid*, 1955, 4 195

is established between virus and host—in other words, a latent infection Although the body remains infected there are no symptoms, and future reinfection with the virus, which would normally cause active disease, produces no effect. This state of affairs can be studied readily in the bacterial viruses. when a bacterial culture is attacked by a specifically active virus, some of the bacterial cells are lysed but others survive and are symbiotically infected with the virus the daughter cells inheriting the infection when the parent cells divide These symbiotically infected bacteria or lysogenic strains are immune to further attack by the same kind of virus although they remain susceptible to other viruses Some animal viruses have a less specific effect by which infection with one kind of virus protects against attack by another kind This protection may be due to saturation of vulnerable sites in the body by the first virus so that there is no suitable accommodation for the second intruder Another suggestion is that sometimes the second virus may be excluded by starvation, because the first has monopolised all the available metabolic activities of the host

It is becoming clear that immunity not attributable to classical antibodies can also arise in bacterial diseases Some protection against toxins can be conferred on animals by giving them large doses of toxoid It may be that specific receptors in the animal body are occupied by the innocuous toxoid so that the toxin is unable to get at these particular sites and hence cannot produce toxic effects Unlike the more usual immunity due to antibodies this protection develops immediately and disappears quite rapidly. In tetanus it has been shown that the attachment of toxin to brain tissue *in vitro* may be blocked by previous exposure to toxoid Further experiments throwing light on the mechanism of this process have been reported recently by DAVIES and WRIGHT[1] They concluded that the administration of toxoid did not permanently block the effects of toxin, but that there was active competition between toxin and toxoid for hypothetical receptor sites in the body On the other hand once the toxin had been fixed to brain tissue the toxoid could exert no protective action Animals which had been only partially protected from the effects of toxin by the administration of toxoid did not show the usual signs of tetanus, but paralysis developed as in botulinum intoxication. The cause might be the unmasking of a further component of tetanus toxin possibly peripheral in its action. There have been doubts about the wisdom of attempting to immunise patients in the so-called negative phase when they have already been exposed to infection. The administration of toxoid or vaccine at this stage might divert the protective mechanisms of the body and neutralise any small amount of antibody present thus allowing the invader to do its damage untrammelled On the other hand, if the immunising agent can exert the blocking and interference phenomena revealed by recent work it may be able to protect even when its administration coincides with exposure to infection. Further experience is needed to judge between these views

The two kinds of protection conferred by vaccines are seen clearly in the case of whooping-cough[2] After a single intraperitoneal dose of pertussis vaccine in animals there is first a sudden but transient protection against pertussis This protection reaches its peak in about ten days and then disappears. EVANS and PERKINS[2] suggested that it might be the result of interference of the type encountered in virus infections and it is presumably due to saturation of sensitive sites by the dead organisms in the vaccine so that the live bacteria introduced in the infective inoculation are unable to become established and multiply The second phase of protection—that dependent on the production of antibodies—appears more slowly but lasts much longer Protective antibodies cannot be detected in the blood after a single injection of vaccine but a second injection gives rise to detectable antibody. These observations can be applied in testing the potency of pertussis vaccines Animals are given the vaccine and later challenged with a live virulent culture to find what protection they have It is necessary to measure the lasting protection conferred by antibody formation and not the temporary interference effect. hence, the challenge dose should be given when the transient interference effect has subsided and the more permanent antibody effect alone remains With pertussis vaccines therefore the challenge dose should be given 30 days after the administration of vaccine and not as recommended[3] at present after 14 days, since the protection measured at that stage is produced by the precocious interference

Annotations

THE GUILLEBAUD REPORT

CHARGED three years ago with inquiring into the financial aspects of the National Health Service,[4] the Guillebaud Committee has listened patiently to almost everybody who has views on how the service might be improved Its report on which so many hopes have been founded is being published this week after we go to press but Dr Abel-Smith's article on the cost of the National Health Service which appears on p 198, reviews some very interesting basic evidence collected for the committee under the auspices of the National Institute of Economic and Social Research, which is now produced in book form by Prof R M. Titmuss and himself.

ANTENATAL SEXING

IT seems that a reliable method has been discovered of sexing the unborn child In a letter on p 202 Dr James reports that he has found it easy to determine the presence or absence of the sex chromatin in cells of aspirated amniotic fluid, and with reasonable care amniotic fluid can be obtained at any time after the twelfth week.[5] A preliminary report from Israel by Serr et al[6] has recently recorded the same observation Since it has been shown that the technique of nuclear sexing can be applied to cells scraped from the surface of squamous mucosæ, oral[7,8] or vaginal,[9] it was certain that the amniotic fluid and its cells would soon be investigated from this point of view *A priori*, it might seem unlikely that satisfactory preparations would be obtained. for the skin even of the fœtus yields only non-nucleated squames and the lining cells of the amniotic

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[1] Davies J R. Wright E A *Brit J exp Path* 1955, 36, 487
[2] Evans D G Perkins F T. *Ibid* p 391
[3] *Tech Rep Wld Hlth Org* 1953 no 61
[4] See *Lancet* 1953, i 732 749
[5] Alvarez, H Caldeyro Barcia P *Surg Gynec. Obstet* 1950 91 1
[6] Serr D M Sachs L Danon M *Bull Res Coun Israel* 1955 5B 137
[7] Moore L K. Barr, M. L *Lancet* 1955 ii, 57
[8] Marberger E Boccabella R. A Nelson W O *Proc. Soc exp Biol N Y* 1955 89 488
[9] Carpentier P J Stolte L A. M. Visschers G P *Lancet*, 1955 ii, 874

CHILDREN IN HOSPITAL

SIR,—I very much enjoyed the stimulating paper by Professor Illingworth and Dr Holt (Dec 17) I would say, however, that this matter of children in hospital has been over-dramatised

In my experience—and this must be surely universal too—it is the *only* child, especially of elderly parents, or the *youngest* child of a large *family*, *especially* if spread out chronologically, that is *most* likely to become fretful (It was an only child that was portrayed in *A Two year-old Goes to Hospital*—a film that in my view has exerted an influence disproportionate to its real value, dealing as it does with only one case) In such circumstances it is the mother or both parents who fret more than the child, and who, becoming over-anxious, transmit *anxiety to their offspring*

Compared with other features of many children's lives—such as being left with neighbours while the mother goes to work, the distractions of television and films, and lax discipline at home and (through no fault of the teacher) at school—a stay in hospital is likely *to do little harm to a child's mental health* There is a tendency for certain parents to fob off their own shortcomings on to those of us (doctors and nurses) who work in hospital under increasingly difficult conditions

I entirely agree that every parent has a right to see his child when *ill in hospital, and daily visiting is the* rule here But we should see that the right is not abused, and that a sense of proportion is preserved

Ilford Isolation Hospital I M LIBRACH

TUBERCULOSIS STATISTICS

SIR,—At the end of each year both the Ministry of Health and the Middlesex County Council ask every chest clinic to state the number of patients removed from the tuberculosis register during the past year, because of death I find that this figure is then widely quoted as the tuberculosis mortality rate This is, of course, most misleading and fallacious as an appreciable proportion of the patients have died from some intercurrent disease while having treatable or treated tuberculosis

In my area, which serves a *population of about 150,000* people, the number removed from the register because of death in 1954 was 22, 14 succumbed to the disease itself, but 8 died from a separate condition For 1955 the figure is 22, 15 died from pulmonary tuberculosis and 1 died from tuberculous enteritis, but in 6 the death was not related to the tuberculosis This means that in these two years about a third of the deaths were not attributable to tuberculosis This is an appreciable *proportion*, and is likely to get larger in future years, so the annual number *removed from the* register because of death will become an increasingly worthless figure

We are also told that the *notification rate is not* falling, and that its constant high level is a reflection on the methods used to eradicate this disease *This is, to my mind*, illogical reasoning and quite unjustified

In the past only a small proportion of the total number of infected patients in the community were *found*, and these were for the most part young adults with well established disease accompanied by obvious symptoms *Today, I believe*, because we have extended our search we find most of the infected patients in an area at any given time, and the cases *discovered* now include many people over the age of 60, and a number of young people with minimal symptomless, but active, *disease* The fact that tuberculosis is becoming effectively *controlled* is best demonstrated by the rapidly falling percentage of children and young adults who have a positive tuberculin skin test[1]

For the time being, therefore, I am glad that the notification-rate remains high, as it means that our case-finding methods are effective, and if it is even h next year it will be a matter for congratulation, bec as the number of cases gets less, so the finding of th will be all the more difficult

I would, therefore, suggest that the battle again tuberculosis is being won more rapidly and efficien than certain official statistics would lead us to believe

Ashford Hospital,
Middlesex P E BALDRY

PERSONALITY CHANGES AFTER FRONTAL LEUCOTOMY

SIR,—Because of the repercussions from discussion of my book[1] in various places, including the lay press a as more will have seen these than will have seen the book colleagues have suggested that I comment on the ma issue

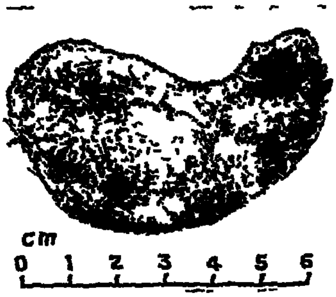
The book does not say that leucotomy is, universally, a bad operation, because it does not deal with this aspect It describes changes in the personality after severance of the frontal lobe by the standard operation, it describes not only the nature but also the extent of these changes Usually they are overshadowed in clinical practice by the modifications (if we may talk of them separately) in the various symptoms for which the operation is performed

Therapeutic procedures—e g, laparotomies—sometimes produce æsthetically undesirable results The consequence is accepted on pragmatic grounds So, after major leucotomy operations, there can be socially significant changes which are undesirable[1] Because of this, modified operations are in use I support the view that, as with *other treatments* in psychiatry, until we have something better they have to be, if appropriately employed, part of our available therapy

Oxford P MACDONALD TOW

TRICHOBEZOAR

SIR,—May I once again draw attention to this very interesting condition? When you published my account[2] of a case in which the hair ball had entered the small bowel of a child and caused obstruction, I thought that this was probably one of the first of its kind to be reported in Britain In 1928, however, Mr C Noon, of Norwich, had recorded[3] a case, in a woman aged 30, of intestinal obstruction due to four separate hair-balls I have very recently removed a hair ball from the small bowel of another child



The patient, a *girl, aged 7, had several* times been in hospital under the care of Mr J S Ramage with developmental anomalies of the renal tract, which included a supernumary kidney and a double urethra She had had *many* attacks of ascending urinary infection, and was *admitted* again on Dec 29 last with abdominal pain and vomiting This attack, however, was rather different, and she appeared to have a small bowel obstruction with a palpable mass in he type 3 strains which have been shown by Ryan nd others[11] to be the cause of pharyngo-conjunctival ever, and Jawetz s strain seems to be a new type hich has been called the Trim or type-8 virus Sero-ogical investigation of the type-8 virus[12] showed that 25 cases of epidemic kerato conjunctivitis occurring between 1951 and 1955 all showed a convalescent serum itre of 1 in 10 or greater, and only 2 of 29 sera from other eye conditions investigated by Jawetz showed such titres

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[1] Grenville Mathers, R *Lancet*, 1955, ii 1341

[1] Personality Changes following Frontal Leucotomy London, 1955

[2] *Lancet* 1954 i, 761

[3] *Brit med J* 1928 i 342

It seems that there is a definite association between epidemic kerato conjunctivitis and these A P C viruses, their known resistance to antiseptics might well explain how transmission occurs by instruments used in ophthalmic practice There is, however, a certain amount of evidence that other agents may also produce the disease, for not only are the viruses isolated by the early workers very different from the A P C group, but there is also a difference in the clinical picture In the more widespread epidemics seen by Wright and by Sanders there were definite constitutional symptoms, which the later workers do not mention Thus, it is possible that the condition may have more than one cause, as is borne out by the occasional isolation of herpes simplex virus from these cases

PROGRESS IN NUCLEIC-ACID RESEARCH

THE self-duplicating plant viruses such as tobacco mosaic virus, are chiefly composed of ribonucleoprotein (6% ribonucleic acid [R N A] by weight), and they have therefore proved important tools for the study of protein synthesis This gives added interest to the report[13] from Stanley s laboratory of the successful splitting of the tobacco mosaic virus into R N A, and protein, and the subsequent recombination of the fragments to form active virus One sample of the virus was treated with dilute sodium carbonate to remove and degrade the nucleic acid, leaving the protein more or less intact, while another sample was treated for a short time with a dilute detergent which degraded the protein but left the R N A intact Both components were demonstrated to be free of intact virus If both fragments were brought together in aqueous solution at pH 6 in the proportion of 10 parts protein to 1 part R N A the solution began to take on the opalescent appearance of a solution of virus and could be shown to contain active virus in amounts which steadily increased reaching a maximum at twenty-four hours Typical particles of virus could be detected in the solution by electron microscopy although none appeared to be present in either of the separate components As earlier work[14] had shown that the virus particle consisted of a strand of R N A surrounded by a helix of protein, the separation of the components had to be achieved without altering the arrangement of the doubtless specific sites on each fragment which bind the two together by salt like links and by hydrogen bonds The first crystallisation of an animal-infecting virus (a strain of poliomyelitis virus) was announced at almost the same time from the same laboratory

Modern views of the function of the cellular nucleic acids, R N A and desoxyribonucleic acid (D N A) tend to associate D N A with the carriers of hereditary features and R N A with morphogenesis and with protein synthesis But a recent important paper by Mirsky and his associates[15] has shown that D N A may also be directly concerned in protein synthesis Isolated calf-thymus nuclei were able to incorporate C^{14}-labelled alanine into nuclear proteins, and this ability was progressively reduced to about 15% of the original level by successive destructions of the D N A by desoxyribonuclease Furthermore, the R N A contained in the nucleolus appeared to be less closely connected with this protein synthesis since 30% of the R N A present could be removed by ribonuclease treatment without affecting the power to synthesise protein from alanine The proteins synthesised under these conditions seemed to be those closely associated with both types of nucleic acid and not the simpler histones of low molecular weight

In general however there seems little doubt that protein synthesis is usually more closely connected with R N A than with D N A For example the only known function of the silk gland (which is very rich in R N A) in the silkworm is to synthesise the protein silk The same is true for all proliferating tissues and for those cells which secrete enzymes Embryonic tissue which is differentiating as well as growing, is also rich in R N A During intense physiological activity unconnected with active protein synthesis (in the heart and kidney, for example), there is no such correlation with R N A content of the organ

Another recent achievement also concerns R N A although it is possible that the results and techniques may be applicable to D N A in due course The R N A macromolecule may be considered as a large number of linked mononucleotides, each nucleotide consisting of a heterocyclic base, linked to a sugar, ribose which bears a phosphoric acid residue (base-ribose OPO_3H_2) Elimination of water between a sugar hydroxyl group and an –OH of a neighbouring phosphoric-acid residue builds up the macromolecule The hydrolysis of the macromolecule to single mononucleotides can be accomplished by alkalis or by enzymes (ribonucleases) but until recently the reversal of this reaction had not been accomplished Ochoa and his colleagues[16] have now found that if an enzyme isolated from *Azotobacter vinelandii* is allowed to act on a solution of a nucleoside diphosphate [base ribose O PO(OH) O PO(OH) OH] then a macromolecule is formed by elimination of inorganic phosphate In this way, Ochoa et al have built up from adenosine diphosphate a poly-adenine nucleotide which had many of the physical and chemical properties of a typical R N A Similarly starting from a mixture of the diphosphates of the naturally occurring ribonucleosides (base-ribose) they could build up an even closer model of a naturally occurring R N A The applications of this work to chemotherapy (by providing a source of "R N A" containing unnatural nucleosides in particular) are exciting At present, the corresponding diphosphates of the desoxyribonucleosides are not available, but when they are, it will be interesting to see whether the same enzyme, or possibly a hitherto unknown one, will be able to convert these diphosphates into a D N A -like macromolecule The four naturally occurring bases in R N A have recently all been detected as nucleoside diphosphates in the acid soluble fractions of animal tissues The early suggestions that this acid soluble fraction would provide precursors for nucleic-acid synthesis[17–19] were strengthened by some of the studies of isotope incorporation[20 21]; and they now seem to have been directly confirmed

PRINTING OF THE LANCET

A DISPUTE in the printing trade is causing difficulty in the production of this and other journals We hope to continue the distribution of our weekly issue at the usual time, but at present we are subject to certain restrictions There may also, we regret to say, be delay in the supply of reprints for scoring When the women had been delivered in Aberdeen Maternity Hospital, their labour was classified by one of the senior obstetrical staff using Stewart and Bernard's classification[3] At no time did the obstetrician or myself discuss the inventory scores or the labour classification As about 90% of all Aberdeen primigravidæ pass through the Antenatal Clinic and are delivered in hospital, any selective factor likely to cause misinterpretation of the results is virtually excluded.

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[11] Ryan, R. W O Rourke J F Iser G *Arch Ophthal Chicago* 1955 54 211

[12] Jawetz, E Kimura S Nicholas A Thygeson, P, Hanna L *Science*, 1955, 122 1190

[13] *Chem. Engng News* Nov 7 1955 p 4794

[14] Schramm G, Schumacher, G Zillig W *Nature Lond* 1955 175 549

[15] Allfrey V G, Mirsky A E Osawa S *Ibid* 1955 176 1042

[16] Grunberg Manago M Ortiz, P J Ochoa S *Science* 1955 122 907

[17] Todd, A R *Harvey Lect* 1951–52, 47

[18] Brown G B *Cold Spr Harb Symp quant Biol* 1948 13 43

[19] Buchanan J M *J Cell comp Physiol* 1951 38 suppl 1 143

[20] Marrian D H *Biochim biophys Acta* 1954 13 282

[21] Goldwasser F *J Amer chem Soc.* 1955 77 6083

50 patients were excluded from the analysis, mainly because of "spoiled" replies or because (in 11 cases) they were delivered elsewhere Of the 850 women who completed the inventory, 259 (30%) had significantly high 'lie" scores, and this agrees with the proportion (32%) in my previous investigation The distribution of major uterine dysfunction between the two groups was as follows

—	High 'lie' score (259)	Low "lie" score (591)	Total (850)
No with major degrees of uterine dysfunction	7 (*2 7%*)	5 (*0 8%*)	12 (*1 4%*)

It will be seen that in labour 1 in 37 patients in the group with high "lie" scores had a major degree of uterine dysfunction, compared with only 1 in 116 patients with low scores

These results support the hypothesis of a "dysfunction temperament," but further research is indicated

I again thank Prof D Baird and Prof W M Millar for their valuable help I am also grateful to Mr W Z Billiewicz, of the Social Medicine Research Unit of the Midwifery Department, Aberdeen, for his statistical evaluation of the results I wish to thank the staffs of the Aberdeen Antenatal Clinic and the records department of the Maternity Hospital for applying the test

Woodilee Mental Hospital,
Lenzie, Glasgow

William A Cramond
Physician Superintendent

EFFECT OF COLCHICUM EXTRACT IN CHRONIC MYELOGENOUS LEUKÆMIA

Sir,—In the following case of chronic myelogenous leukæmia administration of a colchicum extract containing demecolcin caused a prompt and sharp fall in the white blood cell count and an unusual increase in the blood-urea level

A 21 year-old woman was admitted to hospital on Sept 29, 1955, with chronic myelogenous leukæmia On examination there was enlargement of the liver and spleen (28 cm beyond the costal margin) Blood examination revealed Hb 6 4 g per 100 ml, red cells 2,260,000 per c mm, hæmatocrit 20%, and white cells 362,000 per c mm

RESPONSE TO THERAPY WITH A COLCHICUM EXTRACT

Date	Days of therapy	White blood cells (per c mm)	Blood uric acid (mg per 100 ml)	Spleen enlt (cm)	Other manifestations
Sept 29		362 000		*28*	
Oct *5*	1				
,, 7	3	*297 000*			
,, 10	6				Diarrhœa
,, 11	Stopped	86 000		22	
,, 12					Rash
,, 13			51		
,, 14		12 400			Necrosis of lt tonsil
,, 18			5 7		
,, 19				*19 5*	

On Oct 5 treatment with a colchicum extract (containing demecolcin, a new alkaloid isolated by Santavy and Reichstein[4] from *Colchicum autumnale*) 5 mg daily was started, and this was continued for six days (total dose 30 mg) The fir are summarised in the accompanying table

Such a rapid leucolysis with a consequent increase in the blood-uric acid level to 51 mg per 100 ml does not seem to have been reported previously

1st Medical Clinic
Charles University,
Prague II/499, Czechoslovakia

Miloš Netoušek
Director

PLAGIARISM?

Sir,—James Parkinson in his original essay on the Shaking Palsy, written in 1817, describes the onset of the illness as follows

"So slight and nearly imperceptible are the first marks of this malady, and so extremely slow is its progress, that it rarely happens, that the patient can form any recollection of the precise period of its commencement"

Over thirty years later Thomas Addison describes the beginning of the illness now known as pernicious anæmia

"It makes its approach in so slow and insidious a manner that the patient can hardly fix a date to his earliest feeling of that languor which is shortly to become so extreme"

The similarity is striking Can any of your readers confirm or refute that Addison was guilty of *plagiarism*?

Aylesbury, Bucks

V E Lloyd Hart

HYPEREMESIS GRAVIDARUM

Sir,—The value of direct hypnotic suggestion in hyperemesis gravidarum is recognised[1-4] Little, however, has been said of the psychological mechanisms at fault The psycho analytic viewpoint stresses the symbolic ejection of the unwanted fœtus The following case illustrates a modern hazard in the formation of the symptom complex

A multipara, aged 30, was seen in a distressed and dehydrated state She was eight weeks pregnant She said that "a horrible feeling of sickness goes on all the time I cannot keep anything down" During her first pregnancy she had slight vomiting and nausea, which disappeared spontaneously at the thirteenth week Her childhood had been insecure Her father abandoned the family when she was three years old She was the youngest child and was always "spoilt"

She had been an inpatient in hospital for three weeks without improving In view of the gross dehydration and rapid loss of weight, hypnosis was immediately induced and direct suggestions were given to combat the sickness Two days later she reported that the sickness was less and that she had begun to eat a little for the first time in six weeks

No attempt at analysis was made except to say, at the second interview, that these cases represented a desire of the mother to get rid of the fœtus through fear, guilt, or other anxiety The patient denied that this was so in her case She was eating well by the fourth interview, but excessive salivation, both diurnal and nocturnal, proved troublesome At the fifth and last interview she explained that she had been frightened at the first pregnancy by learning that she was *rhesus negative* She was hypnotised and told that she would have no further fear and the salivation would stop On waking the patient said "I have had a sudden thought I was told that if I was rhesus negative I would be all right for the first baby but the second one might be deformed or born dead" This was the crux of the situation She was re hypnotised and told that she would have no further worry about the pregnancy of £6 million in the net cost of the pharmaceutical service resulted from a rise of £12 million in gross expenditure, offset by £6 million in revenue from charges. Increases in quantity, the substitution in prescriptions of proprietary for non proprietary articles, and the development of new products generally have all played important parts in causing the increase in cost. But as a whole we believe that the information collected about this service is sadly inadequate. It is not possible to record in useful quantitative terms what has happened.

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[3] Stewart D B Bernard, R M *J Obstet Gynæc, Brit Emp* 1954, 61 318

[4] *Helv med acta*, 1950, 33, 1606

[1] DeLee J B *Principles and Practice of Obstetrics* Philadelphia 1913

[2] Kroger, W S Hypnosis in Modern Medicine Springfield Ill, 1953

[3] Kroger, W S DeLee S T *Amer J Obstet Gynec* 1946, 51, 544

[4] Palkin M I *Zbl Psychother* 1931 4 273

The trends in cost of the dental and ophthalmic services have been similar. In total they declined in cost by £37 million. The charges introduced in 1951 and 1952 raised £10 million and reductions in the rates of payment of dentists saved £13 million. The remaining fall of £14 million was not entirely due to the indirect effects of changes. There is evidence that demand would have declined anyway after the abnormal arrears of needs had been at least partly dealt with.

A major part of the rise in expenditure by local authorities (£7 million of the £11 million increase from 1949–50 to 1953–54) was the result of rising prices. The rise of £4 million in the real volume of goods and services purchased occurred principally in the ambulance, domestic-help, and home nursing services.

Capital Expenditure

Capital expenditure by the National Health Service (on fixed assets) has been relatively small. About £12 million has been spent each year. As prices of building work and other capital assets have risen substantially over the period, the *real* rate of capital expenditure has progressively declined. The rôle of the health service in national capital formation has been small and declining (from 0.8% to 0.5%). Nearly all the capital expenditure has been devoted to the hospitals. About 10% of expenditure has been on new hospitals and major extension and a further 21% of expenditure has been on ward accommodation. Expenditure on accommodation for staff has accounted for 16% of the total.

The hospital surveys during the 1939–45 war drew attention to the inadequate state of hospital buildings. "Complete demolition" was recommended in a number of cases as some buildings were "unfit for any human habitation." A higher proportion of hospitals required substantial extensions and adaptations. The surveyors wrote of hospital buildings in the North-western area "considering the high place which England takes in the medical world, perhaps the most striking thing about them is how bad they are." It was generally agreed that the hospitals taken over in 1948 were too small, too numerous, and too old. In fact, approximately 45% of all hospitals were originally erected before 1891.

A high level of hospital building was expected to be achieved under the National Health Service. These hopes have not been fulfilled. The rate of fixed capital expenditure on hospitals has averaged about one third of the pre war rate in real terms. At this rate it would take over 200 years to replace our stock of hospitals.

The Hospital Population

The General Register Office generously undertook for us a special tabulation of the 1951 census schedules for all hospitals in England and Wales. This has drawn attention to the importance of demographic and other social factors which influence the demand on hospitals.

Compared with the demands made by single men and women (and, to a lesser extent, the widowed), the proportion of married men and women in hospital, even at the age of 65 and over, is extremely small. Among married men and women, the rise in the proportion in hospital with advancing age is not at all dramatic, it does not reach very high levels even after the age of 75. For all types of hospital, and in proportion to their numbers in the total adult population, the single, widowed, and divorced make about double the demand on hospital accommodation compared with married people. About two thirds of all the hospital beds in the country occupied by those aged over 65 are taken by the single, widowed, and divorced. The married state appears to be a powerful safeguard against admission to hospital, particularly to mental and "chronic" hospitals.

If this "photograph" of the hospital population taken on one night in 1951 is a representative picture of hospital provision, many interesting questions are raised by it. Is marriage a shield against high morbidity ? Is high morbidity a shield against marriage ? How far is the hospital service acting as a family substitute for those who are ill equipped with husbands, wives, and children ? The existence or otherwise of surviving close relatives seems the most important single social factor governing the amount and distribution by age and sex of demand for hospital care—particularly from older people. This being so, it would follow that the past social structure of the population determines in some measure current demands for hospital care. The low marriage rates of forty and fifty years ago represent one important factor. A second is the relatively high mortality rates in the past among married couples in the working classes, which, in addition to the losses caused by the 1914–18 war, led to a higher incidence of broken marriages. One long run effect of the 1914–18 war which has an obvious bearing on hospital demand today is the present "abnormally" high proportion of elderly widows. A third factor is the decline in family size and the survival into old age of more childless married men and women.

As regards the future, the substantially higher marriage-rate which has now prevailed for several decades and the considerable fall in the proportion of marriages broken by death are two encouraging features. The Government Actuary's estimates of the population of Great Britain in 1979 shows no significant change in the actual number of single people of pensionable age. The much publicised increase in the aged is expected to consist very roughly of two million married persons and of half a million widowed and divorced women, the groups which make much lower demands for inpatient care.

The Future

Changes in the marital state of the population would need to be included in any attempt to estimate the future cost of the National Health Service. Information on this aspect, however, was available only for the hospital service, but we were able to assemble some scattered information on the use made of the National Health Service by different age and sex groups of the population. From this, we calculate that a higher proportion of the cost of the National Health Service is devoted to the medical care of those under 15 (including confinements) than to the medical care of those aged 65 and over.

These estimates of the use of the service by different age and sex groups have been used to calculate approximately the additional future costs arising *solely* out of projected population change taken as an independent, isolated factor. Changes in age structure *by themselves* are calculated to increase the present current cost of the National Health Service by 3½% between 1951–52 and 1971–72. A further increase of 4½% is attributable to the projected rise in the total population of England and Wales (using the official projection figures). In total, therefore, population changes *by themselves* are not likely to do much to the future cost of the Service.

All these conclusions should reassure those who feared a continuous and steep increase in the cost of the National Health Service. The real increase in cost has been negligible in view of changes in the population, and the share of the community's resources used on the Service has been declining. The cost of the National Health Service is clearly, if not severely, under control.

His energy spilled outside his work, and in 1950 he was able to preside over the new Manchester Medical Society, which, largely through his efforts, had grown out of the amalgamation of five local medical societies

His leonine physical appearance did not belie his strength. As a student he had been a useful rugby forward, and as he grew older he became an intrepid mountaineer He was a past member of the Council of the Alpine Club and a past president of the Rucksack Club He was a moving spirit in the Mountain Rescue Committee and in 1939 he became chairman Believing that trained rescue parties should be allowed in an emergency to use small amounts of morphine, he drew public attention to this by inviting the Home Office to take legal action against him for supplying morphine for this purpose In court he pleaded guilty and was fined £5 Soon afterwards the Home Office agreed to this extension of the use of morphine

W R D writes

"Quite early it became clear that Wilson Hey was an unusual type and would probably go far This prophecy was fulfilled in his later life His enthusiasm for any work he undertook was impressive He had an unusual quality of brain which almost verged on genius he was certainly original and he never hesitated to express his views in face of the strongest opposition He was not an easy man to know Underneath his suave and charming manner lay a deep understanding of the human element and a great kindliness He would fight to the last ditch for any cause which he decided was right, as was shown in his fight for the supply of morphia to the Mountain Rescue Club He had been ailing for a considerable time, but his work so obsessed him that he refused all advice to retire His name will ring down the corridors of the Royal Infirmary and Christie Hospital for many years to come In the last half century Manchester has produced a number of outstanding surgeons, and amongst them the name of Wilson Harold Hey ranks very high"

Mr Hey leaves his widow, Dr Elsie Hey, with two sons and two daughters, one of whom is a doctor

ARTHUR FELIX

D Sc Vienna, hon D Sc Belf, F R S

Dr Felix, whose death on Jan 14 we announced last week, was pre-eminent in his own field of bacteriology For nearly 40 of his 68 years he had been an international figure

Born in Poland, he completed his studies in Vienna, and during the 1914–18 war he was employed as a bacteriologist in the Austrian army Working for part of the time in field laboratories, often under adverse conditions, he gained much experience of exanthematic typhus, and in conjunction with Weil he isolated the non-motile variant of proteus that reacted specifically with the sera of typhus patients (the Weil-Felix reaction) It was also with Weil that he observed the O and H types of salmonella colonies corresponding to the flagellated and non-flagellated state of the bacteria from this they worked out the two bacterial antigens, the heat-stable O (somatic), and the heat-labile H (flagellar) After the war they collaborated in Prague, and Felix always held Weil in grateful recollection

In 1921 he went to Palestine in accordance with his Zionist principles He remained there, as bacteriologist to the Hadassah Medical Organisation, until 1927, when he came to England and entered the Lister Institute There, happy in his friendship with Ledingham and in the congenial atmosphere he found, he settled down to one of his most profitable periods At first, with Dr Muriel Robertson, he demonstrated H and O forms of the anaerobes *Clostridium tetani* and *Cl septicum*, and from the O antigen of the latter they produced an antibacterial serum, devoid of antitoxic content, which was of theoretical interest, though it had no practical application to the treatment of gas-gangrene His most important work at the Lister Institute, however, was his concentrated investigation of the salmonellas and the discovery of the Vi antigen in the typhoid organism, and it was the characteristics and behaviour of salmonellas that continued to engross him after he joined the Emergency Public Health Laboratory Service in 1939 and became director of the Central Enteric Reference Laboratory and Bureau at Colindale when it was established just ten years ago

Looking back over his career one is struck by the ordered progression of his studies His research outlook was essentially practical, and his activities, applied to the control of infection, seemed to follow a definite plan. He began by investigating the nature of the organism responsible, and establishing exact methods of diagnosis, then he passed to prophylaxis, and finally to the development of biological tools for exact epidemiological inquiries

The Weil-Felix reaction was useful and important, but his contributions to fundamental bacteriology arose out of the very accurate investigations of the proteus X organisms and the non-motile variants, and led to the demonstration of the double antigen complex—somatic and flagellar—in motile bacteria More than ten years previously Smith and Reagh had observed that normal hog-cholera bacilli agglutinated differently from non motile variants, but the significance of the observation had not been fully appreciated In rediscovering the phenomenon Weil and Felix investigated it very thoroughly and showed that the large-flaking agglutination of motile organisms was associated solely with the flagella and that the fine granular agglutination seen with the proteus OX was seen only in non motile organisms

The extension of the proteus studies to the typhoid paratyphoid organisms was the next step, and on the greater part of this Felix worked alone His later observations on the O-inagglutinability of living cultures of some strains of typhoid led to the discovery of the third type of antigen (Vi), and then his endeavour to prepare an improved typhoid vaccine, with the new antigen unimpaired, resulted in the alcohol killed alcohol-preserved T A B vaccine

The persistence of Vi-antibody in a significantly high proportion of typhoid carriers further extended his epidemiological interest, and with the publication of Craigie and Yen's work on the Vi-bacteriophage types of the typhoid bacillus he was quick to seize the opportunity of using this discovery and developing it further for the fine classification of known typhoid carriers and as an epidemiological tool

As a scientific worker, his strongest characteristic was his capacity for studying a problem with persistent attention, and on one occasion he described himself as an instrument tuned to a single note But he never lost interest in any subject he had touched, and to the very end he had as great an interest in the Weil Felix reaction as in the determination of phage-type in an outbreak of paratyphoid fever

H J B writes

"Felix's work was characterised throughout by the simplicity and clarity of the design of his experiments He always used simple equipment and he relied on accurate observation, exact technique in performance, and the inclusion of all possible controls in every test His laboratory records were models of perfection, nearly all in his own neat hand writing on foolscap sheets, carefully filed and stored over the years He had complete confidence in the correctness of his observations and the reliability of his experiments and their records This made him a fearless adversary in any controversy on matters concerning his own work, and if the necessity arose he never hesitated, in this connection, to speak forcefully on what was in his mind

"He did not profess to teach, but he was an excellent instructor whether in person or by his written word My first experience of this came many years before I met him Just after the first world war, when I was working in Constantinople, many cases of typhus fever were being received from the Crimean area, and I found the precise and detailed instructions for the maintenance of the proteus OX strains and the performance of the Weil Felix reaction that originated from him of the greatest help The importance of using only the non motile variant of the proteus X strains for the for mass treatment often suggest that there were sporadic epidemics. Many parishes still had their pest-house—usually a cottage away from the centre of population—but few of these buildings have survived which can be identified with certainty.

A few weeks ago, I went to see Goosehill Camp at Binderton, a remarkable iron-age earthwork over 400 ft up on the eastern face of Bow Hill, which rises on the left-hand side of B 2141 from Chichester to South Harting. Goosehill is, no doubt, an archæologist's paradise, but I was much more interested in a delightful little house some 100 ft further up the hill—in fact, right on the top. This flint cottage has been adapted to suit modern requirements so far as its desolate position will allow but, by what can only be described as a miracle, two doors in it have survived which tell us a little medical history.

The doors are of deal boards polished with age. One shuts off the staircase from the sitting-room while the other does duty for the pantry. They are heavily carved with names and dates. The carving is not mere scratching with a pointed instrument: a really sharp tool in experienced hands made the record that in this cottage I. EVEN was INOCULATED 10th APRIL 1755 and RACHAEL CAPLIN was INOCULATED THE 5 NOV 1758. These two people were, like Jane Peacher (August, 1753), Miss Mary Day (1755), J. Newman (1758), A. Newman (March 19, 1758), Miss Mary Peachey, Mr. Peacher, Martha Adams, Jane Wyatt, and others, occupants of the pest-house. One gentleman who rejoiced in the unusual name of WHICHER SOUTER is said to have CAME TO BOW HILL 27 OCTOBER 1758 on the same day as Richard Caplin. G. Gas was there as late as 1781 and E. Souter in (?) 1788.

I examined the parish registers of West Dean, where entries for Binderton were made after the Commonwealth.

A Jane Peacher was baptised in March 1735-36, so that the person of that name at Bow Hill Cottage in 1753 would have been about 17 years old; she appears to have married James Piggot on Nov. 18, 1762, when Mary Peacher (perhaps her sister) was a witness to the ceremony. A Mary Peacher was married to John Eggar on Oct. 23, 1766, and Jacob Newman was a witness to a marriage performed in 1779. A visit to Stoughton, the parish immediately to the west of Binderton, provided evidence about Richard Caplin. Most of the headstones in the churchyard have been used to form a paved walk, but I found three to members of the Caplin family. A search in the parish registers showed a Richard Caplin as baptised on Aug. 3, 1746, died on Dec. 12, and buried on Dec. 14, 1758—facts which corroborated the epitaph on one of the headstones. Richard would have been 12 years and 2 months old if he was the patient who went to Bow Hill in 1758. On the other hand it may have been his father, also a Richard, who was buried at Stoughton on May 22, 1773.

These are the only links I could discover between parish records and the 19 names which I noted from the doors and their surrounds. One thing I did establish was that the names of none of the 19 people occur in the West Dean or Stoughton burial registers at or about the time of their sojourn at Bow Hill. We may assume, therefore, with some degree of certainty that the inoculations were successful.

It is unfortunate that no overseers' accounts for Binderton, West Dean, or Stoughton have survived to tell us the cost of administering this 18th-century isolation hospital in the heart of the Sussex countryside; but how many such hospitals have the names of former patients cut into their structure? The man who carves his mark for posterity is invariably dubbed a vandal, but for once we must approve the habit: it has given us a fragment of local history which might otherwise have been lost.

In England Now

A Running Commentary by Peripatetic Correspondents

Jimmy was seven years old and had leukæmia. Christmas was near when his mother and father learned the truth. The tragedy of medicine lay bare: neither compassion nor the faintest glimmer of a last hope could soften the cold truth. "We can do nothing. A few weeks perhaps, that's all: nothing more. Only a miracle could—"

With treatment Jimmy gradually improved. On Christmas Day he sat up in bed surrounded by toys and sweets, and his face shone with soap, joy, and cortisone. Soon his blood was normal and his marrow too; his spleen could no longer be felt, and his once enlarged glands had vanished. And his appetite knew no limits. "That's not the way to eat your dinner!" Sister was heard to cry. "Haven't you got a knife and fork?" Chips, ice-cream, strawberry jam, and 'Tizer' were his favourites, and on this diet he rapidly made up the weight he had lost. The day came when he was ready to go home. His pyjamas and slippers were put in a small suitcase, and with trousers, pullover, coat, and school cap, he walked slowly through the hospital gates between his mother and father.

That was two years ago. Since then Jimmy has had another Christmas and two birthdays, two Easters, and five school holidays. He was happy enough before his illness, but each month his parents tried to bring him even more happiness, knowing that it might be his last. Thrice more he walked out through the hospital gates. But the fourth time he was carried by his father, and last week he died.

Philosophers may argue that two years is a fleeting moment in the life of a little boy; that he might have found a greater peace in death two years ago than in two years hence; that a single sorrow borne once is lighter than many borne often. But the light in the eyes of Jimmy and his parents knew nothing of philosophy. We have no regrets.

* * *

I should like to be a nice examiner, but I don't know how. Candidates don't always give fluent and accurate answers in vivas, and they have to be helped along somehow. They don't like this; the bad ones are apt to be suspicious. Of course the examiner can change the subject, but even the dimmest candidate gets increasingly uncomfortable when the eighth topic is reached in seven minutes, and he goes out muttering, "They never gave me time to think about anything." The other extreme is also painful for all concerned. I have met candidates who were apparently willing to be silent *sine die*, but I have never had the nerve to keep quiet after putting one or two questions and see whether silence can be made to last for a whole fifteen minutes. So there is nothing for it but to ease things along on the middle path. Should I tell the candidate when he is wrong? How it demoralises the already nerve-wracked. Should I encourage his ideas? ("The damn swine led me right up the garden path.") I used to think that the only thing that really mattered was to be kind and friendly, and I hope that over the years I have schooled myself to consistent amiability. But now one of my students has come back from an oral examination by an examiner whose graciousness I have always admired. Evidently my student had been off form; some of his inadequacies had been revealed to him, and he was almost in tears about it. "You know, sir, they were so nice about it. That's what I couldn't bear."

* * *

Practice still is rural in the remoter parts of Lincs. True I go round in a car instead of a trap, and I am called by telephone rather than the midnight knock on the postern. But as I go I look for the red flag put out by the hedgeside. It is a signal. A patient at some remote farm has sent down to a road-side neighbour asking us to call. I go along twisting lanes, fortunate if there are no gates to be opened and shut. In the boot of the car are my stock mixtures and tablets, my syringes already boiled and ready for use, dressings, and apparatus for hæmoglobinometry and minor surgery.

from all over the world, and Oertel joined them The time spent in this stimulating and exciting atmosphere coloured his outlook for the rest of his life Wundt made him see the events of history and the phenomena of life from an objective scientific point of view During this stay he also studied comparative anatomy and evolution and the works of Goethe, Lessing, and Gillert

In 1897 he returned to America and in the next ten years he held university posts before in 1907 he was appointed director of the Russell Sage Institute of Pathology, New York In 1913 he came over to Guy's Hospital and worked on experimental nephritis and the development of the kidney In the following year McGill University invited him to become associate professor of pathology there and pathologist to the Royal Victoria Hospital In due course he was appointed to the chair of pathology

W G B writes

"Oertel's contribution to pathology was his insistence that it should be studied from a philosophical point of view and its backbone be composed of a strictly causal comprehension of pathological processes based on logical objective reasoning only This is clearly seen in the preface and introduction of the two books he wrote, *Pathology* (1927) and *Special Pathological Anatomy* (1939) His other contribution was his insistence that organs should be studied whole and that the study of the separate tissues of which an organ was composed did not represent the functional potentiality of the whole organ He made an extensive study of tumours to show that they had the ability to excite the tissues in their neighbourhood to produce stroma, blood supply, and a new nerve supply The steady flow of good papers which came from his institute was based on sound work, much of which was initiated or actually done by Oertel himself

"Oertel was a friendly, urbane, companionable man much absorbed by pathology and philosophy, he had a great admiration for Goethe He enjoyed good living and the company of friends He was a bachelor and since he retired in 1938 he had lived most of the time in London at the Devonshire Club"

JAMES DOUGLAS MONTGOMERY KERR

M D Edin, D P H, D C H

Dr J D M Kerr, a senior medical officer in the Edinburgh public-health department, died on Jan 9, at the age of 32 Born and brought up in Edinburgh, he was educated at George Heriot's School and the University, where he graduated M B in 1946 After serving as house-surgeon at the Royal Infirmary and house-physician at the Royal Hospital for Sick Children in Edinburgh he joined the Royal Air Force On his demobilisation in 1949, he returned to Edinburgh as a clinical assistant at the Sick Children's Hospital, and at the end of this appointment he joined the Edinburgh public-health department as an assistant medical officer in the child-welfare section He took the D C H in 1950

His energy and enthusiasm for work among children led to his being chosen to study retrolental fibroplasia among infants born in the city He submitted the results of his investigations as a thesis for the M D degree, which he obtained in 1953, and he published, with colleagues, several papers on the subject By this time he had decided that his main interest lay in preventive medicine, and in 1954 he took the D P H To enlarge his experience he worked for a time among the aged Two months ago he was appointed a senior medical officer in the Edinburgh public-health department

Two colleagues write "Douglas Kerr always set himself high standards and he showed considerable keenness both in work and in sport Already his researches had shown that he had an incisive and original mind In sport his special interests were rugby, at which he had represented Edinburgh against Glasgow in the inter-city as well as playing for Heriot's F P and London Scottish, and tennis at which he also excelled His cheerful manner and ever-present sense of humour earned him many friends not only among his associates in private and professional life but also among his patients Love of children was a constant feature of his pædiatric and early public-health work and his enthusiasm and sympathetic understanding also won him the confidence and gratitude of the old folk"

Dr H S PEMBERTON

J G F writes

"To some extent Pemberton was a difficult man to know, for he hated anyone to guess that he was a mass of kindness and emotion He did not give his friendship easily, but having done so nobody could be more helpful or more kindly He never forgot the slightest kindness done to him, and would return it a hundredfold, more if possible To him all patients were the same His job was to get them better and this he tried to do with all the skill, all the attention, and all the care he could lavish on them, and not without considerable success He will be remembered with gratitude by many people in Liverpool and district, but particularly by the diabetics At the time of his retirement there were over 1000 patients at his diabetic clinic, all of whom he knew by name and to each he gave individual attention To the hundreds of doctors who in their student days were on Pem's firm he taught that medicine began with the patient, and that the patient as well as the disease must be treated His ward rounds and outpatients were memorable, and no student ever left him without having learnt a great deal about the art of medicine"

Mr E R FLINT

A P B writes

"In the 1914–18 war 'Father Flint' ran the Leeds General Infirmary's surgical beds together with 200 military beds in old Outpatients This was made possible by his cast iron constitution and his indomitable energy His work in the operating theatre was astounding I can remember, as a student, giving 22 general anæsthetics for him for cases of the order of hernia during the afternoon and evening He was fascinating to watch and he had rather a stumpy hand which apparently moved slowly but with such precision that the work was done speedily He had only a student anæsthetist and two nurses to assist him, but the atmosphere of the theatre was serene and no tempers were lost While still R S O he probably opened more abdomens than any other British surgeon in his lifetime"

Appointments

ELLIS, N C, M B, D I H asst M O, Hove and Portslade Health Subcommittee area

FOWLER, P B S, D M Oxfd M R C P consultant physician Chalfonts and Gerrards Cross Hospital, Bucks

GRAHAM I A G, M B Edin senior asst county M O West Riding and school M O Harrogate, Knaresborough and Nidderdale

JONES F T, M B Manc appointed factory doctor, Ruabon, Denbighshire

MACKAY D G, M B Aberd deputy medical superintendent Inverness group of hospitals

NASH JOHN M D Lond, M R C P physician-superintendent, Limerick County council

East Anglian Regional Hospital Board

BUSHBY, ANTHEA M, M B Lpool D A anæsthetic registrar Peterborough Memorial Hospital

GHOSH SOBHA M B Calcutta D G O registrar in obstetrics and gynæcology West Norfolk and King's Lynn Hospital

GIBBON R H M B Camb medical registrar, Norfolk and Norwich Hospital

GREENBERG, M J M B Camb M R C P consultant chest physician Cambridge area

MANSOOR I A M B Bombay orthopædic registrar Norfolk and Norwich Hospital

NEEDHAM BRENDAN, M B N U I D OBST registrar in obstetrics and gynæcology E Suffolk and Ipswich area

WALSH A M M B N U I D OBST registrar in obstetrics and gynæcology Peterborough group of hospitals

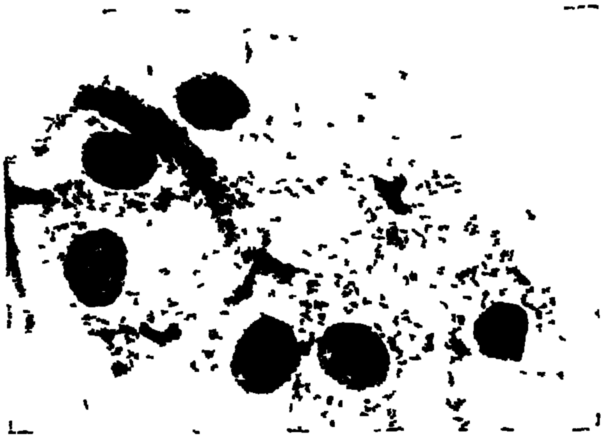
Liverpool Regional Hospital Board

ELLIS D D M B Belf D P M whole time asst psychiatrist

FOLEY MARY M M B N U I D C H D P H whole time tuberculosis M O, Ormskirk area

LANCASTER A P M D Manc D P M whole time asst psychiatrist Deva Hospital

MARSDEN A J M B Lpool F R C S part time consultant general surgeon Ormskirk area



Sediment of amniotic fluid (Papanicolaou stain × 1100)

taken at birth contains many cells With a female fœtus most of these are basophilic with the Papanicolaou staining technique and have large vesicular nuclei Rosa and Fanard[4 5] demonstrated that they are desquamated cells of the fœtal vaginal epithelium Moreover, with fœtuses of either sex other cells are found, probably from the digestive and a few from the urinary tract The material desquamated from the skin consists only of platelets with pyknotic remainders or no nuclei at all

In the large basophilic cells in the amniotic fluid, where the fœtus is female, sex chromatin can easily be demonstrated (see accompanying figure) We found this in more than half of the nuclei suitable for study of morphological detail The Papanicolaou and Giemsa stains both give good results In the case of a male fœtus, most of the nuclei of cells found in the sediment are pyknotic, but some small basophilic cells have vesicular nuclei No sex chromatin could be found in any of these nuclei

It is thus possible to diagnose the sex of the fœtus from the sediment of the amniotic fluid by demonstrating the typical nuclear pattern Where amniotic fluid is tapped for therapeutic reasons the fluid could be tested in this way

Where the sex of a neonate cannot be established immediately after birth, sexing of nuclei could play an important rôle, by its simplicity and speed cytology is here the method of choice, and Moore and Barr's procedure with smears of the oral mucosa should be preferred in these cases

Histological Laboratory,
University of Amsterdam F JAMES

RETIREMENT BENEFITS FOR THE SELF-EMPLOYED

SIR,—Although most members of the medical profession are now accumulating retirement benefits under the National Health Service scheme, there will still be many who cannot make provision so far as earnings from their private practices are concerned, and I am sure that your readers will be as anxious as are other professional people that the proposals of the second Millard Tucker Committee should be implemented in the forthcoming budget

We all realise that since the war the level of taxation has been so high that very few people are now able to provide for their retirement by setting aside savings out of net income Employed persons are increasingly able to use pension schemes of one kind or another which enable provision for old age to be made year by year out of gross earnings

Self-employed persons are not able to enjoy the benefits of such schemes and are thereby placed at a disadvantage compared with those who are employed in industrial or commercial firms which have adopted statutory superannuation schemes The disadvantage is a very real one which is bound, sooner or later, to have an adverse effect on the independent professions

The subject has been most carefully reviewed during the past ten years and it is now two years since the Millard Tucker Committee reported Its conclusion was that the benefits which are available to ordinary employees should apply equally to persons who are self employed

These views were shared by the Royal Commission on the Taxation of Profits and Income, and it can be confidently claimed that there is no responsible body of opinion which would continue to deny to the professional self employed the benefits of pension schemes

So far as the professional men are concerned the cost would certainly be modest, and in any case would to some extent only represent a deferment, since tax would be payable when the pensions are paid Since the relief that is given is conditional upon regular saving, the economic effect would not be inflationary

I hope, therefore, that members of the medical profession will join with their colleagues in other professions in supporting the claim that the Tucker Committee's proposals should speedily find their way on to the Statute Book

Shortlands, Kent E KENNETH WRIGHT

MENTAL NURSING

SIR,—Recent issues of *The Lancet* have been characterised by an unusual and perhaps laudable emphasis on social and occupational aspects of psychiatry in mental hospitals Criticism, much of it ill informed, has been directed against such institutions by various individuals who have assumed the authority or right to castigate hospital authorities for a variety of reasons Hitherto we have dismissed these pontifications with the contempt they deserve The danger, however, is that the popular press will seize extracts from these pseudo authoritative pronouncements to entertain their less erudite readers

Now we are informed by Dr Hunter (Jan 14) that over the past twenty years the advances in psychiatric treatment largely comprise cunningly devised methods of restraint put forward under the guise of therapy Further, the corollary to the proposition, as stated, declares that mental nursing has degenerated to the level of virtually unskilled guardianship, hence the failure of recruitment to the service

It is difficult to believe that any experienced physician will accept such nonsensical pronouncements Dr Hunter's philosophy would suggest that all research in mental disorder should be abandoned and that his skilled team of nurses would thereupon take over This approach, together with perhaps a short course of psycho-analysis, would at once relegate all physical treatments and all sedation to the limbo By extension, he would then similarly treat all cases of traumatic delirium and confusional states associated with bacterial infection or toxæmia, still encountered in general hospitals

May we point out that the most perfunctory inquiry will reveal to Dr Hunter that practically every general hospital, except teaching units, is bedevilled by a similar acute shortage of nursing staff Dr Hunter may or may not have realised that these are times of full employment, that the reserve of both man and woman power is exceedingly small, and that for women greater emancipation and changing economic pressures have thrown open a whole host of vocational possibilities not extant twenty years ago In this regard the size of the nursing staff is by no means correlated with the amount of physical treatment Many hospitals in remote areas with comparatively little in the way of newer therapies experience as much difficulty in recruitment as do the others

We should like to inform him likewise that at the outbreak of war fifteen years ago Springfield Hospital had

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[4] Rosa P A Fanard A E *Bull Féd Gynec Obstet* 1949 1 371
[5] Rosa P A. Fanard A E *Int J Sexol* February 1951, p 1

University of Birmingham

Mr D M Morrissey has been appointed part-time lecturer in surgery, and Mr R F Wrighton, PH D, lecturer in the department of medical statistics

University of Liverpool

At a recent examination for the degree of PH D in the faculty of medicine Dr H Wilson was successful

University of St Andrews

In recent examinations the following were successful

M D —J G Lawson (with commendation), Harry Williams (with honours)

M B Ch B —John Armitage, Doreen M Birley, Dorothea T Grace, J M Hutchison, P J McDonald R B Maclaren Fergus Mitchell, Margaret E Robinson, K E Walling, June P Wilson

Royal College of Physicians of London

On Tuesday and Thursday, Feb 7 and 9, at 5 P M at the college, Pall Mall East, S W 1, Dr R J F Schilling will deliver the Milroy lectures the subject of which will be Chronic Respiratory Disease among Cotton and Other Textile Workers

Royal Society of Medicine

The eighth award of the Hickman medal has been made to Dr Harold Griffith of Montreal, first president of the World Federation of Societies of Anæsthesiologists

St George's Hospital, London

Viscount Ingleby has been appointed chairman of the board of governors of this hospital Lord Ingleby was formerly Mr Osbert Peake

Royal Appointment

Surgeon Rear-Admiral R L G Proctor has been appointed an honorary physician to the Queen in succession to Surgeon Rear-Admiral S G Rainsford

North of England Obstetrical and Gynæcological Society

The following officers have been elected for this society for 1956

President Mr C H Walsh, hon treasurer, Mr C H Walsh hon general secretary Mr C J K Hamilton, vice presidents, Miss E M Mills, Mr J R Bentham Prof A M Claye Mr L B Patrick, Mr F E Stabler, hon reporting secretary, Miss U M Lister

Oxford University Medical Society

The programme of this society for the hilary term includes papers by Dr H E Lewis on the British North Greenland Expedition (Jan 24), by Dr J H Hunt on the future of general practice (Feb 14), and by Sir John Charles on Our Lords and Masters (Feb 28) All the meetings are held on Tuesdays at 8 15 P M at the Radcliffe Infirmary

List of Dispensing Opticians

The annual list of members of the Guild of British Dispensing Opticians is now available It contains 507 addresses in the United Kingdom and overseas, and indicates those where a contact lens and/or artificial-eye fitting service is available Medical eye centres sponsored by the N O T B are also shown. A copy will be sent to any doctor on application to the secretary of the guild, 50, Nottingham Place, London, W 1

Wellcome Museum of Medical Science

Lieut -Colonel C A Bozman has been appointed director of this museum

Colonel Bozman graduated M B from the University of Edinburgh in 1924 and the same year joined the Indian Medical Service He held public health and laboratory appointments in the service including that of director of public health, Burma and became a public health commissioner to the Government of India After his retirement in 1947 he was lecturer in public health at the University of St Andrews health counsellor at the British Middle East Office Cairo and professor of preventive medicine at the University College of East Africa (Makerere College)

CORRIGENDUM *Conn's Syndrome with Severe Hypertension* —In table I of last week's article by Dr T M Chalmers and his colleagues (p 127) the third column should have been headed "Cortisol in whole blood (µg per 100 ml) or 24 hr urine," and the fourth column should have been headed "Aldosterone in whole blood (µg per 100 ml) or 24 hr urine" Fig 4*b* showed a collecting tubule

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The tuberculin dispenser for use with the Heaf multiple puncture apparatus described by Dr Peter Stradling (*Lancet* 1955 ii 252) is now obtainable from Messrs Labex Ltd 49, Ashtree Avenue Mitcham Surrey

Diary of the Week

JAN 29 TO FEB 4

Monday, 30th

UNIVERSITY COLLEGE, Gower Street W C 1

5 P M Dr A Nizet (Liége) Hæmopoiesis and General Prote Metabolism

ROYAL SOCIETY OF MEDICINE 1, Wimpole Street W 1

5 P M *Comparative Medicine* Dr H Churchill Davidson Dr Audrey Smith, Dr H L Rosomoff, Dr B A Cook Mr D N Ross, Mr D G Melrose Hypothermia

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road, W 1

4 P M Dr R H Girdwood Folic Acid and Vitamin B_{12} Deficiency in Man

Tuesday, 31st

BRITISH POSTGRADUATE MEDICAL FEDERATION

5 30 P M (London School of Hygiene and Tropical Medicine Keppel Street, W C 1) Dr D R Wilkie Living Mu

ROYAL ARMY MEDICAL COLLEGE, Millbank S W 1

5 P M Lieut Colonel H J Bensted Bacillary Dysentery

ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington, W 2

5 P M Mr Denis Browne Surgery of the Newborn

INSTITUTE OF DERMATOLOGY, Lisle Street, W C 2

5 30 P M Dr G C Wells Disorders of Sweating

MANCHESTER MEDICAL SOCIETY

4 30 P M (Medical School, University of Manchester) Prof Michael Polanyi F R S Passion and Controversy i Science (University lecture)

Wednesday, 1st

ROYAL SOCIETY OF MEDICINE

5 15 P M *History* Dr W H McMenemey Alexander Phil Wilson Philip (1770–1851), physiologist and physician

8 P M *Surgery and Anæsthetics* Dr B G B Lucas, Sir Rus Brock Mr S M Cohen Application of Hypothermia Surgical Procedures

INSTITUTE OF DISEASES OF THE CHEST Brompton S W 3

5 P M Dr A Cochrane Detection of Tuberculosis in a Community

INSTITUTE OF DERMATOLOGY

5 30 P M Dr J O Oliver Blood and Bone marrow in Sk Diseases

BIRMINGHAM MEDICAL INSTITUTE, 154, Great Charles Stre Birmingham

8 15 P M *Midland Medical Society Section* Dr A M Nusse Dr D L Crombie, Mr Fauset Welsh, Dr K B Roger Antibiotics

MEDICO CHIRURGICAL SOCIETY OF EDINBURGH

8 30 P M (Royal College of Surgeons 18 Nicolson Stre Edinburgh) Dr. I Simson Hall Deafness as a Soc and Industrial Disability

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGO 242, St Vincent Street, Glasgow

5 P M Prof C Heymans Regulation of Blood-pressure a Hypertension (Finlayson lecture)

Thursday, 2nd

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn Fiel London W C 2

5 30 P M. Sir Philip Manson-Bahr Tropical Diseases affect the Throat Nose and Ear

BRITISH POSTGRADUATE MEDICAL FEDERATION

5 30 P M (London School of Hygiene and Tropical Medicin Mr S V Perry, PH D Proteins in Muscular Contractio

UNIVERSITY OF LONDON

5 P M (St Thomas's Hospital Medical School Albert Embankment, S E 1) Prof A Jost (Paris) Hormonal Contr of Sexual Differentiation in the Mammalian Fœtus

ROYAL SOCIETY OF MEDICINE

8 P M *Neurology* Dr Macdonald Critchley Premorbid Litera and the Pattern of Subsequent Aphasia

MANCHESTER MEDICAL SOCIETY

8 P M *Anæsthetics* Dr F W Oliver Carbon dioxide Concentrations in Anæsthetic Apparatus Dr E G Rees Jone The Anæsthetist in Obstetrics

UNIVERSITY OF ST ANDREWS

5 P M (Queen's College Dundee) Prof C A Keele Producti of Pain by Chemical Substances

Friday, 3rd

ROYAL SOCIETY OF MEDICINE

10 30 A M *Otology* Mr I P J MacNaughtan, Mr Tere Cawthorne Chronic Adhesive Otitis Media

2 30 P M *Laryngology* Mr N R Barrett Prof P R All Prof A S Johnstone Dr R E Bonham Carter Unus Aspects of Œsophageal Disease

POSTGRADUATE MEDICAL SCHOOL OF LONDON

4 P M Dr P McG Moffatt Fundus Conditions in Gene Diseases

INSTITUTE OF DERMATOLOGY

5 30 P M Dr L Forman Diseases of the Nails

MIDLAND CENTRE FOR NEUROSURGERY, Holly Lane Smethwick

8 15 P M Mr J B Pennybacker Compression of the Cau Equina

ROYAL MEDICO CHIRURGICAL SOCIETY OF GLASGOW

8 30 P M (Royal Faculty of Physicians and Surgeons of Glasgo Prof C A. Wells Surgery in the Treatment of Hyp tension

"OEDÈME BLEU"

SIR —Dr Ida Macalpine and Sir James Paterson Ross (Jan 14) deem it ' impossible to discuss *œdeme bleu des hysteriques* without glancing at the history of the term ' hysterical ' They achieve this glimpse and in addition aver that the " term has impeded the understanding of mental disorders from earliest times " without mentioning the name of Charcot's great collaborator Pierre Janet

The latter's book on *The Major Symptoms of Hysteria* (1907) is a psychiatric classic Its perusal leaves no room for doubt that the word as used by Janet has secured a permanent place in the history of systematic psychotherapy It has, since his day, been consistently traduced by physicians and surgeons His description of the malady, however, remains of paramount clinical significance

London, W 1 MURDO MACKENZIE

RECRUITMENT FOR THE OVERSEA MEDICAL SERVICE

SIR —From personal experience I would like to support the views put forward by Mr Roaf (Jan. 14) I agree entirely that as a medical ambassador only the best is good enough ' It has to be remembered that many doctors in overseas territories have been trained in this country and know perfectly well who is who To presume that the registrar is able to advise them on the organisation of their medical services is quite absurd Consultants of recognised standing should be able to achieve much more in much shorter time, and a continual exchange of views with experienced specialists from this country would be of far greater value than long-term junior appointments A scheme of short-term secondment of consultants is also likely, apart from the purely technical point of view, to create confidence and good will

Harefield Hospital,
Middlesex. E NASSAU.

ARTIFICIAL HIBERNATION IN HEART-DISEASE

SIR.—In view of the discussions about the use of chlorpromazine that have appeared in your columns we thought it might be of interest to report some effects of artificial hibernation in a new field Our technique, applied in a considerable number of patients, has been essentially Laborit's method—i e , vegetative inhibition by a mixture of chlorpromazine, promethazine, and pethidine in a ratio of 1 : 1 2, supplemented in case of need by hypothermia

Two children with acute rheumatic pancarditis were desperately ill, and their cardiac function had not been improved by repeated digitalisation. Œdema had been uninfluenced by diuretics, and dyspnœa could not be relieved by any means The question then arose whether their chances could be improved by artificial hibernation One hour after treatment began, there was a dramatic improvement in their general state, and dyspnœa was entirely relieved On lowering body-temperature to 31°C and 33°C respectively, the pulse-rate and respiration rate fell to normal Within the next twenty-four hours diuresis was so copious (6 and 8 litres respectively) that œdema practically disappeared The lives of these children could not be prolonged for more than a few days Nevertheless this experience suggests that even in the gravest forms of acute pancarditis artificial hibernation may enable sufficient time to be gained for the condition to be controlled by other means

The diuretic action of hibernation was immediately tested in a number of other patients In two children with chronic rheumatic heart-disease, adequate diuresis could not be induced even by adult doses of mercurial diuretics and theophylline Two doses of the ' lytic cocktail " were given within half an hour, each of them containing 0·25 mg of chlorpromazine per kg body-weight, a mercurial diuretic was given at the same time The resulting diuresis was about three times as great as any previously attained. Both in these and in similar patients there was a rapid decrease in the size of the liver and in the extent of œdema In the same patients a similar diuretic effect was not elicited when, instead of the complete cocktail, one of its constituents was given with the diuretic

1st Department of Pediatrics
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J SZUTRELY
P V VEGHELYI

ALLERGY TO MALE SEX HORMONE

SIR —I have observed a curious allergic phenomenon in a 51-year-old woman during treatment of breast-cancer metastases with male sex hormone

The patient said that as a child she had had morbilli, scarlet fever and diphtheria Menstruation had started at the age of 12 years At the age of 30 she had been operated on for ruptured ectopic pregnancy The menopause began at 45 ; flushes had ceased In November, 1954 a firm nodular tumour was detected in the upper lateral quadrant of the left breast A radical mastectomy was performed followed by X-ray treatment with 6000r She gained 2 kg in weight In February, 1955, she felt tired, became dyspnœic, and had pain, associated with respiration, in the left side of the chest

On admission the secondarily healed mastectomy scar 10 cm. long, was surrounded by a sharply bordered area of pigmentation measuring 4 × 12 cm In the left chest were clinical and radiographic signs of pulmonary metastases and pleural exudate , and histological examination of the exudate revealed malignant cells Blood count . 3,600,000 red cells per c mm , hæmoglobin 72% (Sahli) · white cells 9600 per c.mm (differential count normal) Erythrocyte sedimentation rate 90 mm in 1st hour (Westergren) Urine . pus cells present

Hormonal treatment was started on March 29 with daily injections of 50 mg (2 ml) ' Oreton (testosterone propionate) Four days later the patient complained of itching of the scar The pigmented area became reddish swollen, and tender Administration of ' Antistin ' 0 1 g (2 ml) caused the itching to cease temporarily but continuation of this treatment produced discoloration and renewed itching A scratch test on the forearm revealed faint sensitivity to 0 1 ml oreton and also (a few days later) to 0 1 ml ' Androfort ' (another testosterone propionate preparation) On the same day we injected 0 1 ml androfort into the skin of the pigmented area near the scar , after three days an area of necrosis measuring 0 3 × 0 2 cm developed Control injections with sesame oil and saline solution gave no reaction at all. After four simultaneous injections of oreton and antistin the urticarial reddening subsided and the injections of the hormone were resumed without further reactions The patient went steadily downhill, and she left the hospital on June 13 in an extremely grave condition. She died a few days later at home Permission for necropsy was not granted

It seems indisputable that the reddening and itching of the X-ray-pigmented area was an urticaria-like allergic reaction, and this was proved by the immediate response to anti-histamine substance and the successful desensitisation Obviously the patient developed hypersensitivity to male sex hormone, though she had never before been treated with this The sensitivity was not to a particular preparation of the drug, because the scratch test was positive both to oreton and androfort

The fact that intracutaneous injection of 0 1 ml androfort produced an Arthus-like necrosis in the X-ray-pigmented area favours the assumption that local (sessile) antibodies were present

How did this sensitivity develop ? The short interval between the start of treatment with male hormone and the development of the urticarial reaction is against the possibility of sensitisation to the injected hormone It is, however, well known[1] that physical factors, such as X rays, may cause concentration of the circulating antibodies in the corresponding part of the skin ; and the antibodies thus become localised There are several possible sources of these circulating antibodies (1) the provoking antigens might be breakdown products of the endogenous androgens, this biochemical process having been influenced by the X rays in the highly vascular almost impossible, with the exception of pride of craftsmanship It would, in fact, be easier to attempt to forecast future trends, for the drift away from mining and cotton textile work, in favour of the newer engineering and chemical industries, seems likely to continue, and the further developments in these industries will require a different type of worker from the past, for even a push button operator must know which button to push and why

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[1] Rajka E. *J Allergy* 1942 13 327

The manual worker of my boyhood, with his clay pipe his choker, and his dinner in a red handkerchief, is already a museum piece, and in his place has come a race of people who are already technically proficient, and who, in a short space of time, *must become more so* Such people will lead very different lives from their forebears In this connection it is instructive to note the comprehensive definition of automation presented at the First International Automation Exhibition held in New York in 1954[4] It was there defined as "the substitution of mechanical, hydraulic, pneumatic, electrical, and electronic devices for human organs of observation, decision and effort, so as to increase productivity, control quality, and reduce costs" A more simple definition has been given as "*the operation of machines by other machines*"

Community Living

The first essential is, of course, to be and remain alive and a very considerable portion of the revenue of the country *is devoted to* ensuring that most of us are enabled to do so For the purposes of the present paper, however, we can take these services—health, hygiene, pure and adequate food, and so on—for granted, and concentrate rather on how to "warm both hands before the fire of Life," to quote Walter Savage Landor These measures to preserve life and health are, however, effective only in so far as the people will make them so, and that is a matter of education It is not the prime *function of national health and welfare services to provide* excuses for absence from uncongenial work, or to cure diseases which should not have occurred Similarly the purpose of education is, presumably, to open a wider door than mere ability to read a table of football results, or instructions for the filling in of forms

Excluding his physical needs what *does* a man want? *Here it is tempting to bring out all the well-worn phrases* about a balanced emotional, intellectual, and spiritual *development*, but each man differs and generalities will not suffice First and foremost, however, he needs a sense of purpose, a place, a niche, in his community He needs, if he is a normal person, to feel a sense of personal responsibility for his daily life, and he also needs some outlet for the creative urge which is within everyone, and which if unsatisfied, may appear in the most *bizarre fashions*

It is customary to speak of the home as the place where self discipline, integrity, and a sense of responsibility are learnt, and to point to the association between broken homes and delinquency, but I sometimes wonder whether our educational system is at fault It must be tantalising enough for a child to begin to learn of interesting things, and then have *to concentrate* at an early age on a few special subjects for examination purposes *It must* be even worse for a boy to find himself in the "duds" class, or in a school for backward pupils, especially if he knows that he is only deficient in certain things, while he may be expert in others

Also, how much does our educational system take into account the future *life of the child? Does anyone ever* explain to him the various ways in which he might make his living, and the disadvantages of "dead ends"? Our great industries have many international ramifications Are children taught to associate the factories and workshops in their own town with the geography of their books? It would be a valuable experiment for the management to organise talks to, and visits from schools, and let the men do the talking At least the experiment could do no harm The children would learn something, and the men would benefit by the experience

It is at the next stage, the school leaving age, that the most searching questions need to be asked about the *present system We are, and rightly, proud of our youth* service in Britain It is, in the words of the official handbook, designed to provide for the leisure time activities of young people and to offer them opportunities "complementary to those of home, formal education and work" for observing and developing the personal resources of body and spirit and so help *them to become responsible members of society* But does anyone ever explain to these young people, without practical demonstration on a "*mock up*," how *to make* the best use of a home? Admittedly I have in mind the type of full sized model used by the Building Research Station in their experimental investigations into the comfort and working conditions of the housewife, and such realistic conditions would be too costly to be widely copied But one would imagine that housing authorities, *for* example, might find it profitable, in the long run, to lend an empty council house for this purpose which could then be furnished simply, and water, gas, and electricity boards could supply examples of their wares and demonstrate their proper use Boys would, I believe, enjoy seeing how electrical and other gadgets work, and girls would enjoy being shown how lighting, colour, and the proper *placing of furniture* or fittings, improve working conditions in the home Indeed it is not too far*fetched to suggest that* members of a senior class should "*run*" such a house *for* a week, including the cooking of meals, and thereby gain valuable information on family budgets If the house were open *for* parents to see if they wished, then adults would benefit also Such an experiment might do more good than many lectures on civic and community development

Does anyone gather these youngsters in groups and take them round the various industries in the area? When they have acquired a job, is it anybody's responsi*bility to take them through* the process *from* start to finish, so that they may see the machine of which they form part? In a small office the office boy soon becomes extremely knowledgeable, but a van boy sitting on the tailboard of a truck may know only *the name* printed on the side of it Small wonder if he jumps *off and* goes somewhere else

Quite seriously I would suggest that the federations of employers, the trade unions, and the Government *departments and nationalised* industries concerned, might organise, on an area basis, courses of instruction, with practical demonstrations, *for those* about to enter industry, together with an advisory service for parents For that matter it should not be beyond the wit of man to reorganise part of the National Service machine so that it would function as a preliminary training school for civil as well as military purposes, but without the element of conscription

The Future

It seems to me, as a mere onlooker, that we are stuck *about* halfway along *a* course *for* which the ancient learning has no precedents, for we now have this curious mixture of State control and private enterprise, with the former gaining in importance *It so happens that* I have spent some twenty one years in local and central government service, and, while I have the greatest respect for the civil and local government servants, *there is no doubt in my mind* that the State machine is not an ideal one when considering *industrialisation* and community living Rules drawn up on a national basis must be free from loop holes through *which the* rascal or the stupid may slip, grades must be standardised and rates of *pay adjusted to* those grades, Ministers must be protected and mistakes avoided With such a machine there is little room for experiment, for failures

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The latter's book on *The Major Symptoms of Hysteria* (1907) is a psychiatric classic. Its perusal leaves no room for doubt that the word, as used by Janet, has secured a permanent place in the history of systematic psychotherapy. It has, since his day, been consistently traduced by physicians and surgeons. His description of the malady, however, remains of paramount clinical significance.

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The diuretic action of hibernation was immediately tested in a number of other patients. In two children with chronic rheumatic heart-disease, adequate diuresis could not be induced even by adult doses of mercurial diuretics and theophylline. Two doses of the "lytic cocktail" were given within half an hour, each of them containing 0.25 mg. of chlorpromazine per kg. body-weight; a mercurial diuretic was given at the same time. The resulting diuresis was about three times as great as any previously attained. Both in these and in similar patients there was a rapid decrease in the size of the liver and in the extent of œdema. In the same patients a similar diuretic effect was not elicited when, instead of the complete cocktail, one of its constituents was given with the diuretic.

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J. SZUTRELY.
P. V. VEGHELYI.

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The patient said that as a child she had had morbilli, scarlet fever, and diphtheria. Menstruation had started at the age of 12 years. At the age of 30 she had been operated on for ruptured ectopic pregnancy. The menopause began at 45; flushes had ceased. In November, 1954, a firm nodular tumour was detected in the upper lateral quadrant of the left breast. A radical mastectomy was performed, followed by X-ray treatment with 6000r. She gained 2 kg. in weight. In February, 1955, she felt tired, became dyspnœic, and had pain, associated with respiration, in the left side of the chest.

On admission the secondarily healed mastectomy scar, 10 cm. long, was surrounded by a sharply bordered area of pigmentation, measuring 4 × 12 cm. In the left chest were clinical and radiographic signs of pulmonary metastases and pleural exudate; and histological examination of the exudate revealed malignant cells. Blood-count: 3,600,000 red cells per c.mm.; hæmoglobin 72% (Sahli); white cells 9600 per c.mm. (differential count normal). Erythrocyte-sedimentation rate 90 mm. in 1st hour (Westergren). Urine: pus cells present.

Hormonal treatment was started on March 29 with daily injections of 50 mg. (2 ml.) 'Oreton' (testosterone propionate). Four days later the patient complained of itching of the scar. The pigmented area became reddish, swollen, and tender. Administration of 'Antistin' 0.1 g. (2 ml.) caused the itching to cease temporarily, but continuation of this treatment produced discoloration and renewed itching. A scratch test on the forearm revealed faint sensitivity to 0.1 ml. oreton and also (a few days later) to 0.1 ml. 'Androfort' (another testosterone propionate preparation). On the same day we injected 0.1 ml. androfort into the skin of the pigmented area near the scar; after three days an area of necrosis measuring 0.3 × 0.2 cm. developed. Control injections with sesame oil and saline solution gave no reaction at all. After four simultaneous injections of oreton and antistin, the urticarial reddening subsided and the injections of the hormone were resumed without further reactions. The patient went steadily downhill, and she left the hospital on June 13 in an extremely grave condition. She died a few days later at home. Permission for necropsy was not granted.

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The fact that intracutaneous injection of 0.1 ml. androfort produced an Arthus-like necrosis in the X-ray-pigmented area favours the assumption that local (sessile) antibodies were present.

How did this sensitivity develop? The short interval between the start of treatment with male hormone and the development of the urticarial reaction is against the possibility of sensitisation to the injected hormone. It is, however, well known[1] that physical factors, such as X rays, may cause concentration of the circulating antibodies in the corresponding part of the skin; and the antibodies thus become localised. There are several possible sources of these circulating antibodies: (1) the provoking antigens might be breakdown products of the endogenous androgens, this biochemical process having been influenced by the X rays in the highly vascular

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[1] Rajka, E. J. Allergy, 1942, 13, 327.

THE BILLROTH-I AND POLYA OPERATIONS FOR DUODENAL ULCER

A COMPARISON

J C Goligher
Ch M Edin, F R C S

P J Moir
M C, M B Glasg, F R C S

J H Wrigley
M B Edin, F R C S E

From the Professorial Surgical Unit, General Infirmary, Leeds

The Billroth-I resection is said by many to be followed by much less trouble from post gastrectomy symptoms than is the Polya operation, and for that reason it has been increasingly used in this country in recent years Many surgeons now regard this as the operation of choice for cases of gastric ulcer, to which it is, of course, especially suited The suitability of the Billroth I operation in cases of duodenal ulcer, however, is open to considerable dispute and surgical opinion is sharply divided on this issue To any surgeon who has had much experience of the operation, the objection that it will seldom be technically feasible when the ulcer lies in the duodenum itself will carry little weight, it is surprising how often a really high Billroth-I resection can be performed under such circumstances The criticism that a recurrence of duodenal ulceration is commoner with this technique than with the Polya method is less easily refuted, and reports are conflicting on this point

In view of this divergence of opinion, we have surveyed the late results of subtotal resection by Billroth-I and Polya techniques in the treatment of duodenal ulcer

Case-material

We analyse here all cases of duodenal ulcer admitted during the years 1948–54 inclusive for gastric resection, under the care of one of us (J C G) at St Mary's Hospital or of another of us (P J M) at the Leeds General Infirmary The survey comprises 312 patients (277 males and 35 females) whose ages ranged from 12 to 82 years, the majority being in their 4th or 5th decade Most of the patients had elective gastrectomy, but 20 had emergency operations for bleeding or perforated ulcers

Choice of Operation

Approximately half of the patients were treated by Billroth-I resection and half by Polya resection

The operations were performed by five surgeons of whom three performed Polya resections only and two started with Polya resections but at the end of 1949 adopted the Billroth-I method as the operation of first choice

In 8 or 9 cases early in the series Billroth I resection proved impracticable because of fixity of the ulcer or difficulty in bringing the stomach remnant and duodenum together after a high resection In these cases the operation was completed as a Polya gastrectomy, and was recorded as one of the Polya group

So far as possible with several surgeons taking part a uniform level of gastrectomy was maintained, with removal of at least three quarters of the stomach in all instances, including the Billroth-I cases

TABLE I—NUMBER OF BILLROTH-I AND POLYA RESECTIONS PERFORMED, FOR DUODENAL ULCER, 1948–54

Year	Billroth I	Polya	Both operations
1948		31	31
1949	2	27	29
1950	15	28	43
1951	30	25	55
1952	43	16	59
1953	23	12	35
1954	35	25	60
Total	148	164	312

Table I shows the numbers of both types of operation in the period under review Altogether there were 14 Billroth-I resections and 164 Polya resections In the earlier years relatively more Polya resections were done so the Polya group includes a higher proportion of patients followed up for a long time, this may have a bearing on the relative incidence of recurrent ulceration in the two groups

Losses from Series

Not all the patients were followed up, for, as table II shows, some died after operation, some died subsequently from causes unrelated to recurrent ulceration and some could not be traced

Operative Mortality

There were 12 deaths in the postoperative period, all due to leakage and peritonitis from a sutured duodenal stump or gastroduodenal anastomosis This gives an over all mortality-rate of 3 8% The mortality rate was roughly the same in both groups, there were 6 deaths in 148 patients treated by Billroth-I gastrectomy and 6 deaths in 164 patients treated by Polya gastrectomy, but the latter group included some cases with very adherent ulcers which had been rejected as unsuitable for the Billroth-I operation

TABLE II—DEATHS AT OPERATION, SUBSEQUENT DEATHS FROM UNRELATED CAUSES, UNTRACED PATIENTS, AND PATIENTS FOLLOWED UP

Type of operation	No of patients	No of deaths at operation	No of deaths from unrelated causes	No of untraced patients	No of patients followed up
Billroth I	148	6	1	9	132
Polya	*164*	*6*	*4*	*16*	138

Subsequent Deaths from Unrelated Causes, and Untraced Patients

5 patients died from other causes some time after leaving hospital

2 died from pulmonary tuberculosis one and two years after operation, 1 following prostatectomy four years after gastrectomy, 1 from an unspecified cause one year after operation, and 1 from cardiac failure five years after operation

Despite every effort, 25 patients could not be traced, owing either to a change of address or to their having left the country Several of these patients had been followed up for a short time before becoming inaccessible, but we have considered it best to exclude them from our assessment of the late results

TABLE III—RECURRENT ULCERATION IN ALL PATIENTS FOLLOWED UP

Type of operation	No of patients	Recurrences		
		Proven	Suspected	Total
Billroth I	132	14	6	20 (*15 1%*)
Polya	138	1	1	2 (*1 5%*)

The number of patients who died subsequently and the number who were untraced in each of the two groups were as follows Billroth-I, 1 death and 9 untraced, Polya, 4 deaths and 16 untraced

Follow-up

132 patients treated by Billroth I and 138 by a Polya gastrectomy were followed up (table II) We were interested in three aspects of the late results the incidence

Closing the average laceration took less than half the time eeded for suturing
It was economical
Pain caused by the removal of sutures was eliminated
There were no suture scars

Plastic tapes have been used to close about 100 major urgical wounds There have been no reports of a failure o secure an average or better than average closure, nd abdominal scarring is much less than when the skin s sutured

In a few cases plastic tape has been used to hold kin grafts in place No assessment of its merits can be made until further work is done, but at present this method looks promising

I will gladly send samples of the plastic tape, or further information about it, to any doctor willing to report critically upon his results

8124, Princess Jeanne, N E,
Albuquerque New Mexico

PAUL WILLIAMSON

MODIFIED QUECKENSTEDT TEST

SIR,—Dr Belton seems to be labouring under a misconception the Valsalva manœuvre does not replace the orthodox Queckenstedt test The former will show a significant rise of cerebrospinal fluid (C S F) pressure below the level of the lesion in cases of complete spinal block, as the raised intrathoracic and intra-abdominal pressures are transmitted to the spinal subarachnoid space through the vertebral venous plexuses Thus, if the Valsalva manœuvre is employed, the manometric diagnosis of partial or complete spinal block may be missed Incidentally, the rise of C S F pressure resulting from Queckenstedt's manœuvre occurs so quickly that it must, in part, be due to the sudden swelling of the intracranial veins, which displaces some C S F. into the slightly elastic spinal subarachnoid space

Leicester Royal Infirmary

H J GOLDSMITH

"MUNCHAUSEN'S SYNDROME"

SIR,—On reading Mr Mawson's letter (Jan 14) I recognised that the patient he described had been under my care in this hospital in November, 1955

He was admitted via our casualty department on Nov 23 on a stretcher, having been picked up in the city, suffering from ataxia followed by a blackout He gave a history of three mastoid operations and one for cerebral abscess within the past twenty two months, the last operation having been performed about four months previously He said that he was still "on parole" from a hospital in London He stated that he was an ex male nurse and ship's radio officer, and he was in Dublin to visit his fiancee

Besides some of the findings described by Mr Mawson we found definite slight papillœdema of the right disc, the right visual field was constricted generally Radiography showed almost complete loss of trabecular detail in the right mastoid region, a great deal of bone had been removed in each occipital region, and there were several trephine openings at a higher level on each side opacities resembling Michel clips were present

On the next day, his condition having improved and in view of suspected cerebral abscess possibly necessitating intracranial exploration, he was advised to return to London at once to the hospital where he had received his previous attention In order to expedite his return and as he had not got the full air fare, he was offered a sum of money Of this he took only part, but three days later the hospital had an inquiry from a city mission where he had been seeking further assistance This was the last we heard of him

I write these few notes in the hope that they may help the next colleague under whose care this patient comes

Adelaide Hospital
Dublin

R S W BAKER

SIR,—A seaman answering the description given by Mr Mawson reeled into casualty the other day, now presenting a marked cerebellar gait

His temperature of 101°F could not be shaken He was therefore admitted for observation but refused lumbar puncture Atkinson Morley Hospital had already heard of a man resembling this one, with multiple cranial scars on the right side and a right facial palsy, Princess Beatrice Hospital had dealt with him some time before Following an abrupt but punctilious interview by a physician the following morning, he took his own discharge stating he was Plymouth bound

Croydon General Hospital

F M MOORE

SPORADIC CRETINISM WITH GOITRE

SIR,—I was most interested by the views expressed by Dr McGirr and Dr Hutchison in their letter of Jan 14 It should however be pointed out that their statement "this [Stanbury et al [1]] was the first time that the spontaneous occurrence of diiodotyrosine in the peripheral blood was conclusively proved" is not entirely correct Benua and Dobyns [2] showed that small amounts of mono- and di-iodotyrosine are present in the blood of hyperthyroid and thyroid cancer patients after therapy doses of I^{131} Monoiodotyrosine, but not diiodotyrosine, was excluded as a radiation artefact Further, Benua and Dobyns [2] showed that neither of these compounds was produced from pure I^{131} labelled thyroxine, during their chromatographic procedures

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ROSALIND PITT-RIVERS

OLD FOLKS AT HOME

SIR,—Sir Selwyn Selwyn-Clarke's address, from which you published extracts on Jan 14, suggests many ways in which old people can be assisted But it would be a pity if any reader drew the conclusion that all is well in this field—which is by no means correct

Although several ways and means of helping old people have been mentioned, it has not been made sufficiently clear that, good though these services are, they are not by any means to be found everywhere Indeed some of the examples given are isolated instances of a voluntary body endeavouring to meet a local need after a careful study of the problem It is a great pity that many of these services cannot be reproduced in more places, for I am convinced that the most important task of the voluntary bodies in this field at the present is the provision of properly integrated domiciliary services It is no easy task, for in many instances patience, skill, and devotion are required to a degree not possessed by all There are old people who are anti-social and "difficult" for whom often nothing is done until some near tragedy occurs True the health visitors and the district nurses do wonderful work, but in many places their time is so taken up with family work that they cannot attend to old people as they would wish, and there is, perhaps, less attention given to prevention than to cure I refer here not necessarily to medical treatment but to the support which can be given to old people, by a trained social worker, when they are beginning to deteriorate Too often nothing is done until the failing has gone too far to allow the old person to remain in a place where there is not constant supervision and this leads to an increasing demand for beds on the welfare and hospital services

There are a number of other points on which I should like to comment but there is one particular sentence which cannot fail to be noticed by general practitioners, social workers, and others "But when the nature of the illness or social conditions necessitate hospital care . the patient *will* (my italics) be removed, with his consent, to a hospital" How easy it sounds!

National Corporation for the Care
of Old People Nuffield Lodge
Regent's Park London N W 1

M R F SIMSON
Secretary

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1 Stanbury J B Kassenaar A A H, Meijer, J W A, Terpstra J *J clin Endocrin* 1955 15 1216
2 Benua R S Dobyns B M *Ibid*, p 118

TABLE VI—POST GASTRECTOMY SYMPTOMS NOT DUE TO RECURRENT ULCERATION

Symptom	After Billroth I resection (% of 132 patients)	After Polya resection (% of 138 patients)
Postcibal epigastric fullness	45 4	39 8
Postcibal epigastric fullness with faintness and sweating, &c	15 1	10 8
Bilious regurgitation	9 0	15 2
Non bilious regurgitation and vomiting	6 8	5 0
Persistent weight loss of more than ½ st	20 4	15 9
Quick fatigue	11 3	15 9
Persistent diarrhoea	2 3	2 8

encountering a single instance of definite recurrent peptic ulceration in the stomach or elsewhere

In the present series the higher incidence of duodenal or stomal recurrences after Billroth-I resection than of jejunal ulceration after Polya gastrectomy is surprising in the light of the experimental work of Ivy and Fauley (1931), which gave good reason to believe that the susceptibility to peptic digestion of the duodenal mucosa is less than that of the jejunum On the other hand, the experiments of Mann and Williamson (1923) and others have shown the importance of the neutralisation of the gastric juice by the alkaline bile and pancreatic juice in the avoidance of jejunal ulceration after gastro intestinal anastomoses This factor of neutralisation probably explains why the Billroth I is less satisfactory than the Polya operation

After the Polya operation every drop of bile and pancreatic juice entering the alimentary tract must pass over the jejunal mucosa exposed at the stoma, and this part of the bowel is therefore afforded the fullest possible protection by neutralisation of gastric acidity But after a Billroth I gastrectomy, although there is certainly regurgitation of some bile and pancreatic juice from the second part of the duodenum into the first part and the stomach, a considerable proportion of these alkaline juices is presumably lost distally and cannot protect the duodenal mucosa adjacent to the anastomosis

Treatment of Recurrences

The single patient with a proven recurrence after a Polya resection was treated by vagotomy alone and subsequently had occasional dyspeptic symptoms At the present time, three years after the second operation, the patient is in fairly good health and no definite ulcer can be demonstrated radiographically The patient who had a suspected ulcer after a Polya operation was treated expectantly, he has had no further bleeding and only slight intermittent dyspepsia, and radiographic examination has been negative

13 of the 20 patients with proven or suspected recurrences after a Billroth-I gastrectomy had a further laparotomy After confirmation of the diagnosis, treatment consisted of vagotomy alone in 6 cases and conversion to a Polya type of anastomosis in 7 cases, in 2 of which a vagotomy was also performed All these patients have been seen recently, 4 of the 6 treated by vagotomy alone, and all of those whose anastomosis was converted to a Polya type, are very well 2 of the patients who underwent vagotomy continue to have some pain, as do the majority of the 7 patients treated by dietetic or expectant measures These experiences with vagotomy are of special interest because they suggest that the combination of vagotomy with a high Billroth-I resection in the treatment of duodenal ulcer would not provide a complete insurance against the development of recurrent ulceration

POST GASTRECTOMY SYMPTOMS NOT DUE TO ULCERATION

The frequency of the commoner post gastrectomy symptoms is shown in table VI There was very little difference between the frequency after the two operations, on the whole these results favoured the Pol method, but biliary regurgitation was undoubted commoner, and was probably more severe, after t Polya operation

THE PATIENT'S FUNCTIONAL STATE

The patient's functional state, and his capacity t work and enjoy life, is, in a way, the most importan point in assessing the results of any operation W employed a system of grading closely modelled on th recommended by Visick (1948)

Excellent meant that the result was perfect in every respe

Very good meant that the result was perfect in the eyes o the patient but that some symptoms were elicited by us T patients had largely forgotten about these symptoms, becau they were able to dispel them by minor adjustments to th diet and mode of life A persistent weight loss of up to 10 l was allowed for this category, but patients had to be complete fit for their previous work

Fair meant that the patient had fairly severe symptom but he considered that he was better off than before operatio Several of these patients had a persistent, severe weight los and had to seek lighter work

Unsatisfactory meant that the patient was not improve (Most cases of recurrence fell into this category)

Table VII shows the results in our two groups graded according to this system It shows a slight, but definite, superiority in the results of the Polya, compared with those of the Billroth-I, operation, the latter were especially marred by the large number of patients in the "unsatisfactory" category

TABLE VII—FUNCTIONAL RESULTS

Result	After Billroth I resection (no of patients)	After Polya resection (no of patients)
Excellent	50 } (75 0%)	70 } (89 8%)
Very good	49	54
Fair	13	10
Unsatisfactory	20	4
Total	132	138

Conclusions

The Billroth I resection, even when extensive, is an unsatisfactory operation for duodenal ulcer After this operation the recurrence rate (up to 17% on a three year follow-up) is much higher than that after the Polya operation (2%)

The Billroth I operation is no less likely than the Polya operation to be followed by post gastrectomy symptoms not due to recurrent ulceration, except biliary regurgitation

The functional condition of the patients after Billroth I resection is slightly worse than after the Polya operation

Sometimes the Billroth I method is not technically feasible, and if an attempt were made to enforce it as routine in all cases of duodenal ulcer the operative mortality might well increase

We see no reason whatever for using the Billroth I resection as a primary operation for duodenal ulcer when there is available one so excellent as the Polya, but we admit that for the occasional very severe case of bilious vomiting after Polya gastrectomy for duodenal ulcer it may be justifiable to convert the anastomosis to a Billroth I type and accept the increased risk of recurrent ulceration in order to eliminate this incapacitating symptom

REFERENCES

Ivy, A C, Fauley, G B (1931) *Amer J Surg* 11, 531
Mann F C Williamson C S (1923) *Ann Surg* 77, 409
Visick, A H (1948) *Lancet* i, 505

right iliac fossa At laparotomy a hair ball was removed m the lower jejunum, where it was impacted and was eady beginning to ulcerate through the gut wall

The hair ball (see figure) was about 7 cm long and 5 cm de at one end The child had been noticed chewing her ur while in hospital, and her parents stated that she had ways done so from early childhood

Trichobezoar has rarely been reported in man, particurly as a cause of intestinal obstruction My two cases six years suggest that the condition is commoner than e believe

North Staffordshire Royal Infirmary
Stoke on Trent
H S TRAFFORD

CERVICAL VERTIGO

SIR,—It is most interesting to see the different opinions n the ætiology of paroxysmal vertigo, the latest contribution to which is made by Dr Ryan and Dr Cope Dec 31) under the above heading

I myself made a small effort to solve this problem[1] have also observed that pain stimuli in the head and eck, for example, may elicit attacks of vertigo by bending he neck, but not pain alone except in patients with migraine In these particular cases of vertigo I have always found an imbalance of the masticatory apparatus, of which the muscles and joints and also the trigeminal nerve are involved, owing to a faulty bite The vertigo vould be a reaction of the ear to a physical irritant, and I suggested[1] that the paroxysm is caused by myoclonus of the middle ear muscles

In addition to the instability of the sensory organ in the semicircular canals in these cases, there is also an affection of the cochlea This may be fluctuating or permanent, subjective and/or objective, and perceptible by audiometric examination The lesion does not seem to be cervical

Bergen Kommune sykehus
Bergen Norway
H MYRHAUG

SIR,—In reply to Mr Wilmot's comments (Jan 7) on our article (Dec 31) by aural investigation we meant that audiometry and caloric testing were carried out in addition to clinical examination The question of cervical sympathetic involvement in the quoted cases was discussed in the paper, and though we considered it a possible mechanism our reasons for favouring the alternative explanation were given The presence of cervical disease and vertigo does not of itself signify that the two are related What we wished to show was that there is a characteristic clinical picture by which cervical vertigo can be diagnosed

Royal Southern Hospital
Liverpool
S COPE
G M S RYAN

ANÆSTHESIA FOR CÆSAREAN SECTION

SIR,—In an earlier letter[2] I referred briefly to anæsthesia by hexobarbitone, suxamethonium bromide, and nitrous oxide for cæsarean section I have received many inquiries about the technique

Patients come to the theatre with a Ryle's tube in situ, premedicated with gr $^{1}/_{150}$ atropine sulphate The stomach is aspirated immediately before induction

When the patient has been towelled 0 5 g hexobarbitone is given intravenously, followed immediately by 60 mg suxamethonium bromide ('Brevidil M') through the same needle, and the surgeon makes his incision

While the incision is being made the patient's lungs are gently inflated with a mixture of nitrous oxide (75%) and oxygen (25%) until the relaxant has taken effect Then the patient is intubated and the nitrous oxide/oxygen mixture is continued, a Gordh needle is put into a vein on the back of one hand, and the forearm flexed to bring the needle within easy reach of the anæsthetist

Once the delivery has started the nitrous oxide is cut off and the patient's lungs are flushed with pure oxygen until the cord is cut when the cord is separated the patient is put back on the former nitrous oxide/oxygen mixture, and a further 0 5 g hexobarbitone is given through the Gordh needle—by means of which ergometrine has already been given at the time of delivery

Usually the effect of the suxamethonium bromide has worn off by the time delivery takes place, but sometimes either the surgeon is quicker than usual or the action of the relaxant persists unusually long, and the mother is apnœic when the child is born, but on no occasion has the child's respiration been depressed, and it would appear that the suxamethonium bromide is "lost" in the placenta

I have never seen maternal or fœtal respiration depressed by hexobarbitone, and I prefer this technique to any other, including spinal anæsthesia

Gloucester Royal Infirmary
J SHEGOG RUDDELL

UTERINE DYSFUNCTION DURING LABOUR

SIR,—I have suggested[1] that uterine dysfunction may be related to the patient's personality, and have described a "dysfunction temperament" characterised by suppression or repression of feelings of tension, so that little or no overt anxiety is shown Women with this temperament are reserved and difficult to know, they have a slight tendency to develop peptic-ulcer symptoms, and they have a bias towards rigid and conventional forms of behaviour

This bias was deduced from the results of the Minnesota Multiphasic Personality Inventory,[2] which was completed by most of the patients I investigated It was discovered that 45% of the dysfunction group had high "lie" scores compared with 20% of the control group, the difference being significant at the 2% level

The "lie" score is based on the answers ("true" or "false") to the following 15 questions which are so devised that, if answered honestly, they place the patient in a socially unacceptable light

1 Sometimes, when I am not feeling well, I am cross
2 I would rather win than lose in a game
3 I get angry sometimes
4 I do not like everyone I know
5 Once in a while I think of things too bad to talk about
6 Once in a while I put off until tomorrow what I ought to do today
7 I gossip a little at times
8 I sometimes laugh at vulgar stories
9 My table manners are not quite as good at home as when am in company
10 I do not always tell the truth
11 I do not read every editorial in the newspaper every day
12 If I could get into the cinema without paying and be sure I was not seen, I would probably do it
13 At times I feel like swearing
14 Sometimes at elections I vote for a man about whom I know very little
15 I like to know some important people because it makes me feel important

If a patient answered "false" to 7 or more of the 15 questions, her "lie" score was regarded as significantly high, that is to say, she tended to deny in herself venial faults which we all possess, but which we dislike to admit to other people lest we fall in their estimation

In a subsequent investigation the 15 items of the "lie" scale were incorporated in an inventory with 65 other items dealing with pregnancy and with anxiety-producing situations, and the inventories were given to 900 consecutive primigravidæ who attended the Aberdeen Antenatal Clinic during the latter part of 1954 and the first half of 1955

The test was administered by the health visitor in charge of the clinic and the completed inventories were sent to me

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[1] Nord Med 1953, 50, 1107
[2] Lancet, 1955, ii 1138

[1] Cramond, W A Lancet 1954, ii, 1241
[2] Hathaway, S R, McKinley J C The Minnesota Multiphasic Personality Inventory New York, 1940

WATER DEPLETION

Common Cause

Diminished intake in weak or ill patients, especially after operations, and in coma

Note—Normal water requirements are about 2 5 litres a day (average minimum 2 litres) On a normal diet 1 5 litres a day is taken as fluid, and 1 litre is contained in the food. Therefore, if no food is taken, fluid intake must be increased by 1 litre a day Water is required to replace insensible loss (about 1 litre) and to provide 1 0–1 5 litres for daily urinary excretion Normal water intake must be maintained *in addition to replacement of any abnormal fluid loss* Normal saline solution, for instance, does not satisfy water requirements

ELECTROLYTE DEPLETIONS

Na and Cl are mainly involved, and to a lesser extent K

Body fluid containing electrolytes ("electrolyte fluid") may be lost in the following ways

Common Causes

Vomiting
Gastric suction
Intestinal or biliary drainage
Diarrhœa

Rarer Causes—Via the urine in

Diabetic ketosis and coma
Continued use of mercurial diuretics, and repeated paracentesis or acupuncture, especially in association with a low Na intake
Diuresis following anuria
Untreated Addison's disease

MANAGEMENT OF DEPLETIONS

(1) *Object* the correction of existing depletions as soon as possible and the prevention of threatened depletions

(2) *Criteria of success* the maintenance of a normal urine volume of 1 0–1 5 litres per day, with normal urine and plasma electrolyte levels (see notes F and J)

(3) Water depletion is corrected by giving water in excess of normal requirements

(4) Since electrolyte depletion is mainly due to loss of Na and Cl in approximately isotonic fluid, correction is, in the first instance, by replacement with isotonic NaCl (normal saline) solution, the volume required being the same as the volume of body-fluid lost (see para 5 and note G) Although the composition of the replacement fluid will not be exactly the same as that of the fluid lost, the necessary adjustment will usually be made by the kidney (see notes C and D)

Potassium depletion usually appears when a considerable volume of body-fluid has been lost and intake is inadequate Intravenous isotonic solutions of potassium salts should, however, *not* be used for replacement as these are too concentrated The solution of KCl containing 40 m eq of K per litre should be used (see para 5 and note E)

Electrolyte and water depletions may occur together, in which case measures in paragraphs (3) and (4) should be combined

(5) *Routes of Administration of Principal Fluids*

	Mouth or gastric tube	*Intravenous*	*Per rectum*
Water replacement	Tap water 5–10% dextrose solution	5% dextrose solution	Tap water
Electrolyte replacement		Normal saline solution* (155 m eq of Na and Cl per litre) Sodium lactate solution* (155 m eq of Na per litre) Potassium chloride solution* with 3 5% glucose (40 m eq of K per litre, see note E)	
"*Maintenance solution*"		½ normal saline solution* with 4% dextrose (see note B)	

* These solutions can also be given by mouth or gastric tube in appropriate cases (see note K)

In some cases it may be possible to give NaCl and KCl crystals by mouth in capsule form, provided water intake i increased proportionately (see note K)

For the correction of an existing water depletion 1–4 lit of fluid is usually required according to the severity of th depletion For the correction of an existing electroly depletion 1–8 litres is usually required (para 7)

(6) *Use of Chart*

The chart is designed for a period by period comparison o water and electrolyte fluid intake and output with urine an blood analyses

Electrolyte fluid—"Electrolyte fluid loss" in any o period should be directly compared with "electrolyte flu replacement" for the same period The total under the two headings should balance volume for volume (e g, 1 lit from biliary drainage should be replaced by 1 litre of norm saline solution), provided that there is no pre existing electrolyte depletion If there is already a depletion, it should b corrected at the same time as current losses are being replaced the total under "electrolyte fluid given" remaining muc larger than the total under "electrolyte fluid loss," until th pre existing depletion is made good

Water—No attempt need be made to obtain a similar bal ance with water The total volume of water given should b that necessary to obtain a normal urine volume of 1 0–1 litres a day (see notes F and J) The actual volume of urin passed in a period is charted under "urine analysis"

Analyses—Urine and blood analyses are charted alongsi the electrolyte and water intake and output data for eac period

(7) *Treatment of Existing Depletions*

In a fresh case the nature and extent are estimated, b recognition of the cause, the clinical findings, and a *complet* blood and urine analysis as detailed in the chart (urine bein obtained by catheter if necessary)

(*a*) Enter biochemical findings in period 1 of chart, and wri estimated requirements for period 2 (these will fall within th limits given in para 5) on the back of the chart, bottle b bottle These are initialed by the nurse as they are give (Note that details entered on the *front* of the chart are for th period just elapsed, and that fresh orders entered on th *back* of the chart are for the period just begun With a ne *case, therefore, the first orders are entered on the back* period 2)

(*b*) At the end of each period the patient's bladder i emptied, and *all* urine passed in the period is sent with a bloo sample to the laboratory for analysis (see note H) Enter th results of the analyses in period 2, *together* with total (obtained from nurses' fluid chart) for electrolyte fluid los electrolyte fluid replacement, and water intake From th information, and from the laboratory analyses, it will b apparent to what extent existing depletions have been mad *good, and what further losses* have occurred during th period Order appropriate solutions on back of chart for nex period, including normal water requirements

(*c*) Discontinue the above régime when depletions hav been corrected, and source of depletion is under control *Continue thereafter with maintenance solution* (note B) unti normal intake by mouth can be maintained Over treatmen is dangerous

(8) *Treatment of Threatened Depletions* (due, for example, t postoperative drainage from fistulæ, gastric suction, diarrhœa *or vomiting, but where there is no* pre existing depletion)

(*a*) Request complete blood and urine analysis Estimat volume of fluid likely to be lost from body during next perio and order necessary replacement solutions, *including* wate requirements for the period (*It may be necessary to revie the estimate as period proceeds*)

(*b*) At the end of period, empty bladder, send all urine and specimen of blood to laboratory for analysis Enter the analyses on chart, with totals for electrolyte fluid loss, electro lyte fluid replacement, and water intake Review all finding and *order appropriate solutions for next* period on back chart, including water requirements

(*c*) Continue this procedure until source of depletion under control

Notes

(A) Twenty four hour periods of controlled treatment a usual, but in a severe depletion twelve hour periods are ofte necessary at the start All information for one period shoul be obtained before prescribing for the next period

(B) 2 5 litres of the maintenance solution a day will cove both water and electrolyte requirements where electroly

After abolition of the vomiting, by direct suggestion, he patient's excessive salivation apparently symbolised he still present need to rid herself of the fœtus Later eports stated that she was well

"There are many things, the knowledge of which is of little or no profit to the soul" [5]

London, W 1 GORDON AMBROSE

POLIOMYELITIS VACCINE

SIR,—Extensive use of this vaccine in this country is now proposed It may seem a presumption to raise any question when it has apparently such eminent sponsorship, but, as one of the persons who will be concerned with the actual administration of this vaccine, I cannot help feeling some uneasiness It appears that the degree of protection given is not certain and also its duration We are assured that the vaccine is fully safe, but one cannot but recall that poliomyelitis vaccines in the United States last year had disastrous consequences

When this vaccine comes into use it will mean that three materials are being used in this country whose efficacy is uncertain and whose safety is open to doubt

The first is B C G, which is being used on an ever increasing scale although there is as yet no proof that it is of any value, while there is actual certainty that in a proportion of cases it produces damage of greater or less amount

The second is whooping cough vaccine, also being used on a large scale although we have not yet been given any statistics to show its value—if any One had understood that a factual report on whooping cough vaccine was to be published, but so far all that seems to be available are statements as to "clinical impressions" Many of us are not particularly interested in clinical impressions we require figures

Now this poliomyelitis vaccine is to be brought into general use without, to my mind, satisfactory evidence of its efficacy and safety

Although poliomyelitis rightly causes great concern, both because in a small proportion of cases its consequences are disastrous and because it is a disease for which we have no specific treatment, nevertheless a sense of proportion is called for Even in the worst years we have yet experienced, although the number of cases of poliomyelitis infection has amounted to several thousands, they represent a minute proportion of the population at risk, and the number of cases in which death or paralysis has occurred has been small in proportion to the population Is it proper to administer a vaccine of doubtful potentialities to the child population at large to meet so small a risk? I agree that the individual parent, faced with the death of a child from poliomyelitis or with a paralysed child, will rightly regard this as a very great tragedy, but I do question whether the facts justify us, as yet, in undertaking a mass vaccination campaign In saying this I would like to make it clear that I am by no means an anti vaccinationist I am an enthusiastic supporter of immunisation against diphtheria Here the position is rather different, since we are dealing with the use of a chemical substance and not with an organism living or dead I am also a firm believer in the value of anti smallpox vaccination and yellow fever inoculation But I do think it is not unreasonable to suggest that poliomyelitis vaccines are as yet only in the experimental stage, and I do question whether we have any right to carry out a large scale experiment which may have serious consequences I would certainly hesitate myself, in the present state of knowledge, to give myself or my children this vaccine I think that similar doubts may well be felt by quite a proportion of medical practitioners, and I therefore raise this matter to see if we may have some indication in your columns as to the extent of the doubts felt about this and also whether any convincing evidence can be brought forward to settle these doubts

All this, I should make it quite clear, is a purely personal expression of opinion

Accrington, Lancs R C WEBSTER

Obituary

WILSON HAROLD HEY

M B Manc, F R C S

Mr Wilson Hey, consulting surgeon to the Manchester Royal Infirmary, died on Jan 15 at the age of 73 He was a general surgeon with a strong bias towards urology and he will be remembered particularly for his work on prostatic carcinoma and for the method of prostatectomy that he devised

He was born in Colne, which lies in the heart of Lancashire, and he early showed the determination and stubborness said to be characteristic of the palatinate He entered Manchester University with a leaving scholarship from Burnley Grammar School, and he proved himself an outstanding student, with an original mind His retentive memory and capacity for work served him well, and he won many prizes, medals, and scholarships After graduating M B in 1905 he held house-appointments at the Manchester Royal Infirmary, later becoming resident surgical officer and surgical tutor He was awarded the Tom Jones Research scholarship in surgery and in 1908 he took the F R C S Shortly before the outbreak of war in 1914 he was appointed to the honorary staff of the Royal Infirmary, but almost at once he left Manchester to serve as a surgical specialist with the rank of major in the R A M C For his services to French soldiers he was appointed a chevalier of the Legion of Honour

Schmidt Manchester

On his return to Manchester after the war Wilson Hey's surgical technique and his energy soon gained him a large practice In 1919 he was appointed to the staff of the Christie Hospital and he was one of the first surgeons to use radium He also joined the staff of the Ancoats Hospital, and the Manchester Children's Hospital He was lecturer in clinical surgery at the university he was an interesting and stimulating teacher and students flocked to his outpatient department, for he knew how to pinpoint a principle with an unbelievable but also unforgettable anecdote

Despite his large private practice and his hospital and teaching duties, his original turn of mind and energy obliged him to make time for research Urological surgery had long been his chief interest, and he showed that, in his hands at least, the emergency removal of the prostate gland was a safe proceeding His "aseptic" operation was a transvesical prostatectomy (preceded by twelve hours' chemotherapy) in which the trigone was excised and the bladder afterwards closed He was insistent that "technique and route are merely the handmaidens of asepsis in any operation," and he urged that a catheter should never be used before prostatectomy Latterly, he was also investigating the use of hormones in breast and prostatic cancer and shortly before his death he was putting the finishing touches to his record of his results in cancer of the breast for the last thirty years An old patient had left him a large sum of money to establish a hormone research department at the Christie Hospital and he was preparing the plans for this project

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[5] Thomas à Kempis De Imitatione Christi Chapter 2

Laboratory Examinations

The erythrocyte sedimentation rate (E S R) was raised, ranging from 70 to 120 mm in the 1st hr (Westergren) Leucocytosis ranged from 11,000 to 20,000 per c mm , with a shift to the left in the differential count Blood-cholesterol and serum-protein levels were within normal limits Throat swabs yielded micro organisms belonging to the usual flora of the upper respiratory tract (non-hæmolytic streptococci, *Neisseria catarrhalis*, &c) Radiography did not reveal either compression of the trachea or substernal goitre Electrocardiography was normal The basal metabolic rate (B M R) at the time of admission was raised in all the cases, ranging from +13% to +55% The uptake of radioactive iodine by the thyroid gland ranged from 0 to 13%, and its excretion in the urine was correspondingly increased

Treatment

4 of these patients had received penicillin, streptomycin, or chloramphenicol before admission without effect

Two days after admission 3 patients were treated with oral cortisone 50 mg daily Within twenty-four hours after the administration of cortisone the temperature became normal, the pain subsided, and the patient's general condition improved considerably Treatment was continued with decreasing doses up to four weeks No immediate or late relapses were observed

2 other patients were treated with corticotrophin gel 20 mg twice daily The immediate effect of corticotrophin was as beneficial as that of cortisone, but 1 of the corticotrophin-treated patients had two relapses when the dose was reduced Subsequent increase of the dose readily suppressed the signs again No late recurrences were observed

The 6th patient received no treatment, because she had been admitted to hospital in the sixth week of her disease, when she had recovered spontaneously

The E S R was gradually lowered within three weeks in the patients treated with cortisone and corticotrophin gel The leucocyte count returned to normal during the same period

The B M R and the uptake of radioactive iodine were studied in 3 patients three weeks after the institution of therapy, and the results were similar to those obtained at the time of admission

These examinations were repeated in 4 patients four to fourteen months after their discharge from hospital In 3 of them normal values were obtained, but in the 4th a slightly increased uptake (66%) of radioactive iodine was noted The 2 remaining patients were not available for follow-up

Discussion

All 6 patients reported here were women, aged 35–64 The incidence of non-suppurative thyroiditis in women of this age-group has already been noted (Thorn and Forsham 1952, Williams 1950)

During the acute stage the clinical signs and symptoms indicated thyrotoxicosis It has been suggested that these signs may be due to the escape of thyroglobulin from the disrupted acini into the blood stream (Crile 1952)

4 cases were followed up for four to fourteen months In none of them did clinical symptoms and signs of either thyrotoxicosis or myxœdema appear Repeated examinations of B M R were normal, and the uptake and excretion of radioactive iodine was normal in 3 patients and slightly increased in the 4th This finding is in agreement with the cases observed by Robbins et al (1951) for two and a half to ten months On the other hand, McConahey and Keating (1951) reported that myxœdema developed in 6 of 21 cases of thyroiditis It is not clear whether the diagnosis in these cases was confirmed by a study of the uptake of radioactive iodine or by determinations of protein-bound iodine The question whether either corticotrophin or cortisone can prevent the development of myxœdema in these cases is thus left unanswered A longer follow up and larger numbers of patients are needed to clear this up

Krupp et al (1951) reported the prompt effect of cortisone in non-suppurative thyroiditis, and numerous investigators have confirmed this (Crile 1952, Crile and Schneider 1952, Benjamin 1955, Kraft and Wolf 1955) In the present 5 cases treated with either corticotrophin or cortisone the symptoms and signs disappeared rapidly In 1 of these patients two relapses occurred concomitantly with a decrease in the dosage of corticotrophin , but a prompt response was obtained by increasing the dose again Similar relapses were reported by Teitelman and Rosenberg (1953)

Several attempts have been made to explain the beneficial effect of corticotrophin and cortisone in non suppurative thyroiditis Most workers ascribe the rapid clinical improvement to non specific alteration of the tissue response to inflammation (Crile 1952, Kraft and Wolf 1955), but the exact nature of this effect has not yet been elucidated

Summary

6 cases of subacute non-suppurative thyroiditis are described In 5 of them the administration of either corticotrophin or cortisone had a prompt beneficial effect on the clinical symptoms and signs

The uptake of radioactive iodine by the thyroid gland was close to zero in the 5 cases in which it was studied, and returned to normal in the follow-up period of four to fourteen months

Neither late recurrences, nor myxœdema, nor thyrotoxicosis were seen in these cases

We wish to thank Prof M Rachmilewitz for his helpful suggestions, and Dr J A Stein for the determinations of uptake of radioactive iodine

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VACCINIA VERSUS POLIOMYELITIS?

D P MacIver
M C , T D , M D Edin , D P H
MEDICAL OFFICER OF HEALTH, WALTON AND WEYBRIDGE URBAN, CHERTSEY URBAN, AND BAGSHOT RURAL DISTRICTS, SURREY

Since 1947 I have been investigating, by personal visits and by observation in hospital, all cases of acute poliomyelitis occurring in the three county districts for which I act as medical officer of health Early in this work I formed an impression that poliomyelitis seldom attacks children who have been vaccinated against smallpox during the previous few years , and last autumn's outbreak has provided me with clearer evidence that this is so

Observations

In the three districts, which have a total estimated population of 87,340, the number of children born in 1946–54 was 11,842 Of these a small majority (53%) were vaccinated * , and one would therefore expect to reparation of the antigen was not generally understood, and he wide use of the Dreyer technique designed for H agglu ination influenced many workers to allow their culture of roteus OX to revert to the OH form and thus to lose pecificity By slavishly following Felix s instructions I was aved from this error Later I came to know him personally, e corresponded much when I was overseas, and there were ontinual reminders of the clarity of what he wrote He ook infinite pains to express himself clearly in correct English

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* In this paper the word ' vaccinated " means vaccinated against smallpox

'Felix travelled widely and enjoyed travel He knew eminent bacteriologists in most countries, and he liked to visit them in their laboratories Because of this he was a mine of information about most of the personalities in the bacteriological world A hard master he demanded much of his assistants, but he himself was a slave to his own work He believed in the importance of his own department, but he also understood the need for a sense of proportion in a large institute He was not given to great social activities, but he was a thoughtful and generous host, and a loyal and powerful friend, capable of great charm and kindness, and he had a gentleness that sometimes surprised those who did not know him well"

Dr Felix stayed at Colindale as director of the Central Enteric Reference Laboratory until his retirement under the age-limit in April, 1954 Still fully active, and working under a special grant for two years, he was given accommodation at the Lister Institute to complete unfinished work There he continued at full tempo until the very end

ARCHIBALD FRANCIS WRIGHT

M C, M B Edin

Dr A F Wright, pathologist to the Coventry and Warwickshire Hospital from 1924 until his retirement in 1951, has died at the age of 72

He was born at Southport and educated at Monmouth Grammar School, Edinburgh Academy, and the University of Edinburgh, where he qualified in 1906 In the same year he was appointed to the staff of the Monmouth Hospital In 1910 he became bacteriologist and consultant clinician for venereal diseases to the Staffordshire County Council During the 1914–18 war he served with the R A M C as bacteriologist He was mentioned in despatches and awarded the Military Cross In 1920 he visited the West Indies as a member of the Medical Commission to Combat Venereal Diseases

After his demobilisation he decided to specialise in clinical pathology, and he served as pathologist, always with a strong clinical bias, on the staffs of hospitals in the West Midlands, finally coming to rest in Leamington as pathologist, first to the Warneford Hospital, and in 1924 to the Coventry and Warwickshire Hospital He was a far-sighted and competent organiser, and it was thanks to him that between the wars the authorities of the Coventry and Warwickshire Hospital and the Coventry Borough Council were persuaded to set up a joint laboratory service, with a laboratory within the hospital Such an arrangement is now commonplace, but at that time such close cooperation between a voluntary hospital and a municipal health authority was unusual The joint laboratory service proved of the greatest benefit both to the hospital and to the health service of the borough In 1938 he started a blood-transfusion service based on the laboratory, and at the outbreak of the late war it had already enrolled over 10,000 donors He was a founder member of the Association of Clinical Pathologists, and he served on the advisory committee in pathology of the Birmingham Regional Hospital Board from its inception until his retirement

S C D, to whom we are indebted for some of this information, adds

From the beginning of his medical career Dr Wright was imbued with a sense of the importance of the laboratory in clinical medicine, at that time practically unrecognised in British medical practice It may truly be said that he introduced clinical pathology into the West Midlands For some time before and since his retirement, his health was not good, and latterly few of his colleagues had seen much of him It is a sign of their affectionate regard that to them he was always "Pop" With his passing, a figure that had become and will remain traditional has disappeared

CARL EISINGER

M D Vienna, L R C P E

Mr Eisinger, ear, nose, and throat surgeon to the West Middlesex Hospital, Isleworth, died in London on Jan 14 He was born in Vienna in 1895, and he qualified there in 1920 He worked first at the Institute of Embryology, where he became lecturer under Prof H Fischel and published papers on the artificially induced division of unfertilised ova in mammals and the extirpation of the inner ear in amphibia He later turned to ear nose, and throat work and was elected to the staff of the Vienna university hospital under the late Prof H von Neumann He was appointed Dozent in 1934 Four years later, when Austria was taken over by the Nazis he was forced to leave Vienna

When he arrived in England he expected to go to the United States, where he had been offered a post at St Louis, but when he was appointed postgraduate lecturer at the Metropolitan Ear, Nose, and Throat Hospital, he decided to remain in this country In 1910 he took the Scottish conjoint qualification Later he was appointed to the staffs of the Metropolitan Ear, Nose and Throat Hospital and the West Middlesex Hospital During the late war he was honorary lecturer at St George's Hospital Medical School

After the war Eisinger was twice approached on behalf of the University of Vienna, with a view to his taking up the chair in otorhinolaryngology there, but he preferred to stay in the country of his adoption

R S G writes

'I had the good fortune to meet Carl Eisinger over twenty five years ago in Vienna when he was senior assistant in Neumann's department, where he taught many hundreds of postgraduates from all parts of the world In 1938 he came to this country and was welcomed by a large number of otologists who had attended Neumann's clinic, and was induced to stay in this country He was a man of culture, who lived for his profession and love of people, and, with a wide knowledge of his specialty, which he practised with courtesy and dignity, he soon built up a large consulting and hospital practice He was a jovial companion and a most loyal colleague with high ideals In discussion and in committee he freely expressed his opinion with foresight and wisdom By his death we have lost an otologist of high standing with a great international reputation"

Mr Eisinger leaves a widow and a son, Dr George Eisinger

HORST OERTEL

M D Yale

Professor Oertel, who died at the age of 84 in London on Jan 9, was one of the last links between Virchow, the father of cellular pathology, and pathologists of the present time He was Strathcona professor of pathology at McGill University from 1919 until 1938, and during his time he was largely responsible for the building and development of the pathological institute there When it was opened in 1924, A E Boycott travelled from England to give the inaugural address

Oertel was born at Oberlossnitz, near Dresden, and educated at schools at Plaven and Meissen He took his medical degree in the United States, and after graduating M.D at Yale University in 1894 he returned to Germany to begin his postgraduate study of pathology in Berlin He found the medical school there overcrowded, and though he appreciated the teaching of men like Virchow, von Leyden, Gerhardt, and von Bergmann, he moved to Wurzburg, where he acted as junior assistant to Rindfleisch and Borst It was while working at Wurzburg that Oertel decided that if he was to follow an academic career it was essential to have a preliminary training in philosophy, logic, and biology Wundt at Leipzig was attracting students and research-workers poliomyelitis than those of the less well to do. The fact that, among children contracting poliomyelitis at 5–15 years of age, there was no difference between the vaccinated and the unvaccinated supports the view that social and geographical differences are not the explanation of the findings in the younger children.

4. The fourth possibility is that, at any rate in young children, vaccination against smallpox reduces the likelihood of developing paralytic poliomyelitis within the next three years. Why it should do so is not obvious; for, though postvaccinal encephalitis and polio encephalitis resemble one another clinically, I am informed that no serological relationship between vaccinia and poliomyelitis viruses has been recognised. Hence if there is, as I have postulated, an inverse relationship between vaccination and the incidence of paralytic poliomyelitis, it will require further explanation.

Summary and Conclusions

In 1946–55, in a mainly urban area, with a population of 87,000, where a small majority of children are vaccinated in infancy, there were 21 cases of paralytic poliomyelitis in unvaccinated children under 5 years of age but only 4 in their vaccinated coevals. Of the 19 children under 3½ years old who contracted the disease 17 had never been vaccinated and 1 had been vaccinated only four days previously.

The evidence of this small series suggests an inverse relationship between vaccination and paralytic poliomyelitis in young children. The potential importance of such a relationship makes it desirable that its existence should be proved or disproved, for which purpose equally detailed examination of larger material will be necessary.

I have to thank the parents of all the children for their help and for the information they gave me so willingly, sometimes under difficult and distressing circumstances.

NAPHTHALENE POISONING

E. Gidron
M.D. Rome
DEPUTY CHIEF

J. Leurer
M.D. Zürich
ASSISTANT

DEPARTMENT OF MEDICINE OF THE SHA'ARE ZEDEK GENERAL HOSPITAL, JERUSALEM

Since the introduction of naphthalene in 1841 by Rossbach as an internal antiseptic in typhoid fever and in 1842 as an anthelmintic and adjuvant in dermatological conditions, many cases of intoxication with this substance have been reported—mainly as side-effects of therapy. Industrial naphthalene fume poisoning, chiefly with skin manifestations (Touraine and Ménétrel 1934, Fanburg 1940) and especially naphthalene cataract (Bouchard and Charrin 1886, Michail and Vancea 1927) have also been often reported and investigated.

The fact that, though naphthalene is widely used, only 9 cases of poisoning have been reported since 1947, suggests that this condition often goes unrecognised. Perusal of standard textbooks of medicine, pharmacology, and toxicology supports this impression, for naphthalene intoxication is described in but few of them, and some current textbooks still recommend the therapeutic use of naphthalene.

We therefore report here another case of attempted suicide with naphthalene, review previous publications, and present a comprehensive clinical and pathological picture of "moth-ball anæmia" (*Lancet* 1949). It is to be hoped that naphthalene poisoning will find its way into the new editions of textbooks of medicine, and that naphthalene will be dropped from the modern therapeutic armamentarium.

Case-report

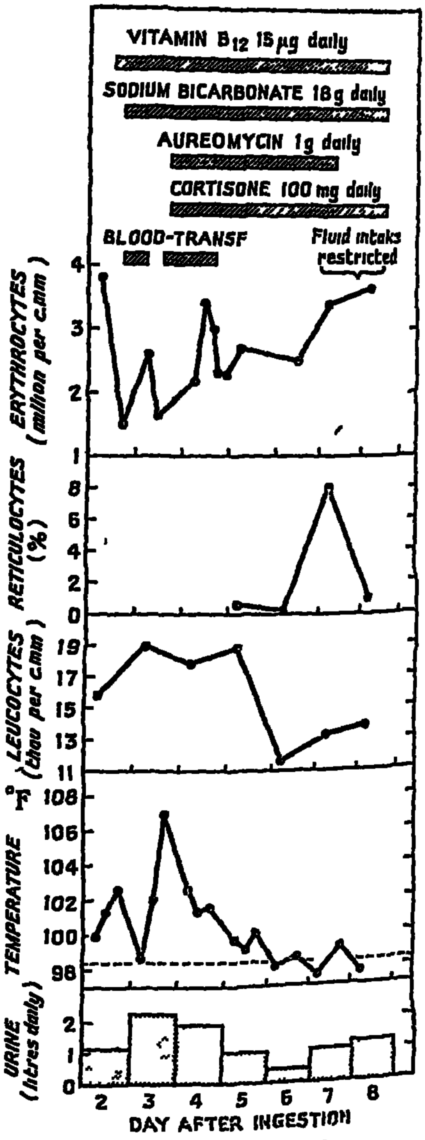
A girl, aged 16, an immigrant from Kurdistan, was admitted to the medical department of this hospital on Dec. 2, 1954, with the history of having taken, 24 hours earlier, about 6 grammes of naphthalene in order to commit suicide. For the 12 hours preceding admission she had increasingly suffered from vertigo and generalised abdominal pain, and had passed four yellow stools. In the evening a physician had given her an emetic, whereupon she had vomited twice.

Dec. 2.—On admission she was in good physical and mental state, not especially pale, and not icteric. The only abnormal findings at physical examination were tenderness of the abdomen, especially to the left of the umbilicus, and marked tenderness in both loins. Liver and spleen was not palpable. Temperature was slightly raised. The girl was quiet but alert.

Dec. 3.—Next morning she complained solely of vertigo, but during the afternoon she became pale and apathetic, complaining of vertigo and of pain in both kidney regions. The red-cell count, which had been 3,500,000 per c.mm. in the morning, had decreased to 1,500,000. The urine, which had been bright-brown (negative for naphthalene and naphthol) in the morning became dark-brown, although benzidine negative. A blood-transfusion (800 ml.) was given, and sodium bicarbonate 3 g. 4-hourly was administered to keep the urine alkaline and to reduce the risk of renal damage from deposition of hæmoglobin.

Dec. 4.—She was now strongly icteric. In the afternoon she complained again of vertigo, and euphoria was noted. Her temperature, raised since admission, reached its peak (41.6°C, 106°F) that evening, and treatment with chlortetracycline (aureomycin) 1 g. daily was started. The red-cell count was 2,000,000 per c.mm. in the morning, but dropped to 1,050,000 at noon. Another blood-transfusion (800 ml.) was given and a constant drip transfusion was set up. The blood-plasma was cherry red, and the urine port-wine coloured and benzidine positive. In an attempt to stop the hæmolysis treatment with cortisone 100 mg. daily was started.

Dec. 5.—The red-cell count was 3,400,000 per c.mm. at noon and 3,000,000 in the afternoon (when the blood-transfusion was stopped). In the evening and during the night the count was 2,300,000, at which value it became steady. From the afternoon of Dec. 5 onwards the patient started to recover also subjectively. The destruction of red cells, on Dec. 4 and 5, was at a rate of 1,000,000 per c.mm. every 3 hours.



A case of naphthalene poisoning

Notes and News

POISONS RULES

AMPHETAMINE and dexamphetamine have lately been added to the fourth schedule of the Poisons Rules[1] Accordingly these drugs may now be sold by retail on prescription only

VISITING CHILDREN IN HOSPITAL

THE Ministry of Health, which has more than once urged hospitals which admit children to allow frequent visiting[2] has again brought this need to the notice of hospital authorities[3], and it expresses the hope that existing arrangements for children visiting their parents in hospital will be extended

The Ministry finds that only 10% of hospitals admitting children now restrict visiting to one day a week or less, such hospitals include 28 which still prohibit all visits except in emergencies The Standing Medical Advisory Committee has reported to the Minister that at infectious diseases hospitals frequent visiting, subject to safeguards, can be allowed, and indeed at some is already being allowed The safeguards include a sufficiency of single bed wards, enough nursing staff to supervise visiting parents, the wearing of protective clothing by visitors, and the application to them of routine measures for preventing the spread of infection, the total prohibition of visitors in the case of some diseases, and the limitation of visiting in general to parents and guardians Many hospitals which do not allow daily visiting give as the reason the undesirability of admitting visitors on days when there are operating sessions, but the committee suggests that there is no general reason why all visiting on such days should be prohibited The visiting of children admitted for tonsillectomy may not be necessary where the child's stay is for twenty four hours or less, but it is undesirable for a child to be denied visitors if it is to be in hospital for three or four days Daily visiting in mental deficiency and other long stay hospitals is desirable, even though this may interfere with the hospital's routine Daily visiting should be allowed even in remote hospitals, so that parents can at least choose the most convenient days, and it would be helpful if these hospitals arranged for the shelter and refreshment of visitors and for accommodating other children whom the parents may be obliged to bring with them Where children have to be admitted to wards for adults there is no good reason for prohibiting daily visiting, even if this arrangement differs from that for the visiting of adult patients

The Ministry hopes that daily visiting will become the general practice of hospitals which admit children, and it says, "it may even be that visits can be allowed more frequently than once a day"

AMŒBIASIS

A DISCUSSION by the Royal Society of Tropical Medicine and Hygiene, on Jan 19, made it clear that amœbiasis is important in Britain, partly because the infection is quite often found in people who have never been abroad, partly because it is a common and sometimes serious cause of ill health in those who have lived in the tropics, and partly because the many drugs advocated in recent years need careful and critical assessment

Dr A R D Adams, of Liverpool, speaking of intestinal amœbiasis only, declared that for the acute attack nothing has so far equalled emetine, that to eradicate the infection a three week intensive course of emetine bismuth iodide should be undertaken, that of the arsenicals acetarsol is probably the best, that retention enemas of 'Chiniofon' are sometimes useful, and that the antibiotics have not justified themselves for routine treatment, and should be reserved for exceptional cases and used with care

Prof A W Woodruff and his colleagues, Dr S Bell and Dr F D Schofield, described several hundred cases treated during several years on a careful plan to evaluate the various drugs used Like Dr Adams, Professor Woodruff was unequivocal that emetine bismuth iodide is at present the drug of choice in chronic intestinal amœbiasis (with emetine itself for the acute attack), and he cited a known relapse rate of 3% in his series—possibly a rather low estimate in view of the difficulties of prolonged observation, but nevertheless comparing favourably with other courses This team of workers also tested chloramphenicol (poor), aureomycin (poor), oxytetracycline (unsatisfactory), fumagillin (disappointing), 'Camoform' (unsatisfactory), 'Glaucarubin (not so good as emetine bismuth iodide, but useful and cheap), and a new drug 'Entamide' (fairly useful and cheap) Some of these drugs have considerable value, but they did not stand comparison with emetine bismuth iodide, nevertheless, lack of toxicity and cheapness are factors Prolonged use of the antibiotics may be risky

Sir George McRobert referred to the historic importance of the introduction of emetine for amœbiasis by Sir Leonard Rogers forty five years ago, but made the important point that emetine bismuth iodide is still too expensive for the Indian peasant There is danger in relying on antibiotics in cases of amœbic hepatitis, which responds to emetine or chloroquine Accurate diagnosis is supremely important, and there are distressing stories of prolonged treatment with all the latest drugs in patients who have never had the disease Sir Philip Manson-Bahr agreed that in India and Africa the diagnosis has been grossly overdone, and he too advocated treatment with emetine bismuth iodide, as he always has done Group Captain W P Stamm thought that the toxicity of emetine has been much over stressed, and like some other speakers he doubted the value of retention enemas Major General A Sachs, and other speakers, referred to the psychological effects of an attack of acute amœbiasis—itself a condition materially affecting the health and comfort of the patient

MOZART'S DEATH

FEW men have made such a generous contribution to music as Wolfgang Amadeus Mozart, who was born at Salzburg two hundred years ago, on Jan 27, 1756, and who composed and played instruments at the age of five and died, at the peak of his powers, only thirty years later Over 600 of his compositions have been published, including 20 masses, 23 operas 49 symphonies, and 27 piano concertos

There has been much speculation about the disease which killed Mozart at so early an age, and the many and conflicting reports have lately been discussed by Dr B Juhn[1] Five of Mozart's brothers and sisters died in infancy, apparently of inanition there was a belief in his family that children should be fed on water and not milk His father probably died of coronary thrombosis, and his mother's death was certified as *maladie du cœur* At a very early age Mozart began a nomadic life which was later spent in search of patronage and a living He was desperately poor, and was in the habit of working late at night, he was dogged by worries, fears, disappointments, hunger and illness He had scarlet fever in 1762, typhoid fever in 1765, smallpox in 1767, an undefined febrile illness the next year, and pneumonia in 1781 Because of Mozart s active life, Dr Juhn dismisses one suggestion that he had rheumatoid arthritis and endocarditis, and another that he had tuberculosis, it is true that at the age of six a physician found a nodular skin eruption on his shins, elbows, and buttocks which could have been erythema nodosum, but hæmolytic streptococci may have been responsible

Mozart began to ail in the late autumn of 1791 and he believed he had been poisoned Œdema of his hands and feet developed, and he complained that he could "taste death on his tongue"—a probable indication of excess urea and ammonia in the saliva Attacks of dyspnœa followed, with convulsions, delirium and severe headaches, and he died in coma on Dec 6, 1791

The cause of his death was certified as *Hitziges Frieselfieber* or "sweat rash," an epidemic and often fatal disease of those days, but Dr Juhn suggests that all the evidence points to malignant nephrosclerosis producing uræmia and heart-failure the nephrosclerosis could have been a result either of nephritis following scarlet fever, or of malignant hypertension Some people at the time, however, thought that he had typhus, and he was buried in Vienna, in a pauper's grave, the position of which is not known

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Plans for new Hospital at Hong-Kong

The Hong Kong government have approved plans for a new hospital of 1275 beds to be built in Kowloon The estimated cost is £3¼ million, and when completed in 1960 it will be the biggest hospital of its kind in the Commonwealth

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[1] Statutory Instruments 1955, no 1978

[2] See *Lancet* 1953, i 531, 539

[3] H M (56)6

[1] Juhn B Mozart's Illness and Death *Ciba Symposium*, February 1956

TABLE III—FREQUENCY OF SIGNS AND SYMPTOMS OF NAPHTHALENE POISONING IN TEN CASES

Case no	Systemic manifestations	Hæmatological manifestations	Urinary manifestations
10		Hæmolysis	Urine port wine coloured
9		Leucocytosis	
8	Pallor	Reticulocytosis	
7	Fever	Raised serum bilirubin level	Hæmoglobinuria
6	Jaundice gastro intestinal symptoms		Albuminuria, white cells
5	Palpable liver	Immature red cells in film	Granular casts
4	Palpable spleen		Red cells
3	Neurological symptoms	Raised serum urea level	General urinary symptoms, raised urobilinogen level
2			Naphthalene metabolites found
1		Heinz bodies, Howell Jolly bodies, sickle trait	Bilirubin, naphthalene odour

vitro *α* naphthol was the strongest hæmolytic agent, while naphthalene was not hæmolytic at all, injected intravenously into rabbits only *α* naphthol was hæmolytic Zuelzer and Apt (1949), however, produced hæmolysis with naphthalene in dogs and noted the following sequence of events (1) diarrhœa, leucocytosis, and Heinz bodies in erythrocytes, (2) apathy and hæmolysis, (3) reticulocytosis, and (4) recovery They also found slight hæmolytic activity in the serum of one of their patients

3 necropsies (Wiedow 1914, Konar et al 1939, Schafer 1951) did not reveal any lesions characteristic of naphthalene poisoning In 2 of these necropsies deposits of hæmoglobin were found in the kidneys, and naphthalene was found in the gastro intestinal contents, urine, and tissues

Discussion

In 1920 Smillie treated 81 cases of hookworm infestation with β-naphthol Only 4 of the patients showed signs of intoxication, and Smillie thought that their history of malaria was of ætiological importance The cases reported by Zuelzer and Apt (1949) were all in Negro children, of whom only 1 had sickle cell trait (although there was pronounced sickling during the acute phase) Ullmann (1947) emphasised the hæmolytic tendencies in the sector of the community his patient came from However, cases were reported from Germany and England and in white Americans It seems, therefore, that no known factor is responsible for increased sensitivity to naphthalene Zuelzer and Apt (1949) have assumed that the different responses to naphthalene depend on variations in intestinal absorption of naphthalene and/or the detoxifying efficiency of the liver No better explanation can yet be offered

Therapy consists mainly of replacement of hæmolysed red cells Whether cortisone acts unspecifically by combating stress or specifically influences the hæmolytic process is unknown

The prognosis rests on two factors—the extent of hæmolysis, and the degree of kidney damage Some workers report oliguria and transient anuria, Schafer (1951) found deposits of hæmoglobin in the kidney collecting tubules at necropsy. Blockage of the tubules by hæmoglobin cylinders and lower nephron nephrosis may cause death

As shown above, the number of leucocytes increases before hæmolysis takes place This early leucocytic response is caused apparently by gastro intestinal damage, symptoms of such damage being the very first an sometimes only signs of naphthalene intoxication I would be interesting to observe the hæmatologic response to parenteral naphthalene

The neurological symptoms are caused mainly b cerebral anoxia Typical in this respect was the euphor in our patient—similar to air pilots' euphoria at gre heights Convulsions, sometimes reported (Goetze 189 Zuelzer and Apt 1949), are possibly caused by blockag of cerebral capillaries by hæmoglobin

The early abdominal pain is undoubtedly due to gastr intestinal irritation Later pain has been reported in th regions of the gall bladder and the spleen This latte pain was complained of by our patient, but on palpatio the tenderness appeared to be in the region of the kidney The same may have been true of the other reported cas of pain in the spleen and gall bladder regions

The frequency of signs and symptoms in the recentl reported cases and ours is summarised in table III

The clinical picture of naphthalene poisoning emergin from the review of these cases is as follows

During the first 24 hours after ingestion only gastro intestinal symptoms of varying severity are noted, mainl nausea and vomiting

On the 2nd day fever and leucocytosis appear, which la several days

These are followed on the 3rd day by pallor, prostration, an rapid destruction of erythrocytes, accompanied by the usua signs of hæmolytic jaundice and hæmoglobinuria The urin assumes a characteristic port wine colour The spleen and live may be enlarged, and signs of kidney damage may appear albuminuria, hæmaturia, and granular casts in the urine Naphthol may be demonstrable in urine at this time

After 5–6 days, the leucocytes revert slowly to norma numbers, the hæmolytic process comes to an end, and there i a well marked reticulocytosis Oliguria or anuria, due to a lower nephron nephrosis or to blockage of renal tubules with hæmoglobin, may now supervene, or convalescence may begin, which, in absence of complications, is rapid

Summary

A case of suicidal naphthalene poisoning is reported, and published cases are reviewed

The clinical picture comprises gastro intestinal disturbances, fever, leucocytosis, hæmolysis and jaundice, signs of cerebral anoxia, hæmoglobinuria, renal damage, and eventual recovery

A plea is made for wider recognition of this syndrome

ADDENDUM

Since this paper was written another patient who had attempted suicide with 10 g of naphthalene was admitted to our department within 4 hours of taking the drug Treatment with 100 mg cortisone daily was started at once and no symptoms of intoxication developed, although 24 hours after admission naphthalene derivatives were found in the urine and Heinz bodies in blood films It remains to be demonstrated experimentally whether cortisone can prevent naphthalene induced hæmolysis or whether individual susceptibility varies greatly

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INDUSTRIALISATION AND COMMUNITY LIVING *

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IN medieval as in ancient times, children were taught to work with their hands from an early age—e g , from about 4 or 5 years—and the apprenticeship system meant that by the time a man had reached his teens he was already experienced in his craft, and a few years later was a master-craftsman The short duration of life at that time, and its uncertainty, were therefore compensated, to some extent, by this early start With the growth of mechanical power, and the rise of the industrial towns, the use of child labour was extended, and life became even more brief and uncertain , for many of these unfortunate little waifs never reached adult life because of the shocking conditions under which they worked Those who did remained the slaves of the machines, and had neither the opportunity, nor the satisfaction, of becoming craftsmen

Conditions in Britain today would appear Utopian to the workers of the early years of last century Hours of work are now less than half, wages are high, health and welfare services are secure, housing is reasonably good, and there are more facilities for the use of leisure Would the medieval craftsmen have been as envious ? I doubt it, for they would find something missing The swing of the pendulum has carried those who work in industry into large and impersonal undertakings , their homes are often in dormitory areas remote from the life of the city or town centre, and much of their leisure is spent passively, in watching, rather than creatively

No one would wish to return to the brief and hard life, the smells and squalor, of a medieval city , but the fact remains that the men of those times were able to take pride in producing, by their own skill, works of the highest quality and beauty , the spinsters really did spin, and life, though short, was truly communal Which all boils down to saying that they had certain incentives which are lacking today Or, if you prefer alternative definitions, they had motives, provocations, or spurs, that roused them to live their short lives fully What were those motives ? Firstly, as already noted, life was brief and uncertain, death came readily to the young as well as to the old, and "men feared death as children fear the dark" Secondly work was a natural thing As Francis Bacon said, in his *Advancement of Learning*, "But men must know, that in this theatre of men's life it is reserved only for God and angels to be lookers on" Thirdly, skill was an essential, and "He that hath not the craft let him shut up the shop" to quote an ancient proverb Most important, the standard of workmanship was judged by fellow-craftsmen, for "a workman is known by his work" Finally, the numbers of the people were relatively small, and life was lived in common, whether in town or village

It will be noted that I have omitted the greatest incentive of all, the spiritual , not because I do not believe in it, but because no amount of academic discussion will replace it if it has been lost

The Current Picture of Industrialisation

Before we attempt to compare those times, and incentives, more closely with our own it will be advisable to examine the magnitude of the problem with which we, in this country, are trying to grapple According to the 1955 edition of the *Official Handbook on Britain*, the United Kingdom is one of the most highly industrialised countries in the world[1] , for ten people work in mining manufacturing, and building, for every one in agriculture Of the total number of persons in civil employment in 1950 about 22½% were said to be employed by public enterprise and 77½% by private enterprise In manufacturing and building 96% of the persons engaged were employed by private enterprise "Also in terms of employment, only about 30% of the public utilities—gas, electricity, water and transport—was the concern of private enterprise"[2] An interesting mid century position in which to find ourselves

Over a quarter of all employees in manufacturing industries are in establishments employing from 100 to 500 persons , but there is a slow and significant trend towards an increase in size, for in May, 1952, establishments with 1000 or more employees were found to employ 2,224,000 persons—more than twice as many as in 1935 It should, however, be noted that a single firm or combine may own many different establishments

We have thus three main components as a result of industrialisation The employers and their associations (there are about 270 national federations and probably about 1600 other employers' organisations) , the State, which is also an employer , and the workers with their trade unions The State departments concerned include the Treasury, the Ministry of Labour and National Service, the Board of Trade the Admiralty, the Ministry of Supply, the Ministry of Agriculture, Fisheries, and Food, the Ministry of Fuel and Power, the Ministry of Transport and Civil Aviation, the Ministry of Works, the Ministry of Housing and Local Government, the Ministry of Health, and the Post Office—a formidable and impressive list

At the end of 1952 there were in Britain 690 separate trade unions with a total membership of 9,525,000, but 67% of all trade unionists were in 17 big unions The total working population of the United Kingdom in 1954 was just over 24 million—i e , some 47% of the total population About 95% of British men of working age (15 years to 64) were in or seeking gainful work The remainder were students, severely disabled persons, or of independent means The proportion of women of working age (15 years to 59) working or seeking gainful work was about 45% There were about one million older men and women still at work, in addition to those of normal working age Of these vast numbers only about 1¾ million were employers or self-employed The majority of the female labour force was under 35 years of age[3]

Nearly 45% of those in civil employment were engaged in the mining and manufacturing industries and only about 5% in agriculture and fishing Women in industry were chiefly employed in the manufacture of textiles, clothing, food, drink, and tobacco, and in the distributive trades and professional and miscellaneous services

Among the changes of this century has been an increase in those employed in administration, including 1,400,000 women clerical workers and typists (1951 census, one per cent Sample Tables), an increase in nurses (now nearly a quarter of a million) and women teachers (220,000) There has been a decline in employment in coal mining, cotton textiles, and agriculture, and in private domestic service On the other hand, employment in metals, engineering and vehicles, and the chemical groups of industries, has doubled in the past twenty years There has also been a considerable increase in the numbers employed in the distributive trades

It is clear, therefore, that with a labour force five times the total population of England in the time of Elizabeth I, and an annual import and export of goods measured in thousands of millions of pounds sterling (in 1953 total imports c i f were £3345 million and exports of United Kingdom goods f o b £2582 million), comparisons with the conditions of medieval times are several attacks of laryngeal spasm caused cyanosis, and it was feared that tracheotomy might become necessary, but laryngeal toilet and a little more thiopentone proved effective The nasal catheter undoubtedly increased secretion and eventually caused ulceration with a sanious discharge

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* From a paper given to a conference of the Industrial Welfare Society on Oct 21, 1955

Nursing

The patient was nursed in a darkened room, making all procedures more difficult The patient was turned hourly, changed often, sucked out as required, and observed continuously so that, if necessary, the doctor could be summoned quickly

Progress

On the fourteenth day of anæsthesia the thiopentone was omitted from the intravenous fluid for a few hours, and not much increase in muscular tone was observed Next day 500 ml of blood was given to correct anæmia Intravenous therapy was discontinued on the sixteenth day Chloral was given for twenty four hours, during which the boy gradually regained consciousness, cried, and drank some water Convalescence was complicated by staphylococcal septicæmia, which responded slowly to antibiotics During this period he overheard a statement on a ward round that he had been in hospital for three weeks He resentfully insisted that he had only been in for a week He had of course no memory of his fortnight's anæsthesia The boy's temperature became normal four weeks after admission, and after some re education in walking, he was discharged

Follow up

When he was seen as an outpatient two weeks later it appeared that after a week's country holiday he had returned to the physiotherapy department demanding another week of exercises "so as to be good and strong for school" He is a bright boy

Discussion

Tracheotomy, with its dangers and difficulty of management, may be avoided if spasms are controlled with central depressants only In some cases even severe spasms can be controlled with central depressants without bad effects, and even more than 40 g of thiopentone may be harmless to a healthy child

The nutrition of a patient with tetanus must be maintained because his need for calories is increased, whether or not he has spasms (Holmdahl and Thoren 1954) His nutritional and electrolyte needs can be supplied by continuous intravenous and intragastric fluids An indwelling nasal catheter should be either used intermittently or changed often from one nostril to the other to avoid ulceration The staphylococcal septicæmia of our patient was possibly introduced by such ulcerations

This case shows that neither a short incubation period, nor a short interval between the first symptom and the first generalised reflex spasm, is a bar to a successful outcome in tetanus

Summary

A case of tetanus with an apparent incubation period of thirty-six hours is reported with recovery after two weeks' anæsthesia maintained with thiopentone

Relaxants were only used for short periods on two occasions for the passage of nasal catheters

My thanks are due to Mr F G Badger, under whose care this patient was, for guidance in the management of the case and in the preparation of this paper, Dr L J Wolfson, Dr D Bigley, and Dr R E Graham for advice on anæsthesia, Dr Mary Fisher for long periods of observation, and the nurses for their watchful care of the boy

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CHIARI'S DISEASE

A CASE DIAGNOSED DURING LIFE

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PRIMARY thrombosis in the hepatic veins has been recorded comparatively rarely since Chiari's (1899) account of 1 man and 2 women who died from this disorder Chiari suggested that the thrombosis was the result of endophlebitis

Armstrong and Carnes (1944) said that about 60 cases of the disease had been described, and that at Stanford University only 5 had been found in 11,979 necropsies—a prevalence of 0 042%

Kelsey and Comfort (1945) found 20 cases in all necropsies at the Mayo Clinic between 1910 and 1939 In only 4 of these was thrombosis of the hepatic veins the major factor, in the remaining 16 it was secondary to some other condition.

Little and Montgomery (1952), who reported 115 cases found that the most common causes were intra abdominal malignant disease, inflammatory conditions, and blood dyscrasias

Thus the disease in many of the cases reported since Chiari's first description was probably secondary to some other illness or was a terminal event

1 patient with the primary condition was first seen with hepatomegaly at the age of 5 and was kept under observation until his death at the age of 28 (Hutchison and Simpson 1930), at necropsy, primary carcinoma of the liver superimposed on obstruction of the hepatic veins was found

Most cases have not been diagnosed until necropsy, an exception was a patient who was admitted to a surgical ward with pyrexia, recurrent jaundice, and hepatosplenomegaly (Baer and Klemperer 1930) Thrombosis of the hepatic veins was considered the probable diagnosis, but cholangitis was not excluded, the former diagnosis was confirmed at necropsy Baer and Klemperer added that portal-vein thrombosis is difficult to diagnose, but the symptoms of hepatic vein thrombosis are more characteristic, comprising right sided upper-abdominal pain radiating to the back, a large, tender liver, splenomegaly, and ascites

Case-report

A male printing machine operator, aged 30, attended the outpatient department on Dec 17, 1952, with a history of abdominal distension and diarrhœa for three weeks, and lower thoracic backache for two weeks From 1941 to 1945 he had served in the R A F as a wireless operator/air gunner but had not lived abroad During and after his service career he had had attacks of epigastric discomfort which were not investigated

On examination he looked ill There was massive ascites which prevented palpation of the abdominal viscera and pressed on the bases of the lungs There was no evidence of heart-disease, the blood pressure was 145/95 mm Hg

Investigations

The patient was admitted the following day and a sample of the ascitic fluid was withdrawn This was faintly bile stained, and it contained 2 4 g per 100 ml of protein and was sterile on culture Chest radiography was normal Hæmoglobin was 97%, and the leucocyte count and blood films were normal, the total serum protein level was 6 g per 100 ml (albumin 3 4 and globulin 2 6 g per 100 ml) the results of this and subsequent estimations are shown in fig 1 Thymol turbidity 5 units, alkaline phosphatase 6 units, and serum bilirubin level 0 2 mg per 100 ml The Wassermann and Kahn reactions were negative

The similarity between this case and the clinical history attached to a specimen of liver (Pearson 1939) in the hospital pathological museum led me to diagnose Chiari's disease

Further Investigations and Progress

The patient remained in hospital for six months, during which abdominal paracentesis was necessary every five to eight days, when 10–14 pints of fluid was withdrawn After the first paracentesis the liver but not the spleen was palpable

On Jan 2, 1953, liver biopsy, by needle puncture, revealed the centrilobular congestion and dilated blood spaces on a national scale are costly. In short it is designed for braking rather than for acceleration.

Much the same comments apply to regional control. For advisory and planning purposes, for distributing the load evenly and strengthening weak places, a regional organisation is excellent. But the men who sit on regional boards can, in the nature of things, know little about conditions in detail in their regions, and nothing whatsoever about the needs of individuals other than those with whom they may come into contact. Are conditions any better under private enterprise? I do not know, but I suspect that the larger the enterprise the less the individual employed in it feels a sense of personal responsibility, and we are unquestionably moving into an era of large enterprises.

I have also found that the most severe judges of a workman are his fellow men, and the iron discipline of some trade unions can be just as harmful as a harsh employer or a remote and impersonal board—indeed more so, for the latter can only operate within certain limits, whereas the former may influence the whole life of a man.

With the vast numbers now employed in industry and the complex machinery of organisation, it is possible, without drawing too much on the imagination, to foresee the possibility of a future in which the individual has no place other than as a unit, to be paid a standard wage (without regard for *good* or *bad* work), for standard hours, provided that he obeys the rules drawn up by the State, the employing body, and his fellow workers. In such a community the penalties for making a wrong decision might greatly exceed the rewards for showing initiative and making the right one, and the punishment for ineptitude might be transferred from the act of being guilty of it to the "crime" of being found out.

It is clear that the requirements of any industrialised country in the future will call for a high level of intelligence in its workers. Unskilled and manual workers will be increasingly replaced by mechanicians and technicians sufficiently familiar with control panels, and laboratory techniques, to take charge of automatic and semi-automatic processes and to be able to detect and remedy causes of breakdown. In such a society it is equally possible to foresee at least a partial return to pride of craftsmanship, particularly if this is fostered by careful preliminary training and regular "post-graduate" instruction, so that the individual is made to feel that he is a part of the whole—"a piece of the main" to quote John Donne. To ensure this will require, in my opinion, more attention to the instruction and advice given to those about to enter industry, and this, in turn, calls for combined action by employers, trade unions, Government departments, and education authorities.

It is also possible that, with increasing ease of control, the hours required to be worked will be shorter, quite apart from the efforts of organised labour in this direction, and the problem of the proper use of leisure, already a considerable one, will loom large. At present we think in terms of a shorter day, or a five-day week, and leave the individual to fill in his spare time as best he can, with the result that, in many instances, he becomes a passive watcher of screens and games, a process which can distil off his earnings without much benefit to himself. Is it too far-fetched to think instead of longer hours of work and longer vacations? If my arithmetic is right, it would be possible to replace a forty-hour week with a fortnight's holiday each year, by a sixty-hour week with three months' holiday, and have some additional 340 hours of work in hand for each individual at the end of the year. It might be asked what would a man do with a longer holiday. My experience of university folk is that they use their vacations to do all the interesting things they cannot do in term-time—such as composing fantasies like this.

I do not suggest that everyone should have three months' holiday each year, but rather that we should get away from the concept of shorter days and shorter weeks, in favour of longer periods of leisure at longer intervals. University teachers can accumulate sabbatical leave term by term, until it amounts to a sabbatical year, which they can then spend in study away from their university. They are not compelled to take it, but the principle is a sound one, and I see no reason why it should not be extended to industry, so that a conscientious worker could accumulate sufficient leave to enable him to do something worth while with it. Some of the arguments against the scheme are obvious: men will then do two jobs, it will cause inconvenience if everyone is away at once, it will interrupt the smooth flow of production, &c., &c., but I do not think that these upset the principle.

I have put forward this proposal on the assumption that the worker of the future will be an intelligent and responsible being, who will prefer to work hard when he is working in order that he may have enough leisure to do interesting things. At the moment the yardstick of prosperity is a material one, as represented by articles which can be bought on a hire-purchase system. If Utopia is to consist of bigger television sets, deep-freeze refrigerators, and more cars on the road, then I am wrong. If it is to comprise opportunities to see and study something of the rest of the world and to live a full life then I am right. Benjamin Franklin who had many sayings about the value of time, wrote truly when he said "Dost thou love life? Then do not squander time, for that's the stuff life is made of". There is more in life than forever fighting for a fatter weekly pay-packet, and then squandering it.

Industrialisation and community living can be made practicable in the future if, (*a*) the worker in industry can be made to feel that he is an essential and integral part of the organisation on which his life, and that of his fellows, depends, (*b*) he is prepared to work for his leisure, and (*c*) that leisure is properly used. There are so many nice things to do, and life slips by so fast. There is more to it than was imagined by Æsop's fly when it sat upon the axle-tree of the chariot wheels, and said, "What a dust do I raise!"

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2. *Ibid*, p. 118.
3. *Ibid*, p. 226.
4. Quoted by Prof. Clyde Dankert in the *Contemporary Review*, September, 1955, p. 159.

"The emergence of middle-aged men as a 'vulnerable group' is the most startling occurrence for a public health movement whose ideas on prevention are based largely on such experiences as maternity and child-welfare work. The nineteenth century epidemics, bred in poverty and malnutrition, arose from failures of the social system. But coronary thrombosis (and there is no reason to suppose it is unique), with its origins apparently in high living standards and our means of achieving these, seems to be arising from what we regard as successes of the social system, and from the essential processes of our new industrial society. There is every reason to expect that, as social progress continues along its present lines, we shall have not less coronary thrombosis in the future but more. Over and above that, it is becoming clear that in the modification of personal behaviour, of diet, smoking, physical exercise, and the rest, which look like providing at any rate part of the answer, the responsibility of the individual for his own health will be far greater than formerly. It will not be possible to impose from without (as drains were built) the new norms of behaviour better serving the needs of middle and old age. They will come about only in a new kind of partnership between community and individual. And if it turns out that the 'wisdom of the body and understanding of the heart' begin with a rather dull *moderation in all things*, perhaps even that is not a negligible message from preventive medicine to these over-excited times."—Dr. J. N. Morris, *Listener*, Dec. 8, 1955, p. 997.

Histological Examination

Extensive destruction of liver parenchyma left only islands and cords of liver cells round some of the portal systems, and nodules of regeneration The rest of the liver consisted of a coarse network of œdematous fibrous tissue containing many dilated blood spaces and veins, some showing proliferation of the intima, others fibrous obliteration and recanalisation Sections through the closed ostia of the hepatic veins showed hypertrophy and fibrosis of the muscularis and œdematous hyaline fibrous tissue with many small channels of recanalisation, replacing the intima and obliterating the lumen

Discussion

This case and that of Pearson are classical examples of Chiari's disease The clinical picture varies with the degree of obstruction of the hepatic vein In total obstruction the illness is short with the rapid development of hepatomegaly, ascites, vomiting, and jaundice, death from hæmatemesis due to ruptured œsophageal varices usually follows When the obstruction is incomplete hepatomegaly and ascites may develop rapidly, but the patient may live for several years, improvement depending on the formation of a collateral circulation and regeneration of the liver The early onset of ascites supports the view of Madden et al (1954) that an important factor causing hepatic ascites is imbalance between the hepatic inflow and outflow of blood

If the disease is suspected diagnosis should not be difficult, because the picture is that of acute hepatic congestion unassociated with hypertension in the superior vena cava, if the patient lives long enough, secondary portal hypertension develops Differentiation from constrictive pericarditis and tricuspid regurgitation rests on the clinical history, the absence of raised jugular pressure, and the absence of the hepato-jugular reflex

Treatment is unsatisfactory, anticoagulants are dangerous because of hepatic damage, and surgery is of doubtful benefit Symptomatic treatment and prolonged rest seem to offer the best prospects of improvement

A clear distinction should be made between cases of primary obstruction, as described by Chiari, and those in which obstruction of the hepatic vein is secondary to another disease

I am grateful to the staff of the Archway Group Laboratory for their assistance in the clinical pathology, especially Dr J G A McSorley and Miss M F Crowley

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SPONTANEOUS HYPOPARATHYROIDISM WITH MEGALOBLASTIC ANÆMIA

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THE following case of idiopathic hypoparathyroidism is reported because of its association with megaloblastic anæmia—an association not previously reported

Case-report

A girl, aged 19, began to have fits at the age of 8 years There was a constant aura consisting in a feeling of stiffness in the right hand lasting some moments Usually this was followed by generalised convulsions The fits might be as many as 12 in a day, but sometimes the patient went 3–10 months without any At the age of 11 years she began to take phenobarbitone gr $^1/_2$ b d and phenytoin sodium gr $1^1/_2$ daily In March, 1953, the latter was increased to gr $1^1/_2$ b.d., but the fits continued, and in April, 1954, the patient was admitted to Claremont Street Hospital, Belfast She had no history of infantile convulsions or of head injury, and she walked and talked at the normal age Menstruation had not begun She was the eighth child in a family of nine There was no history of epilepsy or other neurological illness in the family

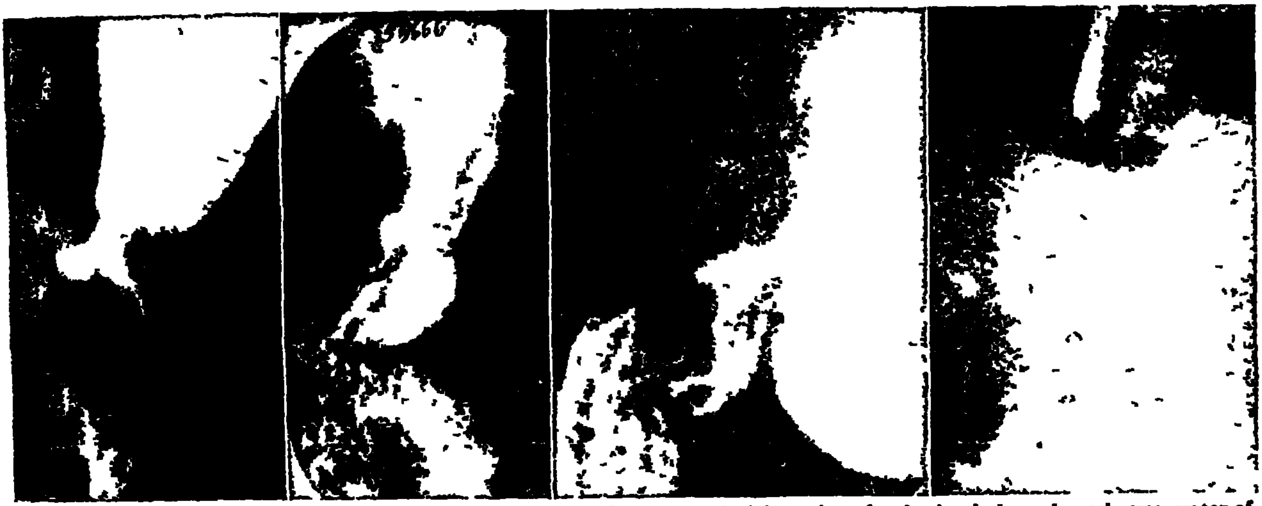
On examination on April 28, 1954, she was cheerful, of average intelligence, small, and plump, with a round face and squat build Height 58 inches, heel to pubis 29 inches, from finger tips to finger tips of outstretched arms 61 inches skull circumference $20^1/_2$ inches Scanty pubic and axillary hair, breasts poorly developed, skin dry, nails apparently normal, but teeth much deformed and widely separated, several being just small stumps There was a butterfly area of brownish pigmentation on the face Chvostek sign easily elicited, Trousseau sign positive Blood pressure 100/60 mm Hg Heart sounds normal, mucosæ pale. Neurological examination negative Lens opacities in both eyes

Investigations—Radiography showed calcification of skull in region of basal ganglia, metacarpals and metatarsals normal, bone age 12 years, no subcutaneous calcification, long bones normal, no abnormal calcification in abdomen. A fractional test meal showed histamine fast achlorhydria Examination of the blood showed Wassermann reaction negative, hæmoglobin 55% (7 9 g per 100 ml), colour index 1 37, packed cell volume 24%, mean corpuscular volume 120 c µ, mean corpuscular Hb concentration 33 g per 100 ml erythrocyte sedimentation rate 57 mm in 1st hr (Westergren), leucocytes 3350 per c mm (neutrophils 48%, lymphocytes 48%, eosinophils 4%), reticulocytes less than 0 5% A blood film showed macrocytosis and poikilocytosis Plasma bilirubin 0 7 mg per 100 ml, plasma protein 9 0 g per 100 ml (albumin 5 8 g, globulin 3 2 g per 100 ml), serum calcium 5 4 mg per 100 ml, serum phosphorus 11 8 mg per 100 ml, alkaline phosphatase 16 King Armstrong units The Ellsworth Howard test showed poor response to intravenous 'Para thor mone' A glucose tolerance test produced a flat curve An insulin sensitivity test was normal A fat balance test (on two occasions) showed 90% and 95% reabsorption Radiography after a barium meal showed a normal intestinal pattern A Sulkowich test showed no calcium in the urine The basal metabolic rate was +17% Intravenous pyelography showed both kidneys normal in size and very good concentration of the contrast medium Blood urea 23 mg per 100 ml The specific gravity of the urine was 1 000–1 020, and a urea concentration test gave 2 6% The Kepler test was negative The urinary excretion of 17 ketosteroids was 2 5 mg in twenty-four hours

Lumbar puncture produced clear cerebrospinal fluid containing protein 35 mg per 100 ml, and leucocytes 1 per c mm, the Wassermann reaction was negative Electrocardiography showed a slight increase in the Q–Tc interval Electro encephalography on May 8, 1954, gave a resting record which showed activity at a wide range of frequencies $1^1/_2$–9 c p.s With hyperpnœa the slow activity was clearly dominant Chromatography showed increased amino aciduria of a general pattern

Prof P J Stoy reported that radiography on June 23, 1953, showed the following teeth erupted $\frac{654321/123456}{7\ 5432\ /\ 2345\ 7}$ The following teeth were present but unerupted $\frac{7/7}{8\ /\ 8}$ The teeth were widely spaced except 7/7, which were erupting, the $\underline{7/}$ being mesio angularly impacted against the $\underline{6/}$ The $\underline{/7}$ was in normal position The roots of all the teeth were incompletely formed and stumpy The lamina dura was prominent and the periodontal shadow broad The dental age of each tooth was as follows (Symington and Rankin being taken as a guide)

$\underline{1/1}$	8 years	$\overline{2/2}$	8 years
$\underline{2/2}$	8 years	$\overline{3/3}$	8 years
$\underline{4/4}$	8 years	$\overline{4/4}$	8 years
$\underline{5/5}$	8 years	$\overline{5/5}$	8 years
$\underline{6/6}$	7–8 years	$\overline{7/7}$	9 years
$\underline{7/7}$	9 years		



Radiographs after barium meal in 4 cases in which Billroth-I gastric resection had been done for duodenal ulcer. In each case crater of large recurrent ulcer is on lesser curve of re-formed stomach just proximal to gastroduodenal anastomosis.

and site of recurrent ulceration, the frequency of post gastrectomy symptoms not due to ulceration (the so called post gastrectomy syndromes), and the functional state of the patient, determined by his fitness for work and his enjoyment of life. To assess these results and make as impartial a comparison as possible between the two operations, each patient was interviewed by a panel of three. To guard still further against bias, the panel usually made its preliminary assessment before consulting the patient's notes, so that its conclusions were often reached in ignorance of the type of operation that had been performed.

RECURRENT ULCERATION

Table III shows the number of patients with recurrent ulcers after the two operations. Proven ulcers were those found at a further operation, or demonstrated unequivocally by radiography or gastroscopy.

TABLE IV—RECURRENT ULCERATION IN PATIENTS FOLLOWED UP FOR AT LEAST THREE YEARS

Type of operation	No of patients	Recurrences		
		Proven	Suspected	Total
Billroth I	80	11	3	14 (*17·5%*)
Polya	106	1	1	2 (*1·9%*)

The difference between the two series is striking: the recurrence rate was 15·1% after the Billroth I resection, and only 1·5% after the Polya resection. These figures do not represent the final picture, because some of the patients treated more recently by these operations may yet have recurrences. However, most of the recurrences appeared within eighteen months to two years of operation, and a slightly more accurate estimate of the risks of recurrent ulceration may be reached by considering only the patients operated on at least three years before the survey (table IV). This also eliminates one of the main points of dissimilarity between the two groups—the duration of the follow up.

These figures confirm the much greater tendency to recurrence after the Billroth I resection. With this operation the recurrence rate after three years was 17·5%, whereas with the Polya operation the recurrence rate was only 1·9%.

Most of the recurrences were in men (who made up the bulk of the series), but 4 were in women, all of whom had been treated by the Billroth I operation.

Sites of Recurrences

After the Polya gastrectomy for duodenal ulcer, recurrence takes place in the jejunal mucosa close to the stoma. By analogy, any recurrences after Billroth I resection would be expected to lie in the exposed duodenal mucosa adjacent to the anastomosis. In the present series some of the recurrences were in the duodenum (table V), but it was surprising to find that the majority were on the lesser curve of the stomach. Findings at the second operation left no doubt that in 3 or 4 cases there were true gastric recurrences. In the other cases, however, the subsequent operations (sometimes a simple vagotomy without opening the stomach, sometimes a Polya conversion with little attention to the exact site of the ulcer) failed to establish the side of the anastomosis on which the ulcer lay, and the radiological diagnosis was accepted. But we were very doubtful about the location of many of these ulcers and wondered whether they were not stomal rather than gastric in position. The radiological diagnosis of ulceration in the region of the lesser curve is difficult because of the niche like appearances often found in this situation after a Billroth-I gastrectomy. Puckering and distortion are produced by the suturing of the upper part of the gastric remnant, which of course constitutes the lesser curve of the re formed stomach. We have therefore been cautious in interpreting radiographs and have restricted definite diagnoses to cases with obvious craters, as in the accompanying figure.

Incidentally, these radiographs give a good indication of the level at which we normally performed our Billroth-I resections. There was no question of the gastrectomy being skimped because a gastroduodenal anastomosis had to be considered.

It is difficult to explain the predilection for recurrent ulceration on the lesser curve after Billroth-I resection for duodenal ulcer, because no such tendency is apparent following this operation for gastric ulcer. In the past six years one of us (J C G) has treated a series of 124 patients with gastric ulcer by Billroth-I resection without

TABLE V—SITES OF RECURRENT ULCERS

Site of recurrence	No of recurrences	
	After Billroth I resection (132 patients)	After Polya resection (138 patients)
Duodenal or jejunal	6	1
On stoma	1	0
On lesser curve of stomach	11	0
Not clearly established	2	1

Reviews of Books

The Treatment of Renal Failure

Therapeutic Principles in the Management of Acute and Chronic Uræmia JOHN P MERRILL, M D, *associate in medicine, Harvard Medical School* New York & London Grune & Stratton 1955 Pp 238 48*s*

IN the past ten years, the underlying pathology of renal failure has been greatly clarified by Jean Oliver's microdissection studies, the conservative regimen of Borst and Bull has justified itself by results, and these patients are no longer filled with fluid (except perhaps in clinical backwaters), and the artificial kidney of Kolff has been modified and tested, and the related procedures of peritoneal and intestinal lavage have been given a trial In short, it was time for a critical review of the treatment of renal failure, based on adequate clinical experience Dr Merrill's book does this admirably

He has treated over 200 patients with acute renal failure, and he has also assessed the value of similar methods in alleviating the discomforts of chronic renal failure This experience enables him to give a balanced and richly documented account of what can be done Yet he is not dazzled, for he reminds us that in the cure, as opposed to the palliation, of renal disease, we are no better off than Richard Bright in 1836, and one of his sections on chronic renal failure is headed *When not to treat* There are some faults for example, it seems questionable to condemn hydrogen resins and allow ammonium resins, which contribute both urea and hydrion to the body

Nevertheless, this is the only book available which is not dedicated to the propagation of one method, but provides an adequately based survey of the different possible forms of treatment. Its merits should make it *the* monograph on renal failure for some years to come

Modern Apparatus for Sterilisation

J H BOWIE, M B, M R C P E London Pharmaceutical Press 1955 Pp 21 2*s* 6*d*

NOT many hospital administrators, or engineers for that matter, have the knowledge to differentiate good and bad dressing-sterilisers But eyebrows will be raised at the first sentence of this admirable little booklet, which reads "About 90 per cent of the sterilisers in use in Britain's hospitals and pharmacies are obsolete" One might suppose that the sterilisers thus decried were bought as the result of efficient sales talk rather than from a knowledge of the physics of steam sterilisation, and the section of the booklet on this subject turns supposition to certainty, for much of the information it gives will come as a surprise even to hospital pharmacists and pathologists whose familiarity with the basic sciences is probably closer than that of anyone else on a hospital's staff In the section on faulty design, it is alarming to discover that the apple of the theatre sister's eye—"the very latest pattern autoclave"—is indeed rotten at the core Although it may only lack a thermometer—as in 55 of the autoclaves which Dr Bowie inspected—and although it may not be acting as a short circuit between the underground drains and the main water-supply of the hospital, as happened with 2 sterilisers

Everyone connected, however remotely, with sterilisation by steam should study this reprint of an address given to the Pharmaceutical Society of Great Britain

The Postural Complex

Observations as to Cause, Diagnosis and Treatment LAURENCE JONES, B S, M D, *visiting orthopodist, Midway Hospital, Los Angeles* Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 156 70*s*

LOW back pain is a heavy burden on every orthopædic department in this country It became even heavier with the recognition that "lumbago" and sciatica were commonly, and some said universally, due to lesions of the intervertebral discs Operations on the discs are not as popular as they were and other diagnoses are coming into their own again, but the results of treatment are still far from satisfactory and many patients are still left with considerable disability Every new idea must therefore be examined and tested without prejudice

It is Dr Jones's theme that most cases of backache and neuralgias in the trunk and limbs (upper as well as lower) have their origin in the feet

The foot cannot roll inwards or outwards without rotation of the leg, if the leg rotates, tension in the iliopsoas alters, the pelvis therefore rotates forwards or backwards, and this, with the resultant changes in spinal curvature, produces alterations in tension in the nerves and spinal cord from one end to the other and consequent "neuralgias" in almost any situation There may be no symptoms whatever in the feet, but Dr Jones maintains that correction of even minor degrees of foot imbalance will cure the pain elsewhere, unless they are of such long standing that "secondary inflammatory changes" have already occurred For such changes, Dr Jones uses more standard methods, but maintenance of improvement depends on foot correction

In preliminary chapters on the morphology of the foot, he emphasises that the foot is becoming an increasingly rigid structure, on which basis he defends his use of "fixed rigid postural shoe corrections" The method he uses for stiffening the shoe before the fitting of the supports, &c, required by that particular patient involves the use of a 'Fiberglas' insert, and considerable apparatus is required to handle this material He is also at great pains to correct any inequality of leg length, which he says is substantial in 40% of subjects

The rationale of this hypothesis and these methods is argued at length in this book That foot deformities can produce rotation of the whole leg and a change in the degree of pelvic tilt is clearly demonstrated, but there is little objective evidence that this produces significant alteration in tension in the spinal cord Nevertheless, Dr Jones writes with enthusiasm and faith, he quotes large numbers of cases, and he is prepared to meet the scepticism which he rightly foresees While it is difficult to believe that this postural complex is either so general or so noxious as he believes, his book will make people think

Radio-Anatomie générale de la tête

ROBERT AUBANIAC, *agrégé d'anatomie*, JACQUES POROT, *assistant d'électro radiologie des Hôpitaux de Paris* Paris Masson 1955 Pp 152

WITHOUT a knowledge of anatomy it would be impossible to interpret radiographs, on the other hand, radiography has often been of value in helping to determine the anatomy of a particular part of the body This book is primarily an illustrated anatomical and radiological atlas of sections of the head in the three principal planes

The structures seen in sections of the head (16 in the coronal plane, 16 in the horizontal plane, and 5 in the sagittal plane) are described with the help of natural size annotated diagrams accompanied by an illustration of a radiograph of each section The description of each section includes comments on the features revealed by the radiograph Radiography has been used to increase the information obtained from the sections, since the radiographs reveal details in the thickness of the section which otherwise could not readily be seen

The text and index are supplied unbound, and the diagrams and radiographs, all well printed on good paper, are supplied as loose sheets in a thin card folder This arrangement has the disadvantage that the loose sheets may easily be lost or damaged, but it has the great advantage that for serious study diagrams of different sections may be removed and compared side by side The cardboard case is rather flimsy and could perhaps be replaced by a proper loose leaf binding

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Textbook of Surgery (2nd ed London Kimpton 1955 Pp 1135 £6)—Only three years have elapsed since the publication of the first edition of this work by Mr H F Moseley, assistant professor of surgery at McGill University, but that is hardly surprising for it is an exceptionally good textbook It is up to date, clear, and comprehensive, and it has achieved wonders in catering for final year and fellowship students at the same time The new edition is enlarged by chapters on radioactive isotopes and on the acute abdomen, and there are now pictures in what was already a well illustrated book An original feature is the addition of film references to the orthodox bibliography

CONTROL OF WATER AND ELECTROLYTE DISORDERS

A SIMPLE CHART

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M.A., M.B Camb, M.R C.P
RESEARCH FELLOW IN MEDICINE

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THE application of modern knowledge of water and electrolyte disturbance is apt to raise difficulties in routine hospital practice, elaborate procedures making impracticable demands on nursing and laboratory staff On the other hand, it is of the utmost importance in both surgical and medical cases to prevent and to correct water and electrolyte disorders Therefore it is essential to devise a system whereby such disorders can be effectively controlled with the least expenditure of time by the hospital staff

Any instructions intended to cover all aspects of imbalance in full detail would clearly be unworkable, particularly as regards the maintenance of record charts House-officers do not have time either to understand or to maintain complicated charts and the primary object would then be defeated

Nevertheless a chart is essential for the following reasons (1) it makes treatment far easier to apply and more effective, (2) progress can be accurately followed and under-treatment or over treatment avoided, (3) impending disorders are more easily recognised and prevented and (4) more accurate control reduces the number of laboratory analyses

A routine chart for recording water and electrolyte balance should be as simple as possible, but at the same time the dangers of over-simplification of an admittedly complex subject must be avoided After prolonged trial and modification such a record chart has been evolved, and instructions, based on the chart, for the control of water and electrolyte disturbance have now been in routine use at the London Hospital for two years The instructions and chart we describe here

Record Chart

The chart is intended to be written up by house-officers from data obtained from the fluid-chart kept by the nurses, and from laboratory analyses (In the nurses' fluid-chart, intake of fluid is recorded as it is given Output of fluid is entered specimen by specimen under the headings of urine, suction, vomit, drainage, and diarrhœa)

The chart is designed for period-by-period comparison of intake and output of water and "electrolyte fluid" (see below) with urine and blood analyses Loss of "electrolyte fluid" can be directly compared, volume by volume, with replacement of electrolyte fluid, thereby rendering control more accurate and reducing demands on the laboratory. Three periods can be logged on each page, which is of the same size as the hospital case-notes, with which the chart is eventually filed

The back of the chart likewise provides for the logging of three periods Solutions prescribed for each period are entered, bottle by bottle, on the back of the chart, each entry being initialed by the nurse giving the fluid Thus there is a clear record of solutions actually given during a period, and this record can be directly compared with data for the same period on the front of the chart It is convenient to keep these orders for fluid together and apart from medicines, injections, and other items entered on the usual hospital treatment-form Space is provided for dietetic instructions for use where intravenous therapy is not indicated or no longer required

The format of the record chart is given in the accompanying table

The results of analysis of blood and urine must be rapidly available, so that accurate control may be maintained It has been found quite practicable to report the results within two hours of the arrival of the specimens in the laboratory, and this is the regular practice at this hospital Normal values for blood analyses are given on the back of the laboratory report

The following instructions are issued with the chart

The Management of Water and Electrolyte Depletions

USING THE RECORD CHART

(For House-officers)

Although the chart can be used equally well in pædiatrics, the following instructions apply mainly to adults.

Front of Chart
(format repeated three times)

WATER AND ELECTROLYTE RECORD CHART
(For use of house-officers)

Record No
Sheet No
Name ______ Ward ______
Date ______ period (12 or 24 hr) from ______ to ______

Electrolyte fluid loss		Electrolyte fluid replacement	Water intake		Urine analysis		Blood analysis	
	ml	ml		ml				
Suction Drainage Vomit Diarrhœa			Mouth Gastric tube Per rectum Intravenous Subcutaneous		Volume Sp gr Cl Na K Urea	ml m.eq /litre m.eq /litre m.eq /litre g /litre	Na K Cl HCO_3 Urea	m.eq /litre m.eq /litre m.eq /litre m.eq /litre mg 100 ml
Total			Total				B.P	

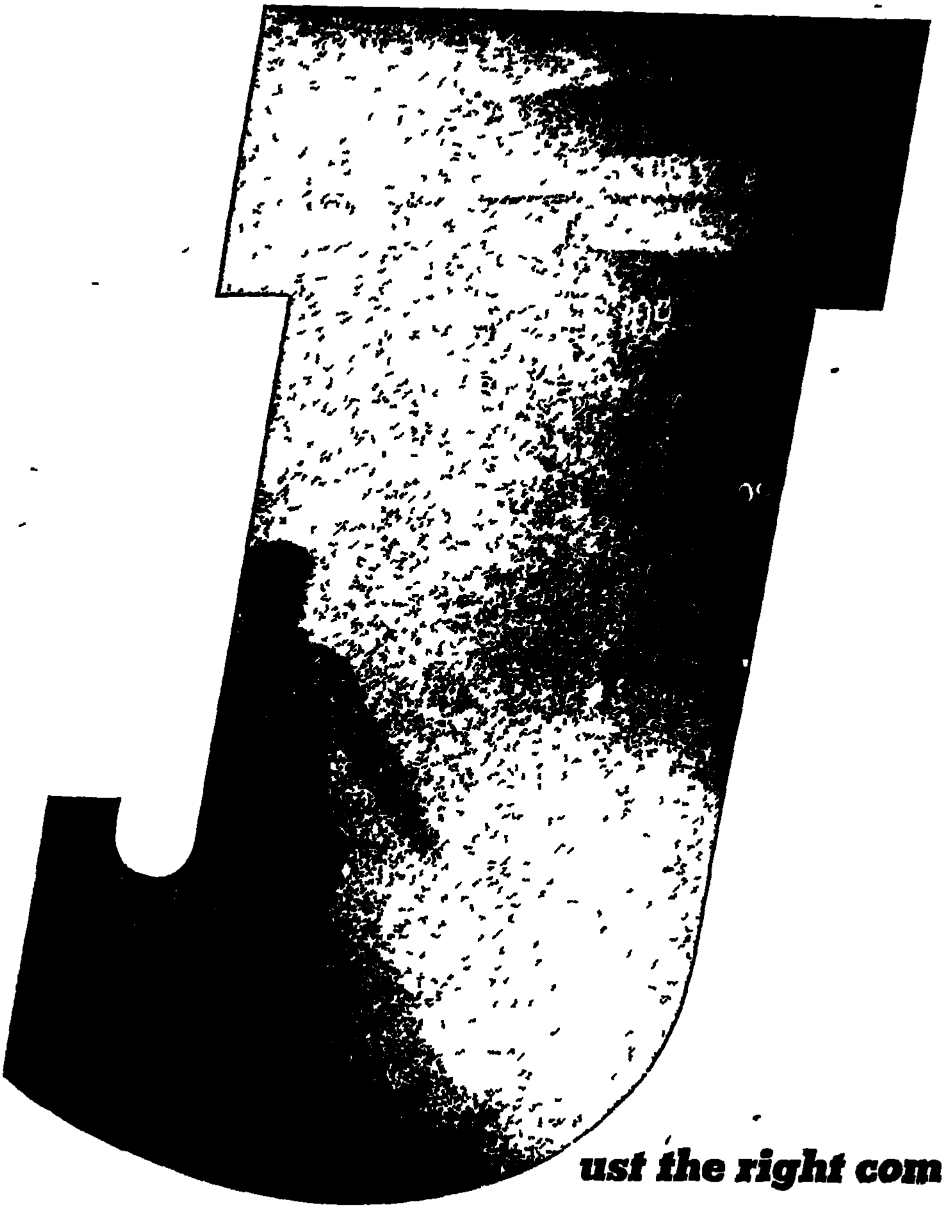
Back of Chart
(format repeated three times)

ORDERS

Date
Period

Diet	Solutions ordered*	Route	Initials as given

* Enter bottle by bottle



ust the right combination...

Cold, damp and smoke — just the right combination to produce the fog which sets people coughing and sends them to their doctor in search of relief

And relief is readily available with 'Phensedyl', the **M&B** brand cough linctus which contains promethazine for its prolonged antihistamine, local analgesic and central sedative action, ephedrine for its broncho-dilator activity and codeine for its depressant effect on the cough reflex

Whatever the cause of cough — whether it is "smog", smoking, the aftermath of influenza, or a more serious condition — these properties of 'Phensedyl' usually bring relief They provide the right combination

Supplied in bottles of 4 and 40 fl oz
(each fluid drachm [3 6 c c] contains

PROMETHAZINE HYDROCHLORIDE	3 6 mgm
CODEINE PHOSPHATE	9 0 mgm.
EPHEDRINE HYDROCHLORIDE	7 2 mgm.)

'PHENSEDYL'
trade mark brand
PROMETHAZINE COUGH LINCTUS
MANUFACTURED BY M&B MAY & BAKER LTD

an **M&B** brand medical product

DISTRIBUTORS PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD DAGENHAM ESSEX

fluid loss is small (as in increased sweating or occasional vomits). It also supplies 100 g. of glucose (400 calories).

(C) Acid-base disturbances often occur in electrolyte depletion. These are usually rectified by the kidney if renal function is adequate, provided correct amounts of Na, Cl, K, and water are given. In severe acidosis or where large infusions of normal saline are required, isotonic Na lactate solution should take the place of a proportion of the normal saline solution. Often an alkalosis associated with K depletion can only be rectified by correcting the K depletion.

(D) Kidney function is often temporarily impaired in electrolyte depletions and after major operations. In these circumstances renal adjustment may be slow or imperfect. This can usually be detected by consecutive urine and blood analyses. Intravenous therapy should be applied with caution in these cases until kidney function recovers.

(E) Intravenous administration of K salts, although frequently essential, is potentially dangerous and should always be cautious. It is suggested that 1 litre of the intravenous KCl solution should be given slowly not more often than once in 6 hours. It may take up to 3 days or more to rectify K depletions completely, particularly if loss continues. K salts can be given by mouth, provided total water intake is increased proportionately (e.g., total intake 2·5–3·0 litres a day). Latent K depletion is often revealed only after a concurrent Na depletion has been rectified. Na depletions must, however, be rectified first.

(F) It is essential not to mistake the oliguria of a primary renal condition (such as acute anuria or acute nephritis) for a simple water or electrolyte depletion. The distinction should be clear from the clinical picture.

(G) In electrolyte depletion via the urine the extent of the electrolyte loss will be evident from blood and urine analyses. The necessary volume and composition of replacement fluid must be estimated from these. Here volume for volume replacement is clearly not applicable.

(H) With a new case complete urine and blood analyses should be made at the start. Subsequently less frequent analyses are required and not all the items on the record chart need be requested. Under "blood analysis" space is available for inserting additional estimations as required—e.g., hæmatocrit, plasma-protein level, &c.

(I) 5% and 10% dextrose solutions are charted under "water intake." It is convenient to chart the maintenance solution (note B) also under "water intake." Normal saline and Na lactate solutions are charted under "electrolyte fluid replacement." KCl solutions are not entered on the front of the chart, but the amounts given will appear among the initialed orders on the back of the chart in the corresponding period.

(J) A normal urinary volume is frequently not attainable in surgical cases on the first postoperative day.

(K) In almost all cases of severe electrolyte depletion intravenous therapy is required to begin with.

(L) In chronic electrolyte depletions—e.g., some cases of pyloric stenosis, diabetic coma, and Addison's disease—the depletions should always be corrected with caution. Cautious treatment allows time for body mechanisms to readjust to more normal conditions. Rapid intravenous infusions, for instance, are dangerous because pulmonary œdema may be precipitated.

Discussion

These instructions on management of water and electrolyte disorders are not meant to be in any way comprehensive but are notes put forward to enable the most efficient use to be made of the chart.

An attempt has been made to keep the number of intravenous solutions at a minimum and the composition of each solution as simple as possible. We feel that there is little indication for the use of more complex solutions. Complex solutions of fixed composition cannot meet the varying requirements of all cases and probably seldom meet fully the requirements of even one case. They may, indeed, give a false sense of security. In particular, the use of solutions containing phosphate has been avoided. Although there may sometimes be an indication for such solutions on theoretical grounds, in practice there are no known clinical features associated with a phosphate deficit alone.

There appears to be a need for an intravenous solution with a disposable cation for use in alkalosis, in the same way that sodium lactate with a disposable anion is used in acidosis. Ammonium chloride has been used but continuation of this practice appears inadvisable until it can be shown that increased ammonium concentration in the systemic circulation is non-toxic.

The management of water and electrolyte disorders must inevitably change as knowledge of water and electrolyte metabolism advances. These instructions and the chart may therefore require modification in the light of future research. However, it is felt that they embody, in as simple form as the subject allows, the essentials of modern management of these disorders.

SUBACUTE NON-SUPPURATIVE THYROIDITIS

TREATMENT WITH CORTISONE AND CORTICOTROPHIN

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Beneficial effects of cortisone and corticotrophin in subacute non-suppurative thyroiditis have been reported by Krupp et al. (1951), Crile (1952), Crile and Schneider (1952), Clark et al. (1953), Teitelman and Rosenberg (1953), Hunter and Sheehan (1954), Benjamin (1955), and Kraft and Wolf (1955).

The ætiology of non-suppurative thyroiditis is unknown, but a virus infection has been suggested (Crile 1952). Pyogenic bacteria have been cultured from suppurative thyroiditis (Thorn and Forsham 1952).

The histological picture of non-suppurative thyroiditis is characterised by the disruption of the acini and by the escape of colloid into the interstitial spaces, where pseudotubercles, giant-cells, and polymorphs are found. These changes are diffuse and usually involve both lobes of the thyroid gland. The lesions gradually disappear, leaving normal thyroid tissue in most cases (Crile and Hazard 1951), but myxœdema (McConahey and Keating 1951) has been reported as a late sequel.

We report here 6 cases of subacute non-suppurative thyroiditis, of which 5 were treated with either corticotrophin or cortisone. Thyroid function was determined by the uptake of radioactive iodine by the thyroid gland and by the excretion of radioactive iodine during and after the disease for up to fourteen months.

Summary of Cases

The history, clinical features, and laboratory findings differed only slightly from case to case and may therefore be presented jointly.

Symptoms and Signs

All the patients were women aged 35–64. In 3 of them the onset of thyroiditis was preceded by an upper respiratory infection one to two weeks earlier. The main complaint was sharp pain at the lower anterior region of the neck, radiating in some of them up to the retro-auricular area. The pain was aggravated by swallowing. There was intermittent pyrexia of 100·4–104·0°F for two to six weeks before admission.

On physical examination all the patients appeared seriously ill, being apprehensive and sweating profusely, with a pulse-rate of 100–120. In some of them a fine tremor of the fingers was observed. In all the patients a diffuse moderate enlargement of the thyroid gland was palpable. The gland was exquisitely tender and firm, and in some patients the skin overlying the gland was reddish, swollen, and hypersensitive. In 2 patients enlargement of cervical lymph-nodes was found. No other pathological signs were noted.

decontrol on such lines as inadvisable if not impossible, the committee concentrate usefully on the means whereby control may be exercised with more knowledge and therefore more delicately and fairly—as indeed has latterly happened to some extent. So that funds may be better allocated and better used, they strongly recommend the development of departmental costing—which will require the willing cooperation of those concerned with hospital administration, not least the doctors. But they well recognise that hospital costs alone do not necessarily reflect the efficiency of hospital management, and the need to find better indices for measuring efficiency is one of the reasons leading them to their important recommendation that the Health Departments should set up a research and statistics department to act as their intelligence branch. This department would consider what information is now lacking and how it can best be got.

But an intelligence branch, helpful though it will be, is not a brain; and the committee has not brought out the fact that the N.H.S. has never had, and still lacks, a policy by which a proper balance between its separate parts is decided and then achieved. At several points Mr. GUILLEBAUD and his colleagues show themselves fully aware that prevention is cheaper than treatment, and that treatment in the home is often cheaper than treatment in the hospital; but only Sir JOHN MAUDE, in his reservation, explains how the present system weights the scales against a reasonable economy. The committee repeatedly urge that people in different parts of the N.H.S. should see the service as one; and they believe (we hope rightly) that habits of cooperation will grow; but they are asking rather a lot of human nature when they suggest that those who run the hospitals so devotedly should remember that whatever they can save may go to balance overspending on something else, such as the pharmaceutical service, and is "not necessarily 'lost' to the National Health Service as a whole." Anyone determined to economise by altering the balance in favour of preventive and domiciliary services would have to recognise that, as the *Times* puts it, "at too many critical points the health service as now organized lacks built-in incentives to economical and efficient administration."

Hospitals are a necessity, and we must not rest until a very much higher standard is achieved in many of those we have today. But this does not mean that the hospital services as a whole ought to go on expanding, bit by bit and year by year. At present, even hospitals that know that they could contract find it hard if not impossible to get into reverse. Demand may fall off with diminishing population, or because of preventive or therapeutic advances: the lightening of the load on children's beds in many populous areas is an obvious example. But from within the hospital the process of cutting down beds and services looks far too much like defeat and far too little like the victory it should be acclaimed to be. Even the distant signs of its happening are a matter for concern: the consultant does not like it to be known that he has difficulty in filling his beds; the matron, the administrator, and the caterer have all been taught to look forward to the day when their hospital will be increasing rather than reducing its complement (their very remuneration is related to the number of beds), and any suggestion of contraction is discouraging and disconcerting. The whole service, in fact, is geared to move only one way—toward expansion. It is to the financial advantage of each general practitioner to have, within reason, as many patients as possible on his list; it is to his advantage, too, to pass as many as possible on to the hospital; and it is to the advantage of the hospital, and everybody in it, to welcome the cases when they arrive, to build up a good rate of occupancy, to develop a larger and better hospital service, and so on. The practices that govern methods of remuneration have been evolved with great care: they are designed to avoid salaries for general practitioners and to preserve freedom for the consultant and a measure of flexibility in the number of sessions assigned to him. It is, too, entirely reasonable to relate salaries of senior categories of administrators and matrons to the size of the hospital in which they work. But we should not forget that when these criteria were evolved it could be taken as axiomatic that the more hospital services we possessed the better. In some areas and for some services this is still, of course, very true; but in others it is true no longer.

With all respect to Sir JOHN MAUDE and others who are anxious for unification of the services under one authority, we would say that it is not the existence of separate machinery that is decisive; for separate machinery in some sense there must be. What may matter more is the fact that the incentives, financial and other, of those who work in the different parts of the service have been allowed to evolve independently, and that nothing has yet been done to solve the problem of fitting them together. We should like to have seen in the Guillebaud Committee's report some indication of the kind of experiment that might be made, which would point the way towards a solution. Were it possible to take a single area—a county borough for instance—and try an entirely different set of financial arrangements, important results might follow. To show how different they could be, let us imagine an extreme case. Suppose that the remuneration of general practitioners in a given area were rearranged so as to involve some deduction in respect of cases passed into the care of the hospital, and a corresponding increase in respect of those treated at home (it might not be impossible to work out a formula); suppose too that the remuneration of the consultants in the area were determined, not by reference to time spent at the hospital, but partly by a fixed rate in respect of availability, and partly by reference to the number of domiciliary visits paid; and suppose that all in administrative positions were paid in accordance with grading or scales which bore no relation to the importance or size of the hospital but on the contrary carried a bonus touched off by any recognisable diminution in the rate of hospital admissions in the community. Suppose all these things, and leave the experiment to run for three or five years, what should we expect to see? Can we doubt that there would be some lessening of the emphasis on hospital services? Though the particular arrangements we have outlined might some of them do more harm than good, they would almost certainly alter the existing balance between hospital and domiciliary work. The existing balance is not necessarily right and it is not unalterable.

find a similar small majority of vaccinated children among those who later contract poliomyelitis In the recent outbreak, poliomyelitis in children of school age was in fact divided about equally between the vaccinated and the unvaccinated smallpox vaccination in infancy evidently does not alter the incidence of poliomyelitis in the age group 5–15 Among the younger children, however, constituting 25% of the cases, the picture is quite different since 1946 there have been 21 cases of paralytic poliomyelitis in the unvaccinated children under 5 years old, but only 4 among the vaccinated This contrast becomes still more striking if we confine our attention to the children under 3½ years old, who were effectively vaccinated in infancy In that age group there were 19 cases of paralytic poliomyelitis, as follows

Case no	Sex	Age at onset of poliomyelitis	Vaccination state	Result	Remarks
1	M	6 wk	No	P 2	
2	F	5 mth	Yes	Died	Died 4 days after vaccination
3	F	8 mth	No	Died	
4	M	11 mth	No	P 2	
5	M	1 yr 2 mth	No	P 3	
6	M	1 yr 2 mth	No	P 2	
7	F	1 yr 3 mth	Yes	P 2	Onset 14 days after inoculation for diphtheria and whooping-cough
8	F	1 yr 3 mth	No	P 3	
9	F	1 yr 6 mth	No	P 3	
10	M	1 yr 6 mth	No	Died	
11	F	2 yr 1 mth	No	P 3	
12	M	2 yr 2 mth	No	P 1	
13	F	2 yr 6 mth	No	P 1	
14	F	2 yr 6 mth	No	P 1	
15	F	2 yr 11 mth	No	P 3	
16	F	3 yr	No	P 3	
17	F	3 yr 4 mth	No	P 3	
18	M	3 yr 6 mth	No	P 1	
19	F	3 yr 6 mth	No	P 1	

Note P 1—Slight paralysis P 2—Moderate paralysis P 3—Severe paralysis

Thus in children under 3½ there were 17 cases of paralytic poliomyelitis (2 fatal) among the unvaccinated, and to these should be added the fatal case (no 2) in which the child died four days after vaccination, at a time when vaccination could not be expected to protect her The correct figure for unprotected children is therefore 18 cases with 3 deaths, whereas for the vaccinated the corresponding figure is 1 case with no deaths

The vaccinated child (no 7) was a girl who had been vaccinated at 6 months in the right leg there had been a severe reaction and (according to the mother) the leg had "gone septic" She was later immunised against diphtheria and pertussis, and at 1 year 3 months she developed paralysis of the left leg, fourteen days after the third injection of the combined vaccine into that limb According to current views this injection may have precipitated poliomyelitis with paralysis, in what might otherwise have been an abortive case

The figures for all cases of paralytic poliomyelitis under 15 years of age, in the period 1946–55, are summarised in the following table, which displays the difference between age groups 0–3½ and 3½–15

Age (yr)	Vaccinated	Unvaccinated	Proportion of poliomyelitis patients vaccinated
0–1	*Nil*	4*	*Nil*
1–3½	1	14	7%
3½–5	3	3	50%
5–15	18†	16†	53%†

* 1 of these children had been vaccinated but died from poliomyelitis four days afterwards

† Approximate figures

During the same period there were 34 cases of paralytic poliomyelitis at ages over 15 None of these patients had been vaccinated within recent years

Comment

The fact that, in this area during these ten years, most of the cases of paralytic poliomyelitis under school age have been in unvaccinated children might be explained in four ways

1 The numbers are small, and the difference demonstrated might be due to chance Personally I am disinclined to accept this explanation, for I have found similar vaccination histories in the cases from three other county districts admitted to our local infectious diseases hospital, where poliomyelitis patients were under my care or observation for the period under review My reason for not including these in my analysis is that these districts were outside my area and I was unable to make personal investigations

2 A recent reduction in the proportion of infants who are vaccinated might account for my findings Supposing, for example, that primary vaccination had virtually ceased in 1950, we should have no difficulty in explaining why so few poliomyelitis cases under 5 years of age have a history of vaccination But in point of fact, though the incidence of paralytic poliomyelitis has risen somewhat in recent years, the primary-vaccination rate has remained fairly constant, as is shown by the following figures

Year	Primary vaccination rate (%)			Poliomyelitis cases under 5 years of age
	Walton and Weybridge (1954 population 40 320)	Chertsey (1954 population 32,640)	Bagshot (1954 population 14 480)	
1955	60	64	50†	9
1954	60	64	47	Nil
1953	45	60	49	1
1952	57	55	53	Nil
1951	55	51	51	1
1950	51	40	47	1
1949	51	30	32	6
	County rate available only *			
1948		46		Nil
1947		57		6
1946		56		1

* The district primary vaccination rate is found to approximate to the county rate over the years 1946–54

† Estimated

3 The difference in incidence of poliomyelitis in vaccinated and unvaccinated children might possibly be related to the child's family or social or geographical circumstances Thus it might be argued (*a*) that parents who take the trouble to have their children vaccinated will also take the trouble to keep them away from infection or (*b*) that children are more likely to be vaccinated if they belong to small families, whose members will be less exposed to poliomyelitis because they have fewer brothers and sisters Neither of these explanations appears likely here

The area is one where social conditions are generally good, and nearly all the children with poliomyelitis have come from homes where they were well looked after

In social class, the fathers of the 25 children under 5 years of age who contracted paralytic poliomyelitis may be roughly classified as professional 5, clerical 5, skilled factory workers 7, labouring 8 The average number of children in these families was 2 6, and of the unvaccinated patients 2 were "only" children

For the fathers of the 25 children over 5 years of age for whom I have similar information, the corresponding figures are professional 5, clerical 7, skilled factory workers 8, labouring 5 In the families of the vaccinated children over 5 years of age the average number of children was 2 4 and in those of their unvaccinated coevals it was 2 3

Actually, if social or geographical factors introduce a bias into the results, one might expect this to be in the opposite direction to that found, for the general belief is that the children of the well-to do are more liable to acute hæmorrhagic leucoencephalitis involving the white matter of the entire central nervous system Atypical pneumonia, with a mononuclear-cell exudate and scattered pulmonary necroses, was also present Post mortem diagnoses of the neurological conditions associated with varicella are too few to substantiate the varied clinical diagnoses which have been made, although certainly many of them appear to be acute disseminated encephalomyelitis In that respect, therefore, this example of acute hæmorrhagic leucoencephalitis as a complication of varicella supports Russell's hypothesis Fowler and French[7] also noted the association with atypical pneumonia Although Lander failed to isolate a virus from either lungs or skin, he inclines towards a virus as the cause, and he suggests that *the disease may* develop after infection by a number of apparently unrelated viruses

PULMONARY EMBOLISM AND 5-HYDROXYTRYPTAMINE

ONE of the puzzles about pulmonary embolism has been the disproportion between the size of the embolus and the subsequent clinical signs When a large embolus blocks a main branch of the pulmonary artery, the results are fatal or very grave But serious circulatory collapse can be produced by an embolus which the subsequent clinical course shows to be quite small The stimulation of pressor reflexes in the lung has been blamed for these widespread symptoms, but no one is really satisfied with this explanation The possibility that a humoral agent might be released at the site of the embolism has also been considered, and recently Smith and Smith[8] have suggested that 5 hydroxytryptamine (5 H T) (serotonin) is the humoral agent responsible 5-H T has been much discussed lately because of its connection with malignant carcinoid tumours of the alimentary tract (argentaffinoma) Patients with these tumours may have a typical syndrome evoked by the 5 H T secreted by the tumour, and the detection of 5 H T or its degradation products in blood or urine during these attacks can be used for diagnosis[9] But, before serotonin was connected with carcinoid tumours, it had been identified as a vasoconstrictor liberated when blood-platelets are lysed in the first stage of clot formation[10] Normally this is only a local action, Udenfriend and Weissbach,[11] for example, showed that the 5 H T liberated is rapidly inactivated, and so long as platelets are intact, 5 H T does not appear It occurred to Smith and Smith that many of the circulatory symptoms of pulmonary embolism resemble those attributed to the secretion of 5 H T in patients with abdominal carcinoid tumours Since there is more or less extensive blood-clotting in pulmonary embolism, both in the vessels and in the infarcted area of the lung, significant amounts of 5-H T may be released, and the Smiths examined this possibility by investigating the results of experimental pulmonary embolism in cats

They allowed blood from the animal to clot spontaneously in a thin film, after one hour the clot was divided into fragments with an average diameter of 2 mm , the fragments were suspended in 1–2 ml of saline solution and injected intravenously This injection caused extensive blockage of the pulmonary arterial bed The effect of this blood clot embolism was a steep fall in blood pressure that lasted for some time the cardiac pulsations became feeble and the heart rate was often slowed at first, later there was a period of hypertension and rapid pulse rate For comparison they injected a similar suspension of starch granules, this either had no effect or caused a transient but profound fall in blood pressure, with cardiac irregularities—a pattern of response quite different from that produced by the injection of blood clot fragments The injection of 10 µg of 5 H T, however produced a response similar in pattern and sequence to that following the blood clot emboli In further experiments to gather more information about this action most 5-H T was found in the lysed buffy layer of blood though considerable amounts were present in the serum and the clot itself Injection of 5 H T or blood clot directly into the right auricle caused a sharp rise of blood pressure in the pulmonary artery, and these and similar experiments suggested that this was the main action of 5 H T If the injections were made so as to by pass the lung beds, the vascular effects were only slight The possibility that histamine or acetylcholine might be causing these vascular changes was excluded by repeating the experiments in the presence of specific antagonists The blood-clot experiments were also repeated in the presence of dibenamine and yohimbine, which are known to antagonise the vascular actions of 5 H T , and of cocaine which potentiates them These drugs acted in the same way with the blood clot injections as they did with 5 H T injections Finally, cats were given 2 ethyl 3 nitroindole, which is known to be an antimetabolite of 5 H T , when blood clot suspension or 5 H T was injected into these treated animals, there was little change in arterial pressure

All these experiments suggest that the release of 5 H T by clotting blood at the site of embolism, or elsewhere in the affected tissue, may play a part in the clinical picture that appears Since experience has shown that heparin often diminishes the unpleasant after effects of pulmonary embolism, Smith and Smith carried out some experiments to see whether heparin antagonises the action of 5 H T Injection of 5-H T into a previously heparinised animal was much less effective in lowering the arterial blood pressure, and in vitro experiments showed that heparin reduced the action of serotonin on the rat colon preparation

These findings raise the question of possible therapeutic measures for reducing or neutralising the action of 5 H T Heparin is already used, and the Smiths' experiments confirm its value 5 H T antagonists might be used, but dibenamine is an anti adrenaline drug still in an experimental stage, and yohimbine is hardly suitable for general use The 5 H T antimetabolite, 2 ethyl 3 nitroindole, takes twelve to forty eight hours to become effective after administration by mouth, and such a delay would make it useless Nevertheless, this work points to a new approach to the treatment of pulmonary embolism, and more appropriate drugs may soon be available

FOOD-POISONING AND DRIED MILK

MOST samples of unpasteurised milk contain *Staphylococcus aureus*, and some of the organisms are strains commonly associated with enterotoxic food poisoning Staphylococci are at least as common on the bovine teat as they are on the human hand and equally difficult to remove Many cows suffer from staphylococcal mastitis, and indeed it is possible that this infection is commoner than it was, owing to the widespread use of penicillin for the eradication of streptococcal mastitis With all the care in the world, some multiplication of bacteria in milk between the teat and the tea cup is unavoidable Nevertheless, only 2% of the recorded outbreaks of food poisoning in 1954 were traced to raw milk and in previous years even fewer[1] The probable reason for this anomaly is that enteritis is caused not by the staphylococci themselves but by the enterotoxin which they produce when they multiply in a suitable medium If milk is kept under conditions which favour the formation of enterotoxin, there will be a simultaneous multiplication of those other bacteria which cause souring and the milk will become unpalatable It is possible too,

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[7] Fowler, M French E L *Med J Aust* 1949, i 267
[8] Smith, G Smith, A N *Surg Gynec Obstet* 1955, 101 691
[9] See *Lancet* 1955 ii 1379
[10] Stefanini M , Dameshek W The Hemorrhagic Disorders New York 1955, p 13
[11] Udenfriend S Weissbach N *Fed Proc* 1954, 13, 412

[1] *Mon Bull Minist Hlth Lab Serv* 1955, 14, 203

TABLE I—INVESTIGATIONS

Day after ingestion	2	3	4	6	7	14
Red cells (million per c mm)	3 8, 1 5	2 6 1 65	2 2, 3 4, 3 0, 2 3	2 5	3 4	4 25
Hæmoglobin (g per 100 ml)	9 9	Estimation impracticable (hæmolysis)		8 5	10 9	12 7
White cells (thousand per c mm)	15 9	19 0	17 9	11 75	13 3	10 2
Erythrocyte-sedimentation rate (mm in 1 hr) (Westergren)	4–7		37–65		62–88	48–85
Serum urea (mg per 100 ml)	42		48			22
Serum-bilirubin (mg per 100 ml)						
Direct			Neg			Neg
Indirect			8 2			0 4
Liver function tests						Normal
Indirect Coombs test			Neg			
Osmotic fragility of red cells			Raised			
Mechanical fragility of red cells			Raised			
Serum hæmolytic activity			Slight			
Urine colour	Brown	Port wine	Port wine	Brown	Yellow	Yellow
Urine quantity (ml per 24 hr)	1150	2250	1900	450	1050	1350
Urinary sediment per high power field						
Leucocytes	–		Some	Some	10–25	Some
Erythrocytes	–		–	8–10	5–8	–
Granular casts	–		–	–	–	–
Albuminuria	–			+	±	–
Glycosuria	–					–
Urinary urobilinogen	Increased		Increased	Increased	Slightly increased	Normal
Urinary bilirubin	Neg		±	Neg		
Benzidine test (urine)	Neg	Pos		Pos		
Urea clearance						Normal
Naphthalene derivatives in urine	Neg					

On 4th day albumin/globulin ratio in serum serum-chloride, serum sodium, serum phosphorus, and serum-calcium levels, and plasma alkali reserve were normal

On 6th day bone marrow showed increased erythropoiesis

The differential white-cell count was always normal except for slight left deviation from 3rd to 5th day

Dec 6—She was still icteric but felt well, apart from tenderness in the left kidney region (complained of as abdominal pain) The colour of the urine reverted to dark-brown, and the number of red cells remained about constant The spleen was not palpable

Dec 7—She was no longer icteric Her urine was bright-brown, but she passed less than half a litre in twenty four hours Her fluid intake was restricted.

Dec 8—The red cell count began to rise, and the urine was yellow and normal in amount

From *Dec 9* convalescence ensued, the girl still complaining of slight pain in the kidney regions for some days

From *Dec 18* to *Dec 20* she complained of heartburn and epigastric pain. Six times she vomited 50–100 ml of bright-red bloody fluid, reporting that the fluid had "somehow suddenly accumulated in her mouth" Examination of mouth, nose, pharynx, and larynx, and radiography of œsophagus, stomach, and duodenum revealed no source for this bleeding It remains doubtful whether this episode has any connection with the intoxication.

The results of investigations are shown in the figure and in table I

Review of Literature

Earlier Cases

Many cases of naphthalene and naphthol poisoning are recorded in the older literature, but in the absence of modern facilities the interpretation of symptoms and signs was inadequate and mortality was high

9 of such cases (Goetze 1899, Nash 1903, Prochownik 1911, Heine 1913, Wiedow 1914, and others) were reviewed by Lewin (1893), Kraus and Brugsch (1923), and Zuelzer and Apt (1949) In at least 2 of them no blood studies were reported 7 of them were caused by therapy, 1 was an accidental moth-ball intoxication, and 1 was a murder 3 were fatal The outstanding symptoms were general urinary symptoms (dysuria, pollakisuria, oliguria, and transient anuria), 7 cases, dark urine, 4 cases, hæmoglobinuria, 3 cases, jaundice, 4 cases, and neurological symptoms (restlessness, disorientation, coma, and convulsions), 4 cases

Gastro intestinal symptoms and eczematous reactions to the topical application of naphthalene were well known Although the darkening of urine was recognised as a symptom—"the darkening of the urine starts usually about five hours after the administration of naphthalene" (Lewin 1893)—this was not appreciated as a sign of acute hæmolysis

Recent Cases

The findings of Ullmann (1947)* together with those of the later reports and ours are summarised in tables II and III

Treatment in all cases was by blood-transfusion Some workers added alkalis and antibiotics and we used cortisone and vitamin B_{12} as well

Mackell et al (1951) and Zuelzer and Apt (1949) also made experiments Mackell et al (1951) tested the hæmolytic activity of naphthalene and its metabolites (the naphthols and naphthoquinones) and found that in

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* The reports of Konar et al (1939) and Taylor and Russell (1932) appeared in journals not available to us in Jerusalem

TABLE II—SYSTEMIC MANIFESTATIONS OF NAPHTHALENE POISONING IN TEN CASES

Case no	1	2	3	4	5	6	7	8	9	10
Age (yr)	18	2	2	2½	2½	3	1½	2½	6 days	16
Fever	+	+	+	–			–	–		+
Neurological symptoms*		–	–	–	+		–			+
Gastro intestinal symptoms†		+	–	+			+	+		–
Abdominal pain	+			+	+					+
Dark stool			+							
Pallor		+	+	+	+	+	+	+		+
Jaundice	–	–	–	+	–	–	+	+	–	+
Palpable liver	–	–	–	+	–			–	–	–
Palpable spleen		–	–	+	–			–	+	–
Death	–	–	–	–	–	–	–	–	–	–
Cause of intoxication	Attempted Suicide				Sucking moth balls			–	‡	Attempted suicide

* Disturbances of consciousness and convulsions † Anorexia, nausea vomiting, and diarrhœa ‡ Clad in naphthalene powdered clothes

Special Articles

NATIONAL HEALTH SERVICE

Recommendations of the Guillebaud Committee

IN May, 1953, the Health Ministers appointed a committee

> " To review the present and prospective cost of the National Health Service, to suggest means, whether by modifications in organisation or otherwise, of ensuring the most effective control and efficient use of such Exchequer funds as may be made available, to advise how, in view of the burdens on the Exchequer, a rising charge upon it can be avoided while providing for the maintenance of an adequate Service, and to make recommendations "

The chairman was Mr C W Guillebaud (now reader in economics in the University of Cambridge), and the members Mr J W Cook, F R S (principal of the University of the South West), Miss Anne Godwin (a member of the council of the Trades Union Congress), Sir John Maude (formerly secretary to the Ministry of Health), and Sir Geoffrey Vickers, V C (treasurer of the Medical Research Council) All these have signed the report published last week,[1] but reservations are appended by Miss Godwin and Sir John Maude

Cost of the Service

In reviewing the present and prospective cost of the service the committee have made use of a memorandum prepared at their request by Prof R M Titmuss and Mr Brian Abel Smith, PH D Summarising this in our last issue, Dr Abel-Smith said that the real increase in the cost of the N H S since 1949–50 has been negligible in view of changes in the population, and that the share of the community's resources used on the service has been declining The committee reproduce the figures leading to this conclusion

The General Structure

The committee reject the suggestion that a National Board or Corporation should be appointed to administer the N H S

Health Authorities

Nor do they want to see the health services unified by the appointment of statutory ad-hoc health authorities which would administer all of them—hospital, practitioner, and local authority services In their view the only form of major reorganisation which calls for serious discussion is one which would add responsibility for the hospital service and/or the executive council services to the present duties of the local health authorities

But they do not feel that a convincing case has been made out for transferring the hospitals to the local authorities

> " Some form of regional authority will always be required for the efficient planning of a national hospital service, and if the service were to be managed by the local authorities, Joint Boards (or some similar bodies) would be necessary to carry out this planning function The service would then be administered through the Health Departments, Joint Boards, local authorities, and presumably hospital managing committees This administrative structure would not be calculated to improve the coordination of the service either at the national level or at the officer level, and would simply create new problems in the relationship between Joint Boards and local authorities Bearing in mind also that some local authorities themselves would be reluctant to accept responsibility for the hospital service that the bulk of the medical profession would be opposed to the suggestion, and that the financial burden would be intolerable unless the Exchequer grant were so substantial that it would render local government responsibility merely illusory, we feel confident that, whatever the merits of the proposal, it is not a practical proposition at the present "

The proposal that maternity, tuberculosis, chronic sick, and infectious diseases hospitals should be transferred to the local authorities is likewise dismissed, since it would *disrupt the hospital service* Sir John Maude would like to see the work of executive councils given to the local health authorities as a step towards unification

General Conclusion

The committee hold that the structure of the N H S was framed broadly on sound lines, and any fundamental change would be premature

> " It is still a very young service and is only beginning to grapple with the deeper and wider problems which confront it *What is most needed at the present time is the prospect of a period of stability*, in order that all the various authorities and representative bodies can think and plan ahead with the knowledge that they will be building on firm foundations Some of the strains and stresses of the National Health Service are attributable to the difficulty experienced by many, who had *grown up under the old system, when called upon to* operate a service administered on different lines Longer experience of the working of the Service and the gradual emergence of a new generation may make comparatively simple many things which now appear difficult or impracticable

An " Adequate " Service

Referring to the word " adequate " in their terms of reference, the committee point out that the amount of the national resources allocated to the N H S must be determined by the Government, the development of the service being one among many public tasks in which objectives and standards must be realistically set and adjusted both to means and to needs As in education, the aim must be to provide the best service possible within the limits of available resources

> " If the test of ' adequacy ' were that the Service should be able to meet every demand which is justifiable on medical grounds, then the Service is clearly inadequate now, and very considerable additional expenditure (both capital and current) would be required to make it so "

The Hospital and Specialist Services

Teaching Hospitals

One of the dangers of a national hospital system lies in uniformity, and the committee (except Miss Godwin) see distinct advantage in preserving the separate status of the teaching hospital They think it would be short-sighted now to subordinate these institutions, " upon which so much depends for the future development of the service," to the regional boards But they emphasise the board of governors' responsibility for coöperating fully with other organisations in the service, and " for the most efficient and economical management within the teaching hospitals themselves " For Scotland no change is proposed

Powers and Functions of Hospital Authorities

For administration of a service dealing with more than 3000 hospitals in England and Wales and some 400 in Scotland, two levels of management are considered essential " The service undoubtedly requires both regional authorities covering areas large enough for purposes of planning and general supervision, and also group management authorities with responsibility for the day to-day running of the service " It should be made clear that regional boards are responsible for *exercising a general oversight* and supervision over the administration of the hospital service in their regions, and the Ministry of Health should leave this task to the boards and not undertake it over their heads

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[1] Report of the Committee of Enquiry into the Cost of the National Health Service Cmd 9663 H M Stationery Office 1956 Pp 309 9s

TETANUS

RICHARD BATTEN
F R C S

LATE REGISTRAR, BIRMINGHAM ACCIDENT HOSPITAL

THE urgent problem in established tetanus is the control of convulsions Hitherto treatment has consisted in sedation with central depressants or in relaxation with drugs of the curare type, or in both

Central depressants are likely to depress respiration, but Forbes and Auld (1955) report 15 cases treated thus without a death, and Grant and McNeilly (1953) describe in detail the successful management of 1 case with thiopentone and pethidine

Relaxants, advocated by so many workers in recent years, are likely to be needed in such large doses that the diaphragm also is paralysed This in turn demands tracheotomy and positive pressure respiration

Tracheotomy—Galloway and Wilson (1953) found that tracheotomy diminished spasms and facilitated the sucking out of secretions Impressed with the improvement that followed routine tracheotomy and positive pressure respiration in bulbar poliomyelitis Lassen et al (1954) recommended curare for tetanus The paralysed and anæsthetised patient was then treated in the same way as one with bulbar poliomyelitis On this regime 3 of their 4 patients with severe tetanus survived Other workers have had variable success with tracheotomy, pulmonary complications apparently not being reduced, though sudden respiratory occlusion can be controlled, Continuous attendance by a doctor, however, is almost essential, and a great strain is thrown on the nurses

Other drugs which may be important in the management of tetanus are chlorpromazine (Bodman et al 1955) and the cortisone group (Lewis et al 1954) Their advantages are still doubtful, and only a few reports have been published

Antitetanic serum—In published cases the quantity, route, and timing of antitetanic serum have been so varied and so unrelated to the outcome that its value seems uncertain Theoretically it seems to be vital for neutralising circulating or unfixed toxin immediately, but convincing experimental and clinical evidence that it does so is lacking Given prophylactically it may be of more certain benefit, but Littlewood et al (1954) report a fatal case of tetanus in a boy who had 1500 units of antitetanic serum two hours after the accident, and anaphylactic deaths from antitetanic serum are not very rare

Management of the *electrolyte balance* has been well studied by Wilson and Care (1955)

Prognosis

The length of the incubation period seems to be clearly related to the severity of the disease, but, as our case suggests, a short incubation period need not make a fatal outcome certain Reported recoveries when the incubation period was less than five days are certainly very few

Case-report

On Aug 22, 1955, a boy, aged 7 years, was playing with his friends throwing lumps of earth at each other He was standing beneath a lamp post when one of the boys shook it, and a small piece of broken glass fell and pierced his scalp His mother found a very small scalp wound, which she did not think worth treatment Next day he walked with a "funny" posture of his shoulders and his jaw became stiff He had a definite convulsive fit at home that night, just thirty six hours after the injury He now could not swallow, and next morning his pillow was soaked with saliva It seems certain that for many weeks he had had no other injury, because his mother insisted that he always presented the most trivial injury to her for inspection and commiseration

Examination and Diagnosis

On admission to hospital on Aug 23 he was pale, looked ill, and had severe painful trismus, a classical risus sardonicus, and neck rigidity His rectal temperature was 99 8 F Tetanus was tentatively diagnosed, and a very guarded prognosis was given to the mother, it was still hoped that the condition might be due to meningitis Lumbar puncture however, produced clear cerebrospinal fluid with normal constituents

Treatment and Progress

Antitetanic serum 100,000 units was given intravenously after an intramuscular test dose of 1500 units The same evening the boy seemed better, his jaw was less tightly clenched and he sat up to play with his toys when visited by his parents, to whom a brighter prognosis was now given In the morning, however, this opinion had to be revised, for during the night a convulsion left him with severe opisthotonos, and next morning he had powerful and almost continuous spasms Rectal thiopentone 1 g in 5% solution produced sufficient relaxation for a polythene cannula to be inserted into the saphenous vein at one ankle to deliver above the knee, thiopentone continuously at the rate of 2 25 g in 1 5 litres of 4 2% glucose in 0 18% saline solution every twenty four hours (0 75 g per 500 ml bottle of glucose and saline solution) Tracheotomy was considered at this point, but, since the reflex spasms were completely controlled with thiopentone, relaxants and controlled respiration appeared unnecessary Continuous anæsthesia was thus maintained for fifteen days The amount of thiopentone needed to relax the hypertonic muscles was 1-2 g in twenty four hours Even then the child continued to have trismus, and the tonicity of his muscles varied from full opisthotonos to mild tightness of the recti abdominis muscles Thrombophlebitis developed in the leg on the fourth day, the cannula was removed, and a new cannula was inserted into the opposite ankle to deliver thiopentone directly into the inferior vena cava This ran successfully for a week and then slipped out unexpectedly owing to the boy's restlessness A third cannula was inserted at the wrist to deliver near the shoulder and ran until it was no longer needed The amount of thiopentone given was controlled by altering the concentration in the bottles as a long term measure or, for quicker action, by injecting a few ml of 2 5% thiopentone into the rubber tubing near its junction with the cannula

Nutrition

Nutrition was maintained partly by the intravenous glucose and saline solution and partly through a nasal catheter to the stomach This catheter was passed with the help of 30 mg of intravenous suxamethonium chloride and was changed by the same technique after ten days By this route a continuous drip of nutrient mixture was supplied, each 500 ml bottle containing 1 pint of milk, 2 switched eggs, 1 oz of sugar, and 1 oz of 'Casilan' to a total of 1 5 litres in twenty four hours, providing 1000 calories Vitamins were added to this mixture in suitable doses The serum electrolytes were estimated at intervals The only abnormality was a lowered serum potassium level on the sixth day, this was corrected by adding potassium chloride to the intravenous fluid

Respiration

Respiration was at first obstructed at intervals when trismus was so severe that the rubber airway was occluded A metal airway of the Waters type was found to resist the boy's bite, and its side tube allowed the pharynx to be sucked clear Atropine gr $^1/_{200}$ three hourly reduced bronchial secretion but increased the viscosity of secretions from nose and throat, making laryngeal toilet more difficult Sulphadimidine via the gastric drip and intramuscular penethamate hydriodide ('Estopen') were given to prevent pulmonary infection Frequent suction was necessary via the nose and mouth to prevent saliva and nasal secretions from running down the trachea, but suction increased secretion and therefore had to be limited On the fourth day of anæsthesia

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experimentally in a limited number of hospitals "Whilst we would agree that the subjective accounts must be retained at least for the time being, we would suggest that their retention be reviewed at a later date"

> "We trust that all concerned with hospital administration —not least the doctors—will co operate to the utmost in order to make a success of this vital aspect of hospital management We should regard it as unfortunate if opposition to the compilation of departmental costs or similar data were to be based on the mistaken idea that any conclusions could be drawn from these figures as to the professional standards or competence of doctors in different hospitals"

Voluntary Contributions

The committee regard it as entirely appropriate that appeals for voluntary contributions should continue to be made by voluntary bodies (for purposes agreed with the hospital concerned) but not by the statutory boards or committees They see no reason why hospitals should not (as many now do) spend endowment moneys on purposes for which Exchequer money could properly be used "It seems to us that the continuance and further expansion of voluntary service is one of the surest ways of maintaining the essential humanity and vitality of the hospital service and preventing the development of that enemy of human welfare—institutionalism"

A Boarding Charge?

Having regard to the relatively low yield likely to be obtained from a hospital boarding charge (after all the probable exemptions have been taken into account), and to the practical difficulties, the cost of collecting the charge, and the strenuous opposition which would be aroused on humanitarian grounds, the committee do not advise its introduction

Staff

Administrative Staff—The committee regret that there should still be no provision nationally for recruitment and training of hospital administrators and recommend such provision as soon as possible

Consultants Whole time or Part-time?—There is, in the committee's view, a valid case under existing conditions for the retention of part-time consultant appointments in addition to whole time appointments

> "We consider it very desirable, however, that Regional Boards should be free to appoint whole time consultants in cases where it is deemed to be necessary in the interests of the service We trust that joint consultation between Regional Boards and the medical consultative committees will lead to agreement between the Boards and the medical profession, and will prevent the emergence of differences of opinion over the conditions of appointment such as have been known to occur in the past
>
> "We are also of opinion that it is undesirable that the financial arrangements relating to the consultant service should be such as to provide a financial inducement to a consultant to apply for a part time rather than a whole time appointment"

A New Specialist Grade?—They welcome the suggestion that, as part of the reorganisation of hospital medical staffing, provision should be made for a new specialist grade, below the grade of consultant, which would offer a permanent position in the career structure of the hospital service

The Medical Administrator

On day-to-day medical administration the committee endorse the views of the Committee on Internal Administration of Hospitals (1954)

> This did not favour group medical superintendents, but wanted the larger general hospitals to appoint, as part time medical administrator for a few years at a time, a consultant in active clinical practice—his appointment to involve no loss of salary Where no such person could be found the work could be done by a younger man in a new R M O or R S O grade

Amenity Beds and Pay Beds

The committee accept the provision of pay beds and amenity beds—bearing in mind that these represent a very small proportion of the total beds in the N H S They remark that all hospital beds, whether free or not should be fully used, but they do not suggest any change in the calculation of charges for pay beds It would be inadvisable to depart from the principle that "the user of a pay bed, having contracted out of the free hospital service, should pay the full cost "

The Family Doctor

Doctor and Patient

The committee are inclined to agree with the Cohen Committee on General Practice (1954) that in general the N H S has not disturbed the doctor patient relationship

Drugs

They are against the introduction "at the present time" of a limited list of drugs prescribable in the N H S But every effort should continue to be made to keep doctors informed about the cost of prescribing generally The advantages obtainable from full pricing of prescriptions are unlikely to be worth the cost Nor do the committee favour the reintroduction of a returnable cash deposit for containers

Central Register of N H S Patients

The existing Central Register is inadequate, and a central alphabetical index appears desirable for the sake of efficiency, economy, and equity

The Family Doctor and the Hospital

The committee associate themselves with various previous recommendations

> Practitioners should have at their disposal hospital beds where they can retain responsibility for their patients They should be encouraged to do part time work as clinical assistants and in the normal hospital grades Diagnostic facilities (particularly radiological and pathological) should be directly available to them wherever possible The rôle of the out patient department should in the main be consultative The general hospital should be a centre of medical endeavour, where the practitioners have right of entry and can meet their hospital colleagues on terms of equality

Concerned, as they are, with the efficient and economical operation of the N H S, the committee say

> "It is desirable that whenever practicable patients should be treated in their own homes by the general practitioner and the local health services, instead of being admitted to hospital where the running costs are so high, and that when a patient is admitted to hospital, he should be discharged at the earliest possible date, any necessary follow up treatment being provided either in the hospital outpatient department or at home by the general practitioner and the home health services"

Dental and Ophthalmic Services

Dentistry

After speaking of the "acute shortage of trained dental man-power (which appears to be growing more serious each year)" the committee declare that in oral disease the opportunities for preventive work are outstanding They hope that the pilot demonstrations of fluoridation of water supplies will be pressed forward, and they urge increased research, more dental health education, and more efficient dental services for mothers and children They discard a proposal that responsibility for the clinic services should be transferred from the local authorities to the Health Departments, but they say that one of the lessons of the past seven years is that some balance must be kept between remuneration inside and outside the clinics Having pointed out that there seems to be a prima-facie case for employing dental ancillaries, they remark that, whatever is done, we cannot hope for an expansion of the service sufficient to meet all needs

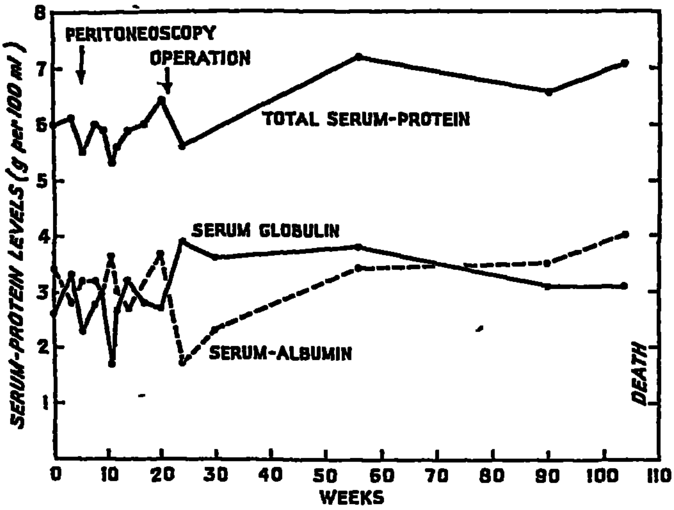

Fig 1—Serum protein levels during illness

On Jan. 10, peritoneoscopy was undertaken by Mr W W Davey, who reported "9 pints of fluid were withdrawn, and good visualisation of the liver was obtained, the anterior sharp edge was rounded with coarse irregularity of the surface and loss of normal architecture Many blood vessels were seen on the surface and there were many recent adhesions between the anterior surface of liver and the parietal peritoneum No superficial hepatic metastases or tubercles were seen the condition is probably acute cirrhosis" These findings were consistent with the clinical diagnosis of Chiari's disease

On Jan 12, treatment was started with phenindione ('Dindevan') 100 mg twice daily, but within twenty four hours the prothrombin time rose from 28 to 75 sec and the treatment was stopped The thymol turbidity was then 9 units, the alkaline phosphatase 16 units, the serum bilirubin 0 2 mg per 100 ml, and the blood urea 20 mg per 100 ml

On Feb 9 prominent, dilated veins on the sides of the chest were noticed, and liver biopsy was repeated This showed engorgement and reticular fibrosis, with dilated, engorged, capillary spaces and inflammatory infiltration in fibrous strands The thymol turbidity was 3 units, the alkaline phosphatase 15 5 units, and the fæcal urobilinogen 27 mg per day

Operation

It was decided that ligation of the hepatic artery might relieve the hepatic congestion no less effectively, and more safely, than a portacaval shunt Mr W W Davey therefore did a laparotomy on April 25 and reported "The spleen was enlarged to twice the normal size, and the liver was adherent to the abdominal wall and to the stomach The portal pressure was not appreciably raised as judged from the appearance of the gastro epiploic veins and the slight bleeding when making the incision The splenic and hepatic arteries were ligated, the latter just proximal to the gastroduodenal artery Both these procedures were difficult because of induration and adhesions" A liver biopsy specimen taken at operation showed "severe fibrosis of irregular pattern with focal hæmorrhage and some regeneration, with slight chronic inflammatory reaction"

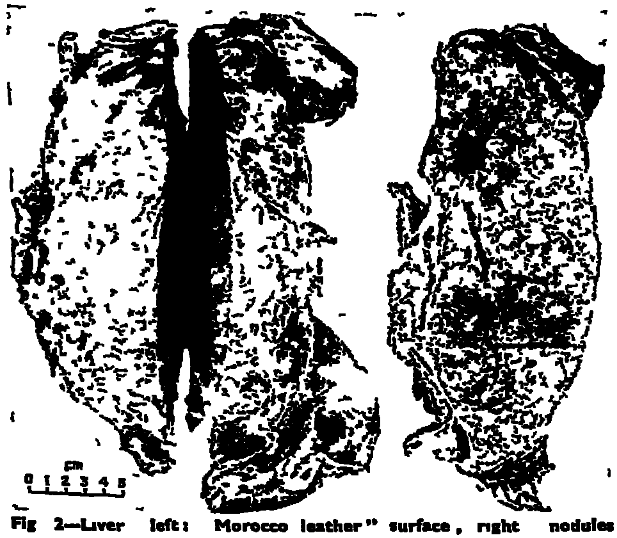

Fig 2—Liver left: "Morocco leather" surface, right nodules of regeneration

Subsequent Progress

After discharge from hospital in June, 1953, the patient continued to attend weekly for abdominal paracentesis, but on Nov 12 he was readmitted with slight hæmatemesis and melæna The veins in the abdominal wall and on the sides of the chest were now more dilated and a barium swallow showed varices at the lower end of the œsophagus He was discharged on Dec 8, and four days later (twelve months after his first admission) the final paracentesis was performed

On Jan 19, 1954, he complained of pain in the breasts and was found to have gynæcomastia, several spider nævi on the face and hands were also noticed There were dilated veins in the flanks, and the liver was hard and nodular

On April 9, the thymol turbidity was 2 units and the alkaline phosphatase 21 1 units He returned to work where he remained until Jan 22, 1955, when he was again admitted with hæmatemesis and melæna Despite blood transfusions his condition deteriorated rapidly and he died in coma on Jan 24

Necropsy (Dr S Robinson)

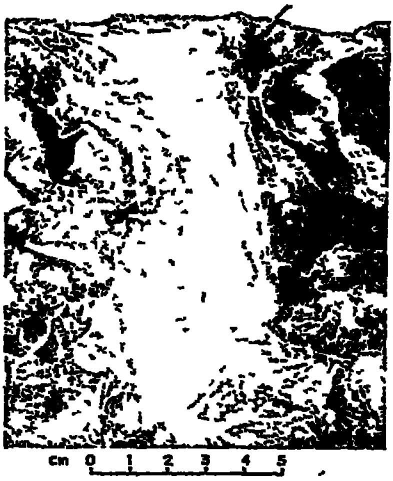

Fig 3—Inferior vena cava, showing fibrosis of adventitia

The *liver* was enlarged (weight 4 lb 13 oz) and firmly fixed to diaphragm, spleen, and stomach by fibrous adhesions bearing many dilated tortuous veins The outer surface was coarsely nodular with a "Morocco leather" appearance (fig 2) The cut surface was mottled with a coarse, grey network of fibrous tissue containing engorged sinusoids and cords of pale yellow surviving liver parenchyma with nodules of regeneration up to 1 cm in diameter (fig 2) The hepatic veins were inconspicuous, and the openings of the left and lower right hepatic veins into the inferior vena cava were completely obliterated, the right upper hepatic vein was blocked by fibrous tissue 1 5 cm from its mouth The *spleen* was slightly enlarged (weight $8^1/_2$ oz) with hyaline fibrosis of the capsule and prominent veins in the adhesions, the cut surface showed engorgement *Heart and blood vessels* the heart weighed $9^1/_2$ oz, and there was œdema of the myocardium There was hypoplasia of the aorta, the circumference of the thoracic portion being 4 cm and of the abdominal portion 3 5 cm There was considerable fibrosis around the adventitia of the inferior vena cava (fig 3) and there were dilated veins in the submucosa of the lower three quarters of the œsophagus with erosion of three veins containing adherent thrombus There were prominent, dilated, tortuous veins in both iliac fossæ and under the skin of the abdomen and back *Stomach* on the anterior wall of the pyloric antrum there was a chronic ulcer measuring 4 × 3 cm which was firmly adherent to the liver and which had several bleeding points in its floor

Adhesions obliterated both *pleural cavities* There were œdema and congestion of the *lungs, brain, kidneys, suprarenals*, and *intestines*

In England Now

A Running Commentary by Peripatetic Correspondents

WHEN the visiting specialist makes a tour of the ward, sister and one of the house-surgeons are in close attendance and behind comes a staff nurse ssh-sshing any patient who dares to so much as breathe noisily A holy hush descends for any doctor and, in a modified degree, for matron's visits Decorum thus prevails during the morning hours, but the noise in a public ward for the rest of the day has to be heard to be believed Conversations are carried on between occupants of beds at opposite ends of the ward probationers retail the latest song hits, community singing is popular, and loud-speakers, tuned eternally to the light programme, add to the din

Many hospitals are built in busy streets Our local infirmary faces a main road, and has a railway shunting-yard behind it and a coach station next door Traffic goes on round the clock and I was surprised to find that after two wakeful nights I hardly noticed it The regular sounds of the ward were much more disturbing My bed was next to a cupboard with sliding doors which seemed to be crashed open and shut about every five minutes all night Screens are rattled about and shut up with a bang Most night-nurses wear shoes that squeak, and the bed of one unlucky patient was next to the bathroom door

Do doctors really believe that, between their visits, the ward is so quiet that you could hear a swab drop ?

* * *

Now that modern mass-production techniques have all but ousted the single-handed preparation of mist , ung , and tab in the little dispensary that once flourished in the lee of every doctor's surgery and chemist's shop, it is, I suppose, old-fashioned to grumble if the names of drugs, as well as the drugs themselves, are mass produced And that is the prospect before us According to the New York correspondent of the *Daily Telegraph* (Jan 20) the baffled boffins of a well-known American pharmaceutical firm have abandoned their self-appointed task of juggling with assorted letters of the alphabet, and turned the whole thing over to an electronic brain

Fed on a diet of word-endings " found to be common in the medical literature of several languages," this machine rejected 22,000 " unsuitable combinations," and then " proceeded to coin 40,000 words," all of a medicinal flavour suitable for drug names Some of the words passed by the machine had also to be consigned by the human editor to the rejects, for the machine is regrettably unable to recognise words that cannot be used in polite conversation

Some of the successful examples such as starycide, platuphyl, chohacyn—certainly carry a vague *soupçon* of the pharmacopœia, though one might be hard put to say just why Certainly they suggest that the heralded new electronic age of innocence will be supremely untroubled by such outdated questions as the meaning of meaning

How doth the lowly *platuphyl*
Avert the psychic pain
Of *starycidal* tendencies
In *chohacyn's* train

* * *

To me, unlike my fellow peripatetic of Jan 14, all airports are much the same airport—they run so much to pattern Were it not for the name picked out in large letters and for striking variations in the temperature I should hardly have known in which hemisphere I was True that Frankfurt had an ornamental lake and waterfalls which might look well floodlit But it was maddening to be set down for three-quarters of an hour in Istanbul and confined within a sort of compound containing only a buffet bar and some inferior toys and jewelry There was a longer, drearier, and stuffier wait at Beirut where the Syrian guards seemed to look at us with the gravest suspicion Still perhaps I exaggerate international monotony At Karachi my wife reported that she had found two Pakistani gentlemen, lightly clad in shorts and vests chattering volubly, and enjoying their lunch while squatting at ease on the floor of the ladies' lavatory I admit you wouldn t see that in England now

Letters to the Editor

HYPERTROPHIC PULMONARY EMPHYSEMA

SIR,—Your leader of Jan 7 follows the familiar pat of articles upon this subject The usual argument f and against its causation by inspiration, expirat coughing, resistance to air-flow, and elasticity (u synonymously with elastic tissue) are set out Then, b convention, the greater part of the article deals with t various physiological function tests in vogue

Your statement that 'any hypothesis should take in account the almost invariable association of hypertro emphysema with bronchial diseases such as chronic bronch or asthma " is misleading Surely it would have been m realistic to have stated that in the ordinary run of p mortem examinations hypertrophic emphysema is alm invariably associated with chronic bronchitis I was unaw that there was any particular association between emphyse and uncomplicated asthma, indeed, emphysema is a unusual finding at necropsy in patients dying from asthma.

The lethal feature of chronic bronchitis is inflammatio of the respiratory unit—namely, the primary lobule an its associated bronchiole Repeated infection leads to progressive lobular and bronchiolar obliteration b fibrous tissue This throws an added strain upon th healthier respiratory units, whose lobules dilate to occupy the spaces previously taken by lobules which have shrunk by fibrosis This mechanism, supplemented here and ther by valvular dilatations, leads to alveolar rupture with a considerable increase in interlobular air drift—in other words, emphysema This process is an inevitable con quence of chronic bronchitis , and the question of whether or not emphysema exists is largely academic, as it inevitably does so, provided the chronic bronchitis i sufficiently severe and lasts long enough If physiological function tests are to be applied as an adjunct to clinical and radiological examination, the most useful in practice are oxygen saturation before and after exercise, and tests of pulmonary function before and after the administration of relaxant drugs when associated bronchospas is suspected

On rare occasions, emphysema develops in the absence of infection Little is known of the pathology in the cases, until detailed studies of the distribution and state of the bronchioles, lobules, blood vessels, and elastic tissue have been made, any explanation of the mechanisms involved is bound to be hypothetical

NEVILLE C OSWALD

London W 1

A PLATELET FACTOR RESPONSIBLE FOR CLOT RETRACTION

SIR,—In the course of platelet transfusion experiment in thrombocytopenic patients it was noted that admin tration of non viable, preserved platelets, although no raising the thrombocyte count, improved the utilisatio of prothrombin and the retraction of the clot[1] Th observation prompted a search for a constituent platelets with the ability to induce retraction of platele poor plasma and fibrin clots Such a factor has bee postulated by Glanzmann[2] and Fonio[3]

Treatment of isolated and thoroughly washed hum or bovine platelets with 75% acetone water v/v or 65 ethyl water v/v mixtures yields an agent which induc retraction of a clot of native platelet free human plas or of purified bovine fibrinogen clotted by thromb This factor precipitates also in ethyl ether at –20 The acetone extract may be freed of thromboplast factor by heating at 56°C for two hours, followed b storage at –20°C for forty eight hours Ethyl eth extracts are free of platelet thromboplastic factor

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[1] Stefanini, M Unpublished observations, 1955

[2] Glanzmann, E *Amer Pediat* 1918, 88 113

[3] Fonio A *Acta hæmat* 1952, 8, 363

On Nov 25, 1954, further radiographs showed both $\underline{8/8}$ ugh up above the still unerupted $\underline{7/7}$ and corresponding o a dental age of 10 years There was no change of calcifica ion in the remaining teeth during the intervening eighteen months but an apical area had developed on the $\overline{|2}$ From this dental evidence some factor appears to have supervened at about the age of 8 years or over, preventing the full development and calcification of the teeth

Progress and Treatment—Idiopathic hypoparathyroidism was diagnosed in view of the low serum calcium level, high serum phosphorus level, normal radiological appearances of the bones, absence of renal insufficiency, and absence of steatorrhœa Despite the patient's suggestive facies and stature, the case was not considered to belong to the pseudo hypoparathyroid variety (Albright et al 1942) in view of the absence of dyschondroplasia and subcutaneous calcification (MacGregor and Whitehead 1954, Robinson et al 1954) The macrocytic anæmia was noted but examination of the bone marrow at this time was inconclusive Anticonvulsant drugs were withdrawn for a week in June, 1954, and treatment was started with dihydrotachysterol 1 ml (1 25 mg) t d s and calcium lactate gr 25 t d s The former was gradually increased to 20 ml daily, but the serum phosphorus level remained higher than the serum calcium level The Hb increased at first but later decreased again In November, 1954, examination of the blood showed Hb 42% (6 2 g per 100 ml), colour index 1 35, leucocytes 2700 per c mm, mean corpuscular volume 110 c µ, reticulocytes 0 8%, and serum bilirubin level 1 4 mg per 100 ml Sternal puncture showed severe megaloblastic dysplasia of the bone marrow Cyanocobalamin 50 µg was given daily by injection The Hb increased rapidly and after five days there was a reticulocytosis of 8% Calciferol 200,000 units daily was substituted for the dihydrotachysterol and the serum calcium level considerably improved No fit had been recorded since March, 1954, and the patient now felt very well, and the signs of latent tetany had disappeared Further electroencephalograms showed improvement On Nov 4, 1954, there was an alpha rhythm at 9 c p s of moderate amplitude and fair symmetry There was excess diffuse episodic theta activity at 3–6 c p s No specific epileptic waves or focus seen On Dec 10, 1954, the electroencephalogram could be considered within normal limits for the patient's age

Follow up—When seen as an outpatient in February, 1955, the patient's Hb was 100%, serum calcium level 8 4 mg per 100 ml, and serum phosphorus level 11 4 mg per 100 ml

Discussion

The nature of the anæmia is an interesting problem Three main possibilities were considered (1) a true pernicious anæmia, (2) the result of long continued dosage with phenytoin sodium, and (3) the result of the hypoparathyroidism

True pernicious anæmia is rare under the age of 40 Murphy (1939), in 550 patients seen personally, found only 1 aged less than 20 Nevertheless the histamine fast achlorhydria, the typical peripheral blood picture, the frank megaloblastic marrow in October, 1954, and the rapid response to cyanocobalamin point strongly to true pernicious anæmia

As regards phenytoin sodium Hawkins and Meynell (1954) described a case in which a megaloblastic change was thought to have been induced by phenytoin sodium Their patient, however, had free gastric acid The hypoparathyroidism is considered to be the least likely cause While the patient was receiving dihydrotachysterol 20 ml daily, her Hb was decreasing rapidly

After a month's treatment with calciferol there was much improvement in the electroencephalograms which could be considered normal for the first time (the first record having been taken in March, 1953) This suggests a definite relationship between the treatment, which produced a rise in the serum calcium level, and the improvement noted electroencephalographically

Robinson et al (1954) suggest that the basic electrical rhythm is responsible for the abnormal pattern in the electroencephalogram, but this case supports the hypothesis that the changes are largely due to a biochemical abnormality

The appearance of the teeth indicates retarded development due to some factor supervening about the age of 8 years The epilepsy in this case also began at 8 years, and one can assume the onset of hypoparathyroidism near that age This dental finding fully agrees with the suggestions of Albright and Strock (1933)

Calciferol was as efficacious as dihydrotachysterol in bringing the serum calcium and serum phosphorus levels back to normal and was less expensive The serum phosphorus level was very high again in February, 1955, although the serum-calcium level was normal. this indicates a renal tubular defect with increased resorption of phosphorus

Summary

A case of idiopathic hypoparathyroidism presenting with epilepsy from the age of 8 years and recently developing megaloblastic anæmia is described

The probable cause of the anæmia is discussed

I wish to thank Dr H Hilton Stewart for permission to report this case, which was under his care, and for his advice

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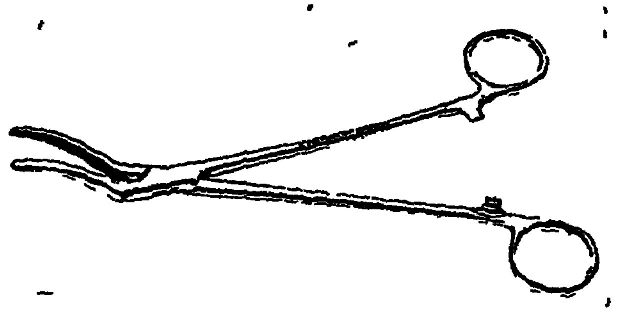
New Inventions

PULMONARY-HILUM CLAMP

The clamp illustrated here was devised about two years ago for use in the thoracic unit in Manchester and has been used by several surgeons in many pulmonary resections

There are occasions when, owing to inflammation or to neoplastic enlargement of glands, the distal ends of the pulmonary vessels are difficult to secure satisfactorily either by ligature or by the commoner clamps—e g, straight Spencer Wells, Roberts forceps, and cholecystectomy forceps



Sometimes a Roberts or a cholecystectomy forceps could be applied backwards to the distal ends of the vessels, or alternatively the vessels could be cut distally and allowed to "bleed back" In such a situation a fairly strong clamp with an angled shank and a reversed curve on its blades, which are longitudinally serrated but no wider than a Roberts forceps, gives most satisfactory control without fear of slipping This instrument has a strong box-joint so that it can also be used, if necessary, as a distal clamp on the bronchus without straining it

I am indebted to Mr H Woodall, of Allen & Hanburys, for having the clamp made to my specifications All inquiries should be addressed to him

P JEWSBURY
F R C S
Blackpool Victoria Hospital

express my opinion that his point of view is superficial, irresponsible, rather superior, and lacking in perception

Beckley, Rye, Sussex C G LEAROYD

SIR,—Dr Comfort attributes the legal attitude to homosexuality largely to emotion, but is it not due to the legal respect for custom? The reasons for custom may or may not be apparent, or valid Incest is taboo presumably because of a "tribal" fear of procreating poor stock On this premise, if the fear is groundless logical argument against incest fails Incest between consenting adults becomes no more culpable than other varieties of sexual relationship between consenting adults

I feel sure, however, that the "tribe" would maintain its taboo on incest without logical explanation Likewise it will maintain its taboo on homosexuality between consenting adult males, which may well have social consequences that are not obvious (Even so, the feminising effect on the passive partner of such relationships seems an obvious social evil)

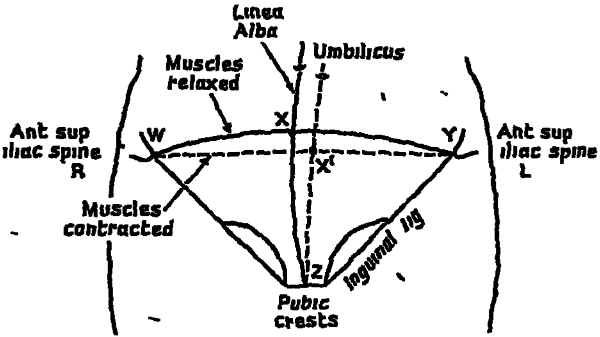
Penalties may be savage and defeat their object, but let us respect the wisdom of our forefathers

Barton on-Humber, Lincs S H F HOWARD

INGUINAL HERNIORRHAPHY

SIR,—I agree with Dr Robinson (Jan 7) that the "fixed point" has meaning only in the coronal plane

In the sagittal plane, as the accompanying figure shows, it moves in the way he describes, moreover, it shows the representation of the points as a pyramid I agree, also, that as the apex of the pyramid, X, moves anteriorly there is a tendency for the gap between the conjoined tendon and inguinal ligament to increase The radiographs referred to by Dr Robinson provide no information on this point The first film was taken with the abdominal musculature relaxed "normally", the second film was taken with the abdominal wall drawn *backwards* by strong contraction No change was detected in the distance between the markers No film was taken with the abdomen "blown out", if one had been taken, an increase in the gap between the markers might have been seen, because the usual clinical method of "bringing down" a small hernia is to make the patient "blow out" the abdomen with a cough



Lastly, I must ask Dr Robinson how the conjoined tendon can contribute to the integrity of the inguinal canal except by literally acting as a "shutter" in the way described by Keith

Mr Forty (Jan 7) asks for the number of recurrences in the group of patients whose "markers" have separated The answer is none at present I agree that if the conjoined tendon is pulled off the inguinal ligament a sheet of fibrous tissue probably bridges the gap If the declared object of sewing the conjoined tendon to the inguinal ligament was to create this fibrous sheet no protest would be necessary, provided it succeeded, but as this intention is not usually understood with this operation, it would appear that the surgeon "succeeds" owing to an accidental event, and is robbed of his satisfaction thereby

With regard to the suture material in some cases catgut was used, in others silk No nylon was employed The relative merit of catgut and silk are being tested in another investigation, which will mature this year, of 100 cases followed up for two years

Tutnall, near Bromsgrove,
Worcs F S A DORAN

WERTHEIM'S HYSTERECTOMY

SIR,—I feel that I must reply to certain points raised by Mr Mills (Jan 14) He refers to the "comparative unpopularity" of the synchronous combined abdomino-vaginal hysterectomy I do not think that his phraseology is quite fair as my colleagues and I have performed over fifty of these operations at St Bartholomew's and other hospitals, and many gynæcological surgeons, both foreign and British, who have come to watch the operation have been impressed with its possibilities

Mr Mills is correct in saying that the operation requires an expert theatre staff and team of assistants, and I have been fortunate in having a series of first-class registrars all of whom have shown themselves most competent operators In my original article I stressed that this operation should only be done in a large and fully equipped department, and my experience with the operation has amply confirmed this

The great advantage of the synchronous combined operation is that the two surgeons, working together, can completely remove the parametrium and paracolpos without changing the position of the patient, and although I commend Mr Mills's idea of an asynchronous combined operation, I do strongly recommend him to try the operation as I described it,[1] when he will appreciate the superiority of the combined technique Apart from providing a wider dissection, the operation is easier and quicker to perform, and he will find the help of his nether colleague of inestimable value when dissecting the bladder from the parametrium and vagina

I would raise, however, one criticism If Mr Mills starts his operation from below and thereby commits himself, he may well find on opening the abdomen that it is not feasible to complete the operation—for instance, if malignant glands are irremovably fixed to the external iliac artery or if the aortic glands are involved Both these complications have occurred in my experience and deterred me from further surgical treatment Our practice now is to open the abdomen with the patient in the St Mark's Hospital position, using the Lloyd Davies

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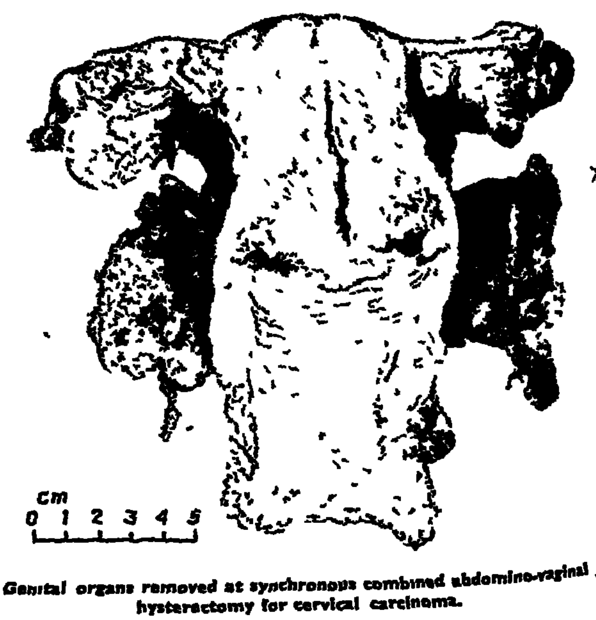
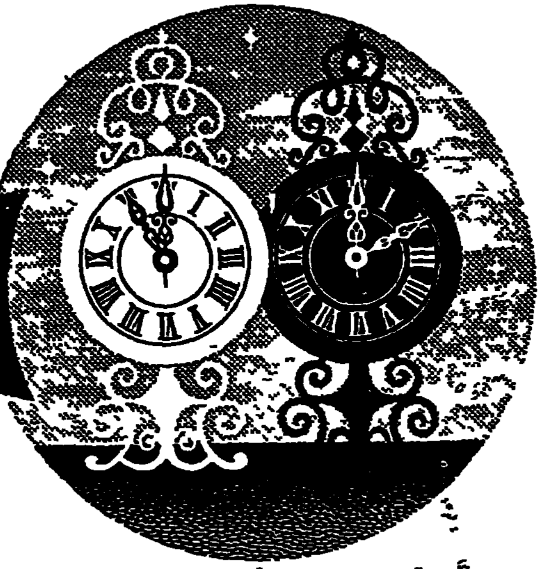
[1] *Lancet* 1951, i, 872



Genital organs removed at synchronous combined abdomino-vaginal hysterectomy for cervical carcinoma.

twofold action



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5 hours.

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view, but in fact supports my own contention, the extreme sensitivity of tocopherols to various physicochemical processes, with consequent loss of biological activity, was demonstrated at the third International Congress on Vitamin E by several speakers in September last

Apart from this divergence of opinion, I endorse wholeheartedly the authors' view that the serum-cholesterol level is not the only, let alone the decisive, factor in the incidence of coronary heart-disease There can be little doubt that the whole blood "chemo cosmos," so to speak, conditioned by the total food intake and the various digestive enzymes, among other factors, has an important rôle

London W 1 L SCHMIDT

Parliament

Guillebaud Report

IN announcing the publication of this report on Jan 25, Mr TURTON, the Minister of Health, said that its main conclusion was that it would be premature at this point to make any fundamental alteration in the structure of the National Health Service In the committee's view what was most needed at present was the prospect of a period of stability so that the authorities and representative bodies could think and plan ahead with the knowledge that they would be building on firm foundations The committee specifically indicated their support, by and large, of the main administrative features of the services, including, for example, the present method of making Exchequer money available for the hospital service With the committee's general conclusion and approach on these matters the Government were in agreement

The committee pointed out that the aim must be to provide the best service possible within the limits of the available resources, and that it must be for the Government to determine as a matter of policy how much of the national resources, in terms of finance, man-power, and materials, could be made available for the health service, regard being had to the competing claims of other social services and national commitments

The committee's recommendations on organisation and management of the service included a recommendation on the desirable rate of capital expenditure in the hospital service The Government decided some time ago that the present level of expenditure should be increased in the years up to 1957–58 The committee proposed that, after that, if the resources could then be made available, £30 million annually would be a desirable level at which to aim over the seven succeeding years

The committee further recommended that when financial circumstances permitted, the existing Exchequer grant towards the capital cost of providing residential accommodation for the aged should be replaced by a 50% grant on the net total expenditure of local authorities on such accommodation This proposal would involve legislation and would also require consideration in the wider context of the relation of local-government finance with the Exchequer There were a number of recommendations either for continuation or for development of measures already in hand or contemplated or for detailed adjustments in the present arrangements These recommendations would require careful consideration He must, moreover, make it clear that in view of the economic situation the Government could not undertake any additional financial commitments in respect of the health services at present

The committee's final comment included a tribute to the service's record of performance and a finding that any charge of widespread extravagance had not been borne out by the evidence

Mr ARTHUR WOODBURN asked whether the Government were bearing in mind that real economy would come when the hospitals could be made more efficient by new capital expenditure A great deal of waste arose from the use of old buildings and appliances and the difficulties experienced by doctors and nurses in carrying on their work He hoped that the Government would realise that cutting down cap expenditure was not necessarily the way to secure econ and that it might be better to spend a little more mon now in order to save over the years In examining the rep he hoped that the Minister would not close his mind t further expenditure if that was necessary to restore an people to work Mr TURTON The Government apprecia those points That is why in the programme for 1956-5 and for 1957–58 there is provision for plant replacem Dr BARNETT STROSS May we interpret what the Minister h said as meaning that as soon as there is an acknowledg improvement in the economic situation of our country th essential recommendations in this valuable report will b given the highest priority? Mr TURTON First we mu study this report and I must have consultations with th local health authorities on many of its detailed recommenda tions Until that has been done it would be wrong for me t make any commitment

QUESTION TIME

Ban on Heroin

Replying to questions, Major GWILYM LLOYD GEORGE, th Home Secretary, said the Government's aim in deciding t ban the manufacture of heroin was to coöperate in a wid spread international effort, to which more than 50 countri had subscribed, to help to eliminate the abuse of the drug i various parts of the world Before reaching the decision th Government had taken the advice of the statutory advisor bodies, namely the standing medical advisory committees i England and Wales and in Scotland The Government ha however, been advised that it was not possible under th present law of this country to prohibit the manufacture heroin There was no similar legal obstacle in the way prohibiting the export and import of heroin, and the Gover ment had accordingly decided to prohibit entirely as fro Jan 1 exports of this drug to countries outside the Briti Islands, except for such small amounts as might be necessa for scientific purposes only, and all imports The Governme had decided to restrict the manufacture of heroin in th country to the quantities actually required for home medi consumption and scientific use

Mr HUGH GAITSKELL Is this a permanent decision abo manufacture? Was not a statement made by the Governme that they proposed to allow manufacture, though not expo for twelve months? Does this latest decision mean th manufacture is to be permanently permitted?—Major LLOY GEORGE The term of the licence is for twelve months in eve instance, although there is a clause which enables it to cut short Twelve months is the normal period of the licen The Government will not at present go beyond this per as the licence itself is valid for twelve months We are touch with the Medical Research Council to ascertain feasibility of developing the other substitutes

Public Health

Influenza in Glasgow

SEROLOGICAL evidence of infection by type-A influe virus has been obtained in 7 cases in Glasgow T illnesses began between Dec 14 and Dec 31 5 w cases of suspected influenza seen in general practi Two strains of type-A virus have been isolated fr infants with pneumonia

England and Wales in 1955

Provisional figures for England and Wales for 1 were recently published by the Registrar Gener The birth-rate was 15 0 per 1000 population, in 1 it was 15 2 and in 1953, 15 5 The death-rate was 11 7 1000 population, compared with 11 3 in 1954 and 11 1953 The infant-mortality rate of 24 9 per 1000 rel live births was the lowest annual rate ever recor in this country It compares with 25 4 in 1954, 26 1953, 27 6 in 1952, and 52 8 in 1938 The stillbi rate was 23 1 per 1000 total live and stillbirths, was lower than the rate for 1954 (23 5) but higher t the rates for 1953 (22 5) and 1952 (22 7)

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[1] *The Registrar General's Weekly Return for England and W for the week ended Jan 14 1956* H M Stationery O Pp 20 1s 3d

THE LANCET

LONDON SATURDAY, FEB 4, 1956

Guillebaud

WHETHER it pays publicly or privately, no nation can hope to have anything like a first-rate modern medical service without spending a great deal of money. Unfortunately the original estimates for the National Health Service were too low; and when, with prices rising, its cost seemed to be higher each year, the increase was widely attributed either to wastefulness or to unreasonable development. Alarmed lest this expenditure should get out of control, the Government in May, 1953, appointed the Guillebaud Committee, with ominous terms of reference: it was to advise how a rising charge on the Exchequer could be avoided while maintaining an "adequate" service, and to suggest means of ensuring "the most effective control and efficient use of such Exchequer funds as may be made available." Faced with these questions, such a committee might easily have sought quick and ruthless answers based on a superficial examination of the facts; but happily this was not the way of Mr GUILLEBAUD and his colleagues. Their eagerness to question and their readiness to listen have been exemplary; and the results of their methodical weighing of evidence are seen in the report now published, which takes up most of the controversial issues in the service, sets out the arguments on both sides, and concludes modestly with "our own view." Even if they had done nothing more, and made no constructive proposals, we could be grateful to them for providing, on so many subjects, the convenient starting-point for all further discussion.

But they have done much more. The review of N.H.S. expenditure made on their behalf by Prof. R. M. TITMUSS and Mr BRIAN ABEL-SMITH, PH.D., and described by the latter in our last issue, shows that costs, as realistically defined, have not in fact been soaring. Nobody would deny that, for various reasons, our medical services now employ far more people than they did before the war or even in 1947; but in terms of 1948–49 prices the net cost of the N.H.S. to public funds continued its initial rise only till 1950–51, and in the next two years it returned to approximately its level in its first full year (1949–50). In 1953–54 it was again a little higher; but, allowing for changes in the age structure of the population, the net cost per head at constant prices was still almost exactly the same as in 1949–50 (£8 15s. as against £8 12s.). During these years the national income rose, and the proportion of the gross national product used by the N.H.S. fell steadily from 3.80% in 1949–50 to 3.42% in 1953–54. "It may come as a surprise to many," the committee truly remark, "to find that the National Health Service has absorbed a decreasing proportion of the country's resources since the year 1949–50." Similarly, the proportion of national investment devoted to the N.H.S. has never reached 1%; and by 1953–54 it was down to 0.53%. In real terms capital expenditure on hospitals has averaged about a third of what it was before the war; and (though these figures are not strictly comparable) the ratio of capital to current expenditure on hospitals in England and Wales fell from 19.6% in 1938–39 to 4.1% in 1952–53—the corresponding figure in the U.S.A. in 1951 being 23.4%. The committee recommend that if possible £30 million a year should be found for the capital needs of the N.H.S. in the seven years after 1957–58 (how much will that be worth then?), and they emphasise the need to look after the buildings we have. Any suggestion that a low rate of capital expenditure has been suitable because the hospitals were in good condition on the appointed day can be rapidly dismissed. TITMUSS and ABEL-SMITH estimate that in England and Wales 45% were originally erected before 1891 and 21% before 1861. Though the running cost of the hospitals has increased progressively since the N.H.S. started, being nearly £30 million higher at 1948–49 prices, in 1953–54 than in 1948–49, they do more (and often better) work for a larger population. In the committee's view:

> "... the experience of the last seven years does not suggest that the organisation has failed to cope with its heavy responsibilities or to control with greater regard for economy than is commonly credited, the large sums of Exchequer money which have been devoted annually to the Health Service. As we have already pointed out, the annual capital allocations for the hospital service have, in our view, been inadequate, but there can be no doubt that the hospital authorities have made very good use of the limited sums made available to them. Any charge that there is widespread extravagance in the National Health Service, whether in respect of the spending of money or the use of manpower, is not borne out by our evidence."

For those of us who did not need this reassurance there is more interest, however, in the Guillebaud Committee's observations on the weaknesses of the service, on which they say:

> "It certainly should not be concluded that we have found the present organisation and administration of the National Health Service to be free from defects. In particular there is much need to integrate more closely the hospital, family practitioner and local health services, and also the welfare services provided by local authorities under the National Assistance Act. We also believe that the hospital service has been somewhat slow to adopt certain methods and techniques of management which have proved their worth in other large-scale undertakings, for example, in making adequate provision for the maintenance of capital assets, making full use of budgetary controls, devising the most economical means of purchasing supplies, making provision for a national recruitment and training scheme on the administrative side of the service, &c."

As may be gathered from this analysis, the remedies they propose are changes in practice rather than in principle. When they were first appointed they were told by witnesses that health could be restored to the service only by loosening controls—the control of the Treasury over the Ministries, of the Ministries over the regional boards, and of the boards over the management committees. At all levels, it was said, good work could be expected only if people were given responsibility for spending their own money and making their own mistakes. But not even for the sake of an entirely novel service are the committee prepared to recommend a change of Parliamentary practice that would give a Ministry, a board, or a committee money which would be theirs to keep if they did not spend it all. Correctly enough, they point out that all that Parliament gives is permission to spend up to a certain sum in a certain period, and they reject pleas both for block grants and for carrying over balances. On the other hand, in dismissing

Royal College of Physicians of London

At a comitia of the college held on Jan 26, with Sir Russell Brain, the president, in the chair, Dr G E S *Ward* was reappointed external examiner in medicine for the Faculty of Radiologists

The following, having *satisfied the censors'* board, were elected to the membership

Philippe Bauwens, L R C P T B Begg, M B Glasg, P F Benson M B *Lond*, C R Blagg M B Leeds, A M *Bradfield*, M B N Z, David Burman, M B Lond, P E *Conen* M B Lond J P H Davies, M B Lond, M F Dixon M B Lond, A M C Duffus, M B Aberd, J R E *Fraser*, M D Melb J R Golding, B M Oxfd, David Greenbaum, M B Lond, G H Hall M B Lond, *squadron-leader* R A F, H F *Hamilton*, M B Lond Joseph Hampson, M B *Edin* J F Hare, M B N Z, D L Hobson, M B Sydney, B R M Hurt M B Sydney, D E Hyams, M B Lond, I C Isdale, M B N Z, W I Kenyon, M B Glasg A H Kitchin, M B Edin, J E *Lennard Jones* M B *Camb*, R *G* Lewis M B Sydney, R D Lowe M B Camb, H M C Macaulay, M D Lond, Om Prakash Malhotra M B Punjab major A M C B L Marks, M D Melb J S Mitchell, M B Camb F R S, Guru Charan Mookerjee M B Calcutta, G H Neilson, M B *Queensland* K H Nickol, M B Lond, Celia M Oakley, M B Lond, J R Rees, M B Camb Imrich Sarkany, L R C P, Edulji Rustamji Sethna M B Bombay, F T *Shannon*, M B N Z, Man Mohan Singh, M B Madras, M D Sumerling, M B Leeds, P K Thomas, M B Lond, P A Zorab, M B *Lond*

Licences to practise were conferred upon the following who have passed the final examination of the Conjoint Board

Chimele Usuwa Abengowe, E S Ainsworth, Christos Angell, Simon Ardeman, Rosemary R *Ashby*, *J D* Atwell, Stanley Austin, J M Barnes, A T Battle, David Beasley, L C D Beregha, D W *Boyd*, K W Browne, Raymond Carlisle, Lawrence Cohen, F L *Cole*, J G *Cruickshank*, J B St C Cumberbatch, H J Davies, Anne C Doulton, P A S *Edmonds*, *Alan* Elsworth, G S Flack, Florence P Forsythe, A G Fraser G B Gasson, G L Goodwin, I D Green, R A Greenwood, P D Griffiths N D Gripper, Mary E Hargest R S Henderson, K T Hesketh, H H Hillman *C E A Holden*, A J Hosking, *J B Illingworth*, *K B Jeves* A J Jouhar, Donald King-Price, J W Kirkbride, D J Llewellyn, J A Lofting, B *C McDermott*, M B R Mackenzie, D M Maclaren, Gerald Maisel, P B Martin Ronald Marx, Joan A Menage, Sadredin Mesbah, D J Moorhouse J A Morgan N V Morgan Morkos Abdel Malak Morkos, G M Morris, A I E Nichini, N W Nicholson, D H G Ogg, Anezionwu Nwankwo Okoro G O Onnaguluchi, Pamela D Osborn, D A Packham D G Paskin R S Peachey, R L V Pearce B N Pickering *Iris C Platt*, *P W Quinn*, M C Rang, *F J Roberts R H Robinson Bryan* Scaife, I A Sewell, Malcolm Sharp M C Sharrard D E Side, J K Skinner, Leon Sloman, Mary Jane *Smal*, *M D B Stephens*, P J Stiles A R Tanser Elizabeth Taylor, R G *Thompson*, M S Tyrell A A P Vince Marguerite A M von Bergen, A C Whitmore, J H Williams, M J *Williams*, *D J Willsher*, F D Wilson, P J E Wilson, C D Wooding

The following diplomas, and those mentioned in our issue *of Jan 21 (p 169)*, were conferred jointly with the Royal College of Surgeons

D I H—D M Evans F P A Garton, E R Gauld, Eric James
D M R T—J E Dalby, Rafael Martinez
D P H—Irene F A Blakeney R S *Cooper M A Fernando*, Betty E Groves, G T B Mackinnell Childs J G P Power Sheila M Robinson Kwaafo Saakwa Mante, J A Tottle Matthias Zeville

Appointments

FOX J A M D Sheff, D P H asst chest physician, Wigan and Leigh hospitals and Wrightington Hospital
JONES *BARBARA*, M B *Birm* D OBST whole time asst pathologist, General Hospital, Nottingham
KELLY L M, M B E M B Lond M O, Ministry of Transport and Civil Aviation, Marine Crews division
POOLE, G H G, M B Lond, D OBST deputy M O H Walthamstow
TOTTLE J A, M B Lond, D P H asst county M O, West Herts *and St Albans division*

Appointed Factory Doctors

CROFT, STANLEY, M B Lpool Rufford Lancaster
JUDGE, J S, M B Glasg Johnstone, Renfrewshire
KIRKWOOD, J M, M B Glasg Cheadle, Staffordshire
MARSLAND, ALAN, M B Manc D L O Middleton, Lancaster

Birmingham Regional Hospital Board

COLLIER, HENRI M R C S, F F A R C S whole time consultant anæsthetist, Birmingham (Dudley Road) group
JEFFERSON, MICHAEL D M Oxfd, M R C P part time consultant neurologist S Warwickshire group
LEOH-LACHOWICZ Z S MED DIP Lwow D M R D part time *consultant* radiologist, West Bromwich and Wolverhampton groups

Colonial Appointments

ADDY, R F M B Wales M O northern region, Nigeria
HUTCHISON C F M B *Lond* assistant bacteriologist, Jamaica
JARDINE D E, M B Glasg M O, Tanganyika
MURPHY MICHAEL L R C P M O, Uganda
MURRAY, J G M, M B Edin M O, northern region, Nigeria
ROBERTSON P A, M B M O, Tanganyika
SIMPSON, E J B, M B Leeds M O, South Pacific health service Fiji
VON HALLER E M B Berlin M O Gold Coast

The London Hospital

At one of the London's series of clinical evenings for ge practitioners on Jan 25, the subjects were neurolog Sir Russell Brain, Dr R A *Henson* and Mr D W Northfield were the hosts

William Hyde Award

The Research Board for the Correlation of Medical Sc and *Physical Education* announce that *this* award has b given *this year to Dr Martin Herford for his studies of* mental and physical problems of young people leaving sc and entering industry

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On Feb 4 Dr R E Rewell is sailing for Madras where he has appointed a visiting professor under the Colombo *plan He is g to set up a postgraduate institute of gynæcological and pædi* pathology

Diary of the Week

FEB 5 TO 11

Monday, 6th

UNIVERSITY OF LONDON
5 30 P M (University College Gower Street, W C 1) K Alder (Cologne) Diene Synthesis
POSTGRADUATE MEDICAL SCHOOL, Ducane Road, *London* W 1
4 P M Colonel W R M Drew Recent Advances in Tro Medicine

Tuesday, 7th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S
5 P M Dr R S F Schilling Chronic Respiratory Disease Am Cotton and Other Textile Workers (First of two M *lectures*)
ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fi W C 2
3 45 P M Dr L M Franks Spread of Prostatic Cancer
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medi Keppel Street, W C 1) Dr J F Stokes Treatmen *Hepatic* Coma
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street W 1
8 P M *Pathology and Orthopædics* Mr A L Eyre Brook, Dr A Thomson, Mr R Barnes Dr H A Sissons Giant Tumour of Bone and Related Conditions
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P M Dr R Magnus Haines Gynæcological *Pathology*
INSTITUTE OF DERMATOLOGY, Lisle Street, W C 2
5 30 P M Prof J B Kinmonth Lymphatics, Œdema and Skin

Wednesday, 8th

UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical Medic Prof Boris Ephrussi (Paris) Nucleus and Cytoplas *Cellular Differentiation*
ROYAL SOCIETY OF MEDICINE
4 30 P M *Physical Medicine* Mr G T Hankey Mr C F Ball Dr G O Storey Affections of the Temporo mandib Joint
INSTITUTE OF DISEASES OF THE CHEST, Brompton, London, S
5 P M Dr J *Clifford* Hoyle Duration of Anti tubercul Treatment
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Histopathology of Mycotic Di
ST MARYLEBONE HOSPITAL FOR PSYCHIATRY AND CHILD GUID 48, Cosway Street N W 1
5 P M Dr W E R Mons Panics and Fears
NOTTINGHAM MEDICO CHIRURGICAL SOCIETY, 64, St James's Str Nottingham
8 30 P M Air Vice Marshal F E Lipscomb Medicine in Royal Air Force
ROYAL FACULTY OF PHYSICIANS AND SURGEONS 242, St Vinc Street, Glasgow, C 2
5 P M Dr H R MacLennan Present day Trends in Gynæcol in Britain and in the United States

Thursday, 9th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P M Dr Schilling Chronic Respiratory Disease Among Cot and Other Textile Workers (Second of two M lectures)
ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Mr Ashton Miller Diverticulum of the Bladder
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M *(London School of Hygiene* and Tropical Medic Lord Rothschild F R S Fertilisation
INSTITUTE OF DERMATOLOGY
5 30 P M Dr A Herxheimer *Physical* Urticarias and Der graphism.
UNIVERSITY OF ST ANDREWS
5 P M (Queen's College, Dundee) Prof B McFarland C genital Dislocation *of* the Hip

Friday, 10th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr Peter Kerley Tumours in the Chest
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Ro W C 1
3 30 P M Mr Maxwell Ellis Nasal Catarrh
INSTITUTE OF DERMATOLOGY
5 30 P M Dr P F Borrie Leg Ulcers

Annotations

PRINTING OF THE LANCET

THIS issue of our journal has been truncated at a late stage in its development, and we have reluctantly had to omit many letters and other contributions intended for immediate publication At the time of going to press we do not know what developments are likely in the present dispute in the printing trade We can do no more than assure readers, contributors, and advertisers that we shall try to produce each week at least a token issue, and if this cannot be printed in more than token numbers we shall send copies later to all subscribers Publication of normal issues will of course be resumed as soon as possible

INTRACRANIAL BRUITS

AUSCULTATION of the skull is often omitted from a neurological examination, but Mackenzie,[1] in a recent account of intracranial bruits, has drawn attention to the importance of this method of examination Travers,[2] in 1809–11, appears to have been the first to record an intracranial bruit, in a patient who in all probability had a carotico-cavernous fistula, and some years later Fisher[3,4] made a number of observations on the "cephalic bellows sound" He found this sign in children with chronic hydrocephalus and congestion, acute inflammation, and compression of the brain, and he thought the bruit resulted from impediment to the free passage of blood through the basal arteries as they were compressed by the diseased brain against the bony channels in which they ran In 1843 Whitney[5] noted a bruit in an adult with an aneurysm of the basilar artery, and in 1898 Hoffman[6] made the first presumptive diagnosis of an intracranial angioma when he heard an intracranial bruit in a patient with a spastic left hemiparesis

An intracranial bruit may be hard to hear, and it should be listened for in quiet surroundings, which are often difficult to find in an outpatient department It is often heard best over one or other eyeball, but auscultation should also be carried out over the temporal fossæ and the mastoid processes The condition most commonly associated with an intracranial bruit (sometimes a very loud one) is a carotico-cavernous fistula, usually the result of trauma but sometimes due to spontaneous rupture of a carotid aneurysm into the cavernous sinus A bruit can be heard in some intracranial angiomas, and it is perhaps in this condition that careful auscultation of the head is of most value The proportion of these patients in whom a bruit has been heard varies in different series Tonnis[7] recorded it in only 4 out of 22 patients, but Mackenzie,[8] in a previous study of 48 patients with intracranial angiomas proved by arteriography, recorded a bruit in 24 He made the interesting observation that a bruit was heard in 65% of the patients in whom the presenting symptoms were epilepsy, periodic headaches, or a hemiparesis while it was uncommon in patients whose initial symptoms were a subarachnoid or intracranial hæmorrhage The importance of listening for a bruit is emphasised by 2 case-records given by Mackenzie A patient aged 23 had had minor epileptic attacks for seven years and 2 major attacks in the fifteen months before she was seen at hospital, the only focal feature about the attacks being a transient aphasia at the onset a bruit heard over the left eyeball indicated carotid angiography and this showed an angioma in and around the left Sylvian fissure Another patient had begun to have attacks of migraine at the age of 12 the visual aura was always on the right and the headache on the left At the age of 26 she had a persistent defect in the right lower quadrant of the visual field At 41 a bruit was heard over the left eyeball and left mastoid process, and arteriography showed a large left occipital angioma

Mackenzie records the rare occurrence of a bruit with a non-communicating intracranial aneurysm, a frontal meningioma and a glomus-jugulare tumour, and for a short time in a patient with occlusion of the internal carotid artery The occasional presence of a bruit in children with raised intracranial pressure is well recognised, and Mackenzie mentions 2 cases of this kind, in 1 the pressure was raised by a pineal tumour and in the other by cerebral thrombophlebitis He emphasises that an intracranial bruit may at times be heard without any other indication of an intracranial lesion, and that the presence of a bruit does not in itself warrant further investigation He refers to a patient in whom a bruit apparently due to a moderately severe anæmia disappeared when the anæmia was corrected Another unpublished observation is in keeping with this, a physician who had had two large gastro intestinal hæmorrhages heard a noise in his left ear which was synchronous with the pulse and which stopped completely on carotid compression, the noise disappeared when the anæmia was corrected by blood-transfusion Although it is not known whether this noise could be heard by an outside observer the patient described it as having the characteristics of an intracranial bruit, a sound with which he was familiar.

The site of origin of an intracranial bruit is usually considered to be the arteriovenous communication which occurs in carotico cavernous aneurysms and many intracranial angiomas but Mackenzie suggests that another mechanism may be important in some cases With intracranial vascular abnormalities there may be increased blood flow through the carotid or vertebral arteries, and he suggests that, particularly in the carotid, there may be a relative stenosis where the artery enters the intracranial cavity This may be the origin of the bruit, and it would explain why it may be heard most easily over the eyeball A similar mechanism of relative stenosis of the basal arteries would explain the bruit in children with raised intracranial pressure—the explanation originally suggested by Fisher in 1838

ACUTE HÆMORRHAGIC LEUCOENCEPHALITIS

ALTHOUGH Wernicke's disease and brain purpura[1] were early differentiated from the many cases of hæmorrhagic encephalitis described during the past eighty years, it is only comparatively recently that further subdivision has been possible Necrotising hæmorrhagic encephalitis[2] and acute hæmorrhagic leucoencephalitis[3] are now usually recognised as distinct entities, although Adams and Kublik[4] maintain that they are a single disease All 16 recorded cases of acute hæmorrhagic leucoencephalitis show a similar pathological picture characterised by severe vascular damage, with fibrin impregnation of the walls of venules, capillary disruption, multiple hæmorrhages of ring and ball types, perivascular necrosis, pronounced leucocytic infiltration, widespread focal and perivascular demyelination, and a microglial reaction

A lead to the understanding of the ætiology of hæmorrhagic leucoencephalitis was given by Russell[5] when she pointed out its similarity to acute disseminated encephalomyelitis and produced evidence suggesting an allergic basis for both conditions Lander[6] records the case of a 36-year old man who had hæmorrhagic varicella ; on the fifth day of the disease he lapsed into coma and he died four days later Necropsy revealed the typical features of

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1 Mackenzie I *Brain* 1955 78 350
2 Travers B *Med-chir Trans* 1809–11 2 1
3 Fisher J D *Med Mag Boston* 1834 2 144
4 Fisher J D *Amer J med Sci* 1838 22 277
5 Whitney S S *Ibid* 1843 6 281
6 Hoffman J *Münch. med Wschr* 1898, 2 1159
7 Tonnis W Quoted by Mackenzie
8 Mackenzie I. *Brain* 1953 76 184

1 Schmidt M B *Beit path. Anat* 1905 7 419
2 Baker A B *Amer J Path* 1935 11 185
3 Hurst E W *Med J Aust* 1941 ii 1
4 Adams R D Kublik, C S *Amer J Med* 1952 12 510
5 Russell, D S *Brain* 1955 78 369, see *Lancet*, 1955, ii, 1282
6 Lander H *J Path Bact* 1955, 70 157

entertain today about this complicated and fascinating problem The man on the bridge between basic research and clinical practice whom I select for this purpose must inevitably bear a certain resemblance to myself, his views will therefore be not a little confused by the fact that I am normally to be found as busily engaged in the direct clinical application of a specialised technique as most of the others on one side of his bridge and at least as biased and full of foibles as the rest This pontine figure of my imagination should look impartially and hopefully to either side, but since his own state of mind is necessarily temporary and subject to change, and since, though most parts of it may be sympathetically regarded from one side or the other, the whole is likely to appear curiously misshapen from both, he should not always expect such tolerance in return It is important that he should have a flexible, sensible, and general view against which he can test the claims that are made and into which he may either fit new knowledge or use it to change his outlook For the rest of my address I shall be attempting to see the cancer problem and some of the people engaged on it as they might appear today from this precarious viewpoint

To my selected middle man, cancer is a human disease process which has only been defined in terms of behaviour He knows that each doctor decides for himself what number and what degree of several abnormal behaviour patterns he will accept in each particular patient before he attaches the diagnosis He sees the mistakes that are made from time to time in this assessment, to the pride and profit of quacks on the one hand, and to the dismay and frustration of clinicians on the other He recognises that growth may be excessive or invasive, or even perhaps metastasising, and still be benign, that a tumour may be a malformation or a neoplasm or neither or both, that the degree of malignancy of undoubted cancers may so vary that one may be far more easily curable than many other diseases and another so catastrophic that the patient disintegrates before our eyes A tumour may progress through every borderline stage in each one of its behaviour characteristics after another and, if hormone dependent or conditional, may still retain this property long after dissemination has occurred or lose it at any time during this progression The process may start in many cells at about the same time in one localised area, in one organ, or in scattered homologous tissue in different parts of the body The distribution of cancer throughout the animal kingdom, the rather similar changes which take place in plants, and the involvement at times of almost every tissue in the human body, suggests to him strongly that this behaviour pattern must be something fundamental biologically The different factors which incite and promote this change in behaviour, the long latent periods which occur, the widely different degrees of growth potential revealed, and the similarity of average age at diagnosis despite a widely different incidence in those exposed and those not exposed to some carcinogenic agents, all seem to favour a balance between growth and growth restraint which weakens sharply with advancing years The fact that so many different stimuli—both internal and external to the cell—can provoke this change in behaviour and that they are not always, or even usually, necessary for its continuance, seems to indicate that the capacity for unlimited growth which is expressed must reside within the cell itself

To him, however, it is an assumption to conclude that this capacity must therefore be unusual, peculiar to the cancer cell, or necessarily due to some special, specific change within it There seems to be little evidence that chemical or structural changes have yet been found in cancer cells which are not present in normal cells in different stages of embryological development and differentiation Unlimited growth potential holds for unicellular organisms, it has to be shown that it does not do so for the multicellular A fragment of chick embryo, doubling its original size every forty-eight hours, has, we are told, been growing in culture for nearly as many years The fundamental behaviour pattern which expresses a capacity for unlimited self reproduction seems no less than life itself There does not appear to be any obvious reason, beyond man's wish to find it, why there should be some special growth potential within the cancer cell thought to be evil which is any different from or any more or less mysterious than that already existing in all living things and thought to be good He suspects the introduction of a value judgment into an exercise devoted to the understanding of a phenomenon of Nature

The emergence of new qualities from increasing complexity of structure is another fundamental biological property which seems to him to be relevant New qualities not present in the various parts which go to make some new whole nevertheless arise from their combination The nuclear physicist's world of fundamental particles is free of quality, while the sphere of the biologist is packed full of them in glorious and confusing abundance An electron is not hard or red or beautiful but, with other particles equally lacking in these qualities, goes to make structures which may appear to be all three Similarly the adding together of cells in a pattern to make an organism produces new qualities which are not inherent in the cells themselves One of the most necessary qualities for survival which must arise is organisation As evolution, by producing increasing complexity, has allowed the development of more and more qualities, so it has demanded and selected better and better organisation

Each cell in the human body, being produced by mitosis as a direct descendant of the original fertilised ovum, carries within it all the inherited potentialities to which the individual is heir These cells do not remain alike, however, most of them by differentiation become type specific, giving up some of their inherited potentialities for expression in growth and form while acquiring specialisation in function

The processes of asexual reproduction, of regeneration and wound healing, and of neoplasia have much in common Some dedifferentiation followed by cell immigration and an increase in mitosis are usual Dedifferentiation is a necessary preliminary to regeneration and, even in tissue-culture, cells normally dedifferentiate to some extent before they begin to divide With controlled regeneration, mitotic-rate and degree of differentiation are inversely related—that is, mitotic rate decreases as differentiation increases—the process being organised, with tumour formation, mitosis is directly related to the degree of dedifferentiation first achieved, but it tends to be maintained at this rate since differentiation fails to return again, the process being disorganised

It is this failure of organisation which appears to be the fundamental factor in neoplasia, distinguishing it from agamic reproduction and regeneration Multifocal origin, variation in degree of change in several behaviour characteristics, progression in those changes, and conditional growth, all seem to be more easily understandable in terms of progressive relaxation of different controls and of cell reversion by varying steps of dedifferentiation to the reassertion of an inherent independence and individuality The multiplicity of causes of relaxation of control and the continuance of the new behaviour pattern, even when inciting factors have ceased to operate, also seem easier to accept on this basis To this middle man, any special intracellular evil, be it mutation, virus, special disorder of nucleic acid metabolism, or any other unnatural agent which increases cellular activity or damages its controlling that multiplication of the souring organisms will check the increase of staphylococci either by competition for nourishment or by the production of some inhibitory substance, such as nisin Perhaps raw milk contains sufficient staphylococcal enterotoxin to produce symptoms only when by some uncommon chance the staphylococci have had a flying start in the multiplication race

Whatever the theoretical dangers, common experience suggests that the milk, raw or pasteurised, which passes through the normal channels of commerce is almost free from risk For this reason eight large outbreaks of food poisoning within a month, all due beyond doubt to reconstituted spray dried milk supplied to its schools by one local authority, gave rise to some alarm [2] While no pathogenic bacteria could be isolated from any of the victims of these accidents, *Staph aureus* (phage-type 42E/53W) was found in all the suspected batches of milk-powder, which were all from one maker Serial examination of the daily batches from this factory showed staphylococci in almost every sample in numbers which varied widely from day to day but which seemed to reach a maximum in the early summer Spray dried milk-powder from other makers showed, with one exception, far lower figures throughout the year Roller dried milk showed no staphylococci at all Since, however, the milk which caused gastro enteritis was drunk within four hours of being reconstituted (a time too short for bacterial multiplication), it was clear that the staphylococci in the powder were by themselves insufficient to account for the effects produced The powder must have contained a large amount of enterotoxin, probably produced at some stage in manufacture and surviving the process of drying

The spray-drying of milk consists essentially of pasteurisation, evaporation to about one third of the original volume, and drying by injection of a fine spray into a current of air at 320°F The raw milk before processing contained many staphylococci, but because it was kept chilled at 40°F it was unlikely to be the source of enterotoxin Laboratory tests confirmed the expectation that few bacteria survived pasteurisation and evaporation Between this stage and drying, it is customary to run the milk through a balance tank which eliminates fluctuations in the flow to the drier At the beginning of the working day, the bacterial content of the milk in this tank was negligible, but within a few hours it rose as high as 100 million organisms per g, and staphylococci were almost invariably present Drying reduced the numbers of bacteria but did not kill them all Since staphylococcal enterotoxin will withstand boiling for several minutes its potency was probably little altered by this last stage in the process

The balance tank in such a plant offers unusual opportunities for bacterial multiplication The evaporated milk is warm It tends to deposit a sludge which can be removed only at the end of the day and which offers excellent pabulum to bacteria as well as slowing the flow through the tank It is less clear how it becomes infected It may be by aerial contamination More probably some sin of omission in the daily cleaning or the working of the pasteuriser allows the entry of a few staphylococci which can then multiply indefinitely It may or may not be important that staphylococci were most abundant in the milk dried in early summer, which is the time when the largest volume of liquid milk reaches the factories and when, in consequence, the drying plant works a longer stint than usual The longer the run, the greater the likelihood of bacterial multiplication to dangerous levels in the balance tank

It would be unwise to make too much of the risks revealed by these accurate and elegant investigations Many hundreds of gallons of reconstituted spray-dried milk are given to children, and the recorded accidents are less than a dozen The practical measures to prevent such accidents in the future must remain the responsibility of those who dry the milk It is probable that small changes in design or operation will do all that is necessary The detection of staphylococcal enterotoxin is impracticable as a routine measure, and we must rely substantially on the good sense of the manufacturers

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[2] Anderson P H R Stone D M *J Hyg Camb* 1955 53 387

ŒSOPHAGITIS

ŒSOPHAGITIS has aroused interest because of its association with hiatus hernia, and the two conditions have become so closely linked in our minds that we may be misled into believing that œsophagitis is always associated with gastric hernia, and Lodge [1] has shown this is not so There is the question of cart and horse, for œsophagitis, leading to shortening of the œsophagus, can draw the stomach up into the thorax, and it may be hard to decide in a late case whether hernia preceded œsophagitis or vice versa Peters [2] has studied 116 cases of œsophagitis selected from 20,000 necropsies, slight and doubtful lesions and those not due to peptic digestion were excluded After analysing the clinical and pathological records, he found that, though the causes were often multiple, in 66 3% the trouble was largely due to factors outside the cardia or hiatus which upset the mechanism responsible for closure of the cardia Repeated vomiting (from pyloric stenosis or pregnancy, for example) and increased intra abdominal pressure (from such causes as obesity, ascites, and pregnancy[3]) may be the start of persistent inflammation Acquired hiatus hernia and congenital enlargement of the hiatus accounted for another 20 3% of cases These observations are important surgically since they emphasise that correction of the hiatus hernia will not necessarily relieve an associated œsophagitis

From the Mayo Clinic, Schmidt [4] gives warning against operations involving the cardia, such as œsophago gastrostomy for cardiospasm or stricture, or a similar anastomosis following excision of a lower œsophageal growth, for œsophageal ulceration ensues in a high proportion of cases Experience at the Lahey Clinic [5] has also shown that resection of the lower œsophagus and cardia for chronic œsophageal stricture, or for megaœsophagus, is disappointing because of subsequent recurrent ulceration, an associated operation to drain the stomach, such as pyloroplasty or gastrojejunostomy has been advised Nevertheless, Neuman and Ellis [6] have shown experimentally that these operations do not reduce the incidence of œsophagitis after œsophagogastrostomy in dogs, and that the condition can be controlled only when the acid-bearing area of the stomach is removed by pylorectomy Thus, Wells and Johnston [3] recognising the failures after repair of hiatus hernia undertaken to relieve symptoms of associated œsophagitis, have performed partial gastrectomy not only to ensure drainage away from an incompetent cardia but also to reduce gastric secretion This procedure defeated its ends in 2 of their patients, for œsophagitis persisted because of the regurgitation of bile, and they now also divert the duodenal secretions with a Roux-en Y anastomosis Whether this technique will introduce further complications, such as anastomotic or jejunal ulceration (as the vagus nerves are also divided, this may be avoided) or steatorrhœa, remains to be seen, Wells and Johnston have met no such difficulties in 12 patients treated so far Their method seems to be a reasonable surgical answer to the otherwise intractable problems of œsophagitis without hiatus hernia and the shortened œsophagus which prevents the reduction of a hiatus hernia

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1 Lodge K V *J Path Bact* 1955 69, 17
2 Peters, P M *Thorax* 1955 10 269
3 Wells C, Johnston J H *Lancet* 1955, i 937
4 Schmidt H W *Arch intern Med* 1955, 96, 717
5 Boyd D P *Ibid* p 724
6 Neuman, H W Ellis, F H *J thorac Surg* 1954, 28, 201

confident They are well aware of the importance of asking the right questions if they are to expect reasonable answers, and in their own fields are unlikely to be caught in this old trap for long In the wider, unfamiliar sphere of cancer to which they bring their special knowledge and skills, however, they too often appear to accept the basic questions put without the same critical inquiry It may be that the worthy, emotional, but unscientific appeal of becoming a public benefactor, or at least of sharing in such benefaction, attracted some of them from the start, so that they entered on their work with an element of prejudgment on questions of discoverable cause and cure which prevented them at the start from stopping to examine these fundamental propositions too closely They are entitled to study whatever aspect of the subject they may choose to follow—this is the privilege of their calling—but much of what they study does not seem to bear much resemblance to what we hoped they had set out to study There are many of them who have become so fundamental that they appear to be looking for a cause of something which seems to be life and for a cure of something which seems to be the second law of thermodynamics

The vast effort which he sees on this side of him is, under the guise of cancer research, mostly directed towards unravelling the basic mysteries of life and living It could hardly have a more worthy object, it demands our increased support That so much basic biological work should be financed through its cancer relationship may possibly be a mistake, however, since this may have tied it too closely to the demand for an answer to a specific problem which has not even been properly set Cancer research achievements have been great, they are only underrated because they have supplied no simple solutions to the questions of cause and cure of the disease process to which they are officially dedicated Judged, as they should be, on their own merits, they are seen to have made important contributions to an immense range of scientific inquiry which is in itself a fascinating story The twin compulsions of an emotional desire to rid mankind of a killing disease and the constant demand for answers from those who provide the money do seem, however, to have had some ill effect on cancer research A few workers have rashly abandoned their privileged seclusion at times to announce in public that they are on the trail and that a capture may shortly be expected The almost hysterical note to be heard in some demands for cancer-research expansion, carrying an implied threat that if they are not met the public cannot expect the solution in a reasonable time, has not always been confined to the administrators This unhealthy and unscientific atmosphere for the quiet pursuit of fundamental knowledge may not be widespread but there is enough of it to be clearly seen The middle-man may well feel that another look at the proposition that there is no single simple solution, no specific intracellular evil, and no universal cure for them to discover might blow this mist away What he wants from these research workers is knowledge about the fundamentals of life and living, of biological organisation and disorganisation, and an understanding of growth, development, and decay They may take their time, they have all the time there is Each new discovery is a welcome gain in knowledge They should be content with this, their proper heritage in cancer research as in other fields, the responsibility for the application of their work is not really theirs If they feel an obligation to produce results which both please the public and advance the cause of science, the middle man wonders why they do not more often help to put a few extra people on his bridge

Clinical Cancer Work

To the other side of the bridge as he looks towards the clinical cancer workers, he sees quite another scene Here is no group diverse in training and devoted to a single aim, but the whole of medicine Doctors with much the same basic training in fact but of whom few are primarily engaged in cancer work though most of them have regular and direct contact with it It is perhaps surprising how few doctors are deeply and daily concerned with a large range of cancer patients Those surgeon whose interests have centred on one part of the body, and who have acquired by long experience special skill in dealing with malignant disease at this site, are primarily concerned with the advance of their specialty and have not often paid much attention to more general cancer problems This trend has been of the greatest value in diagnosis, in studying the natural history of the disease, and in local treatment, but, as a result, it has been left to comparatively few surgeons to take an active interest in the whole wide field

The situation is temporarily rather different for the radiotherapists They see more patients with a far greater variety of tumours than any of their colleagues, and a bigger proportion of those they see have advanced disease Specialisation is now developing within the larger radiotherapy departments, for the very same good reasons which led to specialisation in surgery in the past Cooperation in special clinics between surgeons and radiotherapists with similar interests has greatly improved the quality of the treatment given but emphasises still further the need for clinicians with a wider research interest in this whole process of disordered growth

Our middle man recognises that it does not seem very important to some people that physicians and surgeons concerned with cancer should have any very profound knowledge of this disease process The steady fall in the incidence of mouth cancer which has followed better dental care and a decline in pipe smoking, the dramatic change in diagnosis of lung cancer and the improvement in results of treatment of testicular tumours, are random examples of advances which have not been dependent on any very fundamental understanding of growth and organisation Nevertheless he feels that a change of outlook on this great medical and social problem by doctors might have important consequences

One thousand eight hundred years ago Galen classified tumours as being according to nature, exceeding nature, and contrary to nature, and a better division of this fluctuation in growth and control, if nature in this context means organisation, has not since been made One hundred and eighty years ago Percivall Pott described occupational cancer, carcinogenesis, the curability of localised tumours, the importance of factors outside the tumour, and the disappointments of palliative treatment He wrote

> "The disease, in these people, seems to derive its origin from a lodgment of soot in the rugæ of the scrotum, and at first not to be a disease of the habit In other cases of a cancerous nature, in which the habit is too frequently concerned, we have not often so fair a prospect of success by the removal of the distempered part, and are obliged to be content with means, which I wish I could say were truly palliative"

Although the carcinogenic hydrocarbons have since been discovered and an immense amount of work has been done on relative potencies of tumour inciting and promoting agents, there have only recently been signs of a real advance in understanding The simple view that the whole trouble lies in a specific evil within the cell resulting in its autonomy, which has become so widespread, threw the emphasis away from medicine and on to the chemist and the cytologist The result has been that ideas no longer flow as easily as they should from clinical to basic research interests Too many research workers feel that the clinician has nothing more of interest to say since he knows little of intracellular mechanisms, and too many clinicians feel that

Prior Approval of Expenditure.—At present regional boards and boards of governors have to seek approval from the Health Departments for capital works costing more than £10,000, and the Health Departments approval from the Treasury for capital works costing more than £30,000. These limits should be raised to £50,000 and £100,000 respectively.

Appointment of Staff and Establishments.—The existing controls over the appointment of consultants and junior hospital medical staff in England and Wales should be retained, but the controls over other categories of staffing establishments should be relaxed as far and as fast as possible. The hospital authorities should themselves regularly review their establishments. There were reasons why in the early years the Ministry should send out its own establishment review teams; but henceforth, responsibility for ensuring economy in the use of hospital staff should remain fairly and squarely with the regional hospital boards and boards of governors—with the proviso that the Boards must seek the authority of the Ministry for any additional consultant appointments.

Medical Consultation at Regional Level

The committee have little doubt that the medical profession would welcome the appointment of statutory medical advisory councils in all regions; but they see objections. Taking these together there is sufficient weight in them to deter the committee from recommending the establishment of statutory medical advisory councils for all regional hospital boards. But they urge all boards to review their arrangements for joint consultation with the medical profession, and to consider whether medical consultative committees could with advantage be set up at regional level to ensure that decisions on medical matters of wide general import are not taken without proper consultation with those who will be affected.

Circulars

The committee do no more than recommend that the Health Departments should keep the number of directions to a minimum.

They do not ask the Ministry to adopt the Scottish practice and in future issue circulars only to regional boards and boards of governors—never direct to management committees. They think this would put the regional boards to a lot of unnecessary work which would increase the cost of the service without necessarily increasing its efficiency.

Regions and Groups

Any extensive rearrangement of regional boundaries, or the creation of new regions would, it is felt, be wasteful and undesirable.

As for hospital groupings, the committee would like the larger groups to be broken down. Where this cannot be done, the management committee should delegate more responsibility to the hospital secretaries in the group, or should strengthen the position of some of its house committees. This, however, should be quite exceptional. House committees are doing excellent work; but in the ideal hospital group there is insufficient room for two bodies (management committee and house committee) with executive and spending powers.

The committee think it preferable for mental hospitals and mental-deficiency institutions to be managed separately and not in combination with one or more general hospitals.

Committee Work

There is a real danger of the administrative side of the N.H.S. getting bogged down in a morass of committees. Any unnecessary committee work is an unmixed evil.

> "Accordingly we recommend that all Management Committees and Boards of Management should now review their arrangements with the aim of simplifying their committee structure and reducing the volume of work, for example, by increased delegation of authority to responsible administrative officers. We are confident that this delegation would be facilitated if the hospital secretary were given a higher status in hospital administration and if the post of hospital secretary were to become a normal starting point to a hospital administrative career at group or regional level."

Appointment of Boards

The committee hold that the Health Minister must reserve the sole right to decide who shall be appointed to the regional boards. He could not accept an arrangement which would bind him to accept the nominations of the outside bodies concerned.

Medical Membership of Boards and Committees

Should doctors serve on administrative bodies? The committee are against exclusion of doctors. But they were surprised to find that in one board the proportion of medical members has reached 42%, and they think that, *unless circumstances are quite unusual, it should not exceed 25%*.

Current Expenditure

Rewards for Efficient and Economical Management.—Direct financial rewards for underspendings could not be made to one management committee in a region without injustice to others which have budgeted closely and spent up to the limit of their estimates.

Block Grants.—The weight of argument is against the adoption of block grants to meet current expenditure in the hospital service. The analogy with quinquennial grants to universities is not really a valid one, because universities have important revenues of their own and their grants are truly grants-in aid. Moreover there is a big difference in scale between £25 million a year for universities and £320 million for hospitals.

Unspent Balances.—It has often been argued that, to encourage them in economy, hospitals should be allowed to carry forward their unspent balances. But the committee agree with the Select Committee on Estimates (1950–51) when it said:

> "... the amount of money included in a year's estimates of a hospital authority was not the year's income of that authority, but was merely the limit of permission to spend. When a saving has been made on an estimate it generally means that the authority has found itself able to provide the service in question at a lower cost than was allowed for in the estimate; it follows that the Ministry ought not, in the absence of some special reason, to approve an estimate in the following year for the same purpose and of the same size as before."

Capital Expenditure

"Having regard to the advanced degree of obsolescence of many hospitals in this country, and to the very large arrears of capital expenditure resulting from the virtual cessation of hospital building since 1938," the committee suggest £30 million a year as a desirable rate of capital expenditure at which to aim over the seven years succeeding 1957–58. Of this £30 million some 10% should be used specifically for revenue saving schemes.

The maintenance of assets is of great importance, and regional boards should be responsible for ensuring that the fabric of the hospitals in their region is being suitably maintained.

Block Grants and Carry over of Balances.—The arguments for these are not deemed strong enough to warrant a recommendation involving a revolutionary change in Government finance. The committee welcome the innovation whereby the Health Minister recently announced probable capital allocations for three years ahead.

Hospital Costing

Costing systems should be regarded not as a means of imposing restrictions but as a means of ensuring that the best value is obtained for money spent. The committee think that departmental costing should be started they had peripheral vascular disease and that their presenting symptom was *intermittent claudication* Since dilatal stimulates gastric secretion, patients with peptic ulcers were excluded, and, as the makers suggest that it is unwise to give dilatal to patients with angina or with hyperthyroidism, these too were excluded Instead of using a random distribution table to select those who should have the active drug and those who should have inactive placebo tablets, it was decided, in consultation with a statistician, first to divide the patients into separate groups according to the nature of any previous treatment Three groups according to previous treatment were required

(1) Those patients who had had no previous treatment for their intermittent claudication

(2) Those who had been given tolazoline hydrochloride ('Priscol')

(3) Those who had been treated by sympathectomy

Each member in each group was then paired off with a patient of similar age in the same group One member of each pair was given the active drug and the other the placebo The patients were unaware of the activity of the preparation with which they were supplied 2 of the patients taking the placebo tablets had to be dropped from the trial because of illnesses unrelated to their peripheral vascular disease Thus 50 patients completed the trial, 26 of them taking dilatal and 24 acting as controls Various tests were applied to individual legs Since 1 of the patients taking dilatal was an amputee, the reported results refer to 51 legs in the trial group and 48 legs in the controls

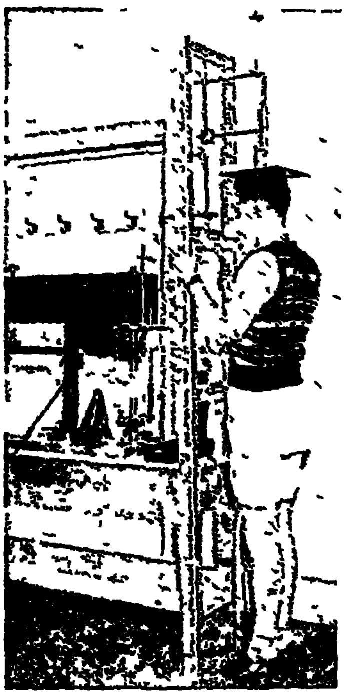

Fig 1—Patient ready to perform exercise test

Each patient made two visits to hospital for the purpose of this trial On the first visit, after being subjected to the various tests described below, the patient was given a tablet of the drug or of the placebo according to whether he was selected for the trial or for the control series, and was observed for half an hour In this way it was possible to ensure that no patient who was going to take dilatal was hypersensitive to it In fact, none of the patients showed hypersensitivity to dilatal The patients were given a supply of tablets to last 9 weeks, together with instructions for taking them At some time between the 8th and 9th week the patient made his second visit to hospital, where he was subjected to the various tests for a second time and asked to state whether in his opinion the course of tablets had made him better, not affected him, or made him worse If in the patient's opinion he was better he was asked to estimate the increase in his walking distance

Acute Clinical Experiments

In 12 patients the immediate effect of dilatal on the blood-flow in the calf muscles at rest was observed The patient rested supine on a couch At the end of about half an hour, when a basal rate of blood flow in both legs had been established, dilatal was given, and the subsequent calf-muscle blood-flow rates were observed every 15 minutes for 2 hours In these tests different doses of dilatal were used, 6 patients received 2 5 mg by mouth, 3 patients 5 mg by mouth, and 3 patients 5 mg intramuscularly

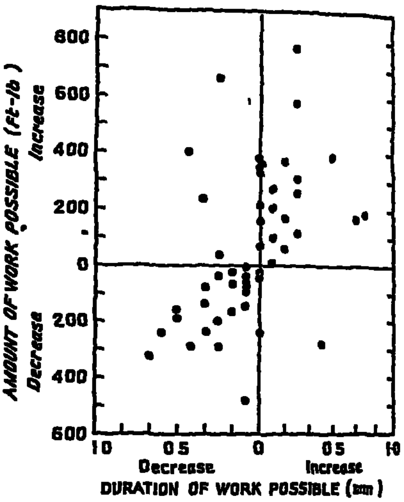

Fig 2—Change in amount and duration of work possible by each leg separately after course of dilatal

Experimental Detail

Muscle blood flow measurements were made with a mercury-in rubber strain-gauge type of plethysmograph similar to that described by Whitney (1953) This was applied to the calf, and the observed flows (calculated as ml per 100 g per min) assumed to represent muscle blood-flow (Grant and Pearson 1938) Venous occlusion was secured by inflation of 7-in wide rubber cuffs incorporated in the legs of a specially made pair of "*shorts*"

The exercise test was made both before and after the 8-week course of either the drug or the placebo On arrival at the clinical laboratory the patient was weighed and prepared for the test by fitting on him the necessary pieces of apparatus A rest of an hour was allowed, during which the patient sat at ease on a chair He next stood up and steadied himself by holding on to the two vertical uprights seen in fig 1 His left leg was tested first As soon as a steady resting blood-flow could be observed, the patient was asked to lift the leg not under test clear of the ground by flexing the knee on that side, and then to raise his body up on to the toes of the side being investigated and down again in time with a metronome (each cycle being timed to last 2 sec) Care was taken that the patient did not assist himself by using his arms He continued to go up and down on his toes in time with the metronome until either the pain of intermittent claudication became so severe that he could do no more or until he had exercised for 2 minutes Immediately the period of exercise stopped, the patient stood still with both feet on the ground The blood-flow was measured from immediately after the exercise until reactive hyperæmia had passed After a rest of 5 minutes the right leg was tested in a similar way

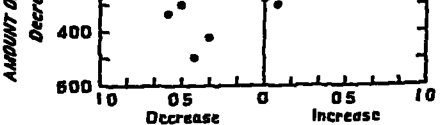

Fig 3—Change in amount and duration of work possible by each leg separately after course of placebo

They doubt whether the work of the Dental Estimates Boards could be done in ways less expensive in money or man-power.

A Comprehensive Hospital Eye Service?

There is certainly scope for some further development of the hospital eye service, but the weight of evidence is against abolishing the supplementary ophthalmic service and substituting a comprehensive hospital service.

Charges to Patients

The committee's rejection of a boarding charge for hospital patients has already been mentioned. Similarly in the practitioner and local-authority services they do not advocate new charges. (Miss Godwin would abolish existing charges.)

Charges for Dentures.—The present charges should be retained so long as there are not enough dentists to meet potential demands.

Charges for Dental Treatment.—These seem to be impeding a number of people from using the general dental service, and the reduction of their incidence should have the highest priority when resources become available. Meanwhile the committee strongly favour the proposal that if financial conditions permit, "the dental treatment charge should be refunded to patients who have received comprehensive treatment, been made dentally fit, and have sought treatment within a specified period of time (say, once every 12 months)." This would enable people to contract (as it were) into a free service and would make an effective contribution to prevention.

Charges for Spectacles.—It seems that these form a barrier to a proportion of the people who need to make use of the service, and priority (second only to adjustment of the dental treatment charge) should be given to a substantial reduction.

The Shilling Prescription Charge.—Removal of this charge would not, at present, improve the working of the service to an extent commensurate with the cost.

Local Health Authorities

In the best interests of local government, the cost of local health services should be shared equally, as at present, between the local rates and the Exchequer. But the committee think that the lack of any Exchequer grant towards the running costs of residential accommodation for the aged "will become increasingly an obstacle to the smooth development of the hospital and local authority services" and may ultimately distort the pattern of the N H S.

Hence they recommend that, as soon as circumstances permit, the existing Exchequer subsidy towards the cost of new residential accommodation under the National Assistance Act be abolished, and that instead the net expenditure (both capital and current) incurred in providing all residential accommodation of this type should attract a 50% Exchequer grant. In return, the Health Ministers could require local welfare authorities to develop their services on a scale commensurate with the needs.

Prevention

So far as the N H S vote is concerned, the committee "know of no wide fields on which large sums of money might now be spent so as to bring the preventive services more into line with the curative services.

" those who have criticised the Health Service for spending far too much on disease and far too little on prevention have tended to overstate their case. It is true that a number of preventive health measures could be initiated, with advantage, outside the National Health Service, one of the most important of which might be the elimination of air pollution. It is true also that some of these measures might cost a great deal of money."

Within the health service, however, they would like to see special attention given to (1) development of the home health services, (2) inquiries "designed to reveal the broad fields in which preventive medicine might be extended profitably," and (3) development of the chiropody service.

Maternity and Child Welfare Services

The maternity services are in a state of some confusion and their organisation should be reviewed soon. New thought is needed as to the rôles of the local authority clinic, the practitioner, and the outpatient department.

Care of the Aged

The committee agree with those who say that it is the "inadequacy" of the services, and not the form of administrative organisation, which is the root cause of the problems now arising in the care of the aged. It is perhaps this inadequacy that has led some to advocate "half-way houses" to fill the gap between local authority and hospital provision, and, though they are far from criticising the very useful half-way houses set up by voluntary organisations and others, the committee do not wish the notion to develop that there is a gap that can be filled only in this way.

Ambulances

This service should not be transferred from the health authorities to the hospital authorities.

Whitley Council Machinery

Among hospital authorities there is still considerable irritation at their not having more discretion to determine rates of pay, to reward staff for outstanding efficiency, and to make bonus payments to employees for whom there is no promotion outlet. But the loss of the autonomy formerly enjoyed by hospital authorities in this field is an inescapable result of the introduction of a national service. The Whitley Council agreements themselves need not always be rigid and inflexible, and the committee think that they should allow a measure of flexibility to meet local variations whenever the need arises—a problem faced and solved by many large scale undertakings. This flexibility, however, should be built into the national agreements and not left to the discretion of individual managing bodies, who might compete between themselves for man-power.

An Intelligence Service for the N H S

The Health Departments are advised to set up a Research and Statistics Department. This would be the Departments' intelligence branch, working with their administrative and medical staff, and it would constantly search for information which would enable administrators to make right decisions for future development.

Coöperation within the Service

Coordination is needed at three levels: (1) centrally, (2) where national policies are applied to local circumstances, and (3) where individual workers must cooperate to help a particular patient. The committee put little faith in new coordinating machinery: "in the areas where cooperation is still lacking, what is now needed more than anything else is a change of heart among those concerned, and particularly, we feel, on the part of hospitals." Further improvements in cooperation will be achieved chiefly at the "working level." Besides recommending regional boards to review their arrangements for consulting the medical profession, they propose that the medical officer of health or one of his staff should have an honorary appointment on the medical staff of a hospital, taking charge of outbreaks of infection.

Final Comment

"Looking to the future, it is clear that there are long-term problems of high importance confronting the National Health Service, not a few of which can only be solved by the medical profession itself, and which will call for all the qualities of statesmanship and adaptability that it can command."

tion, which may show spontaneous remission or changes in severity from day to day

The fact that the patients on dilatal estimated that they had improved in the distance that they could walk to an extent which was significantly better than the improvement claimed by the controls, whereas our tests of exercise tolerance did not show any such statistically significant difference between the two groups, led to a critical assessment of the tests to find if some salient point was being missed A possible source of error might be that dilatal produced a very transient effect For instance, if after the administration of a tablet the blood-flow improved for only a few minutes, the improvement might be noted by the patient but missed by our tests applied about an hour after the last tablet had been taken by the patient Consequently twelve acute experiments were made in which the blood-flow in the legs at rest was measured over $2^1/_2$ hours during which dilatal was given Table II shows that the resting blood-flow increased in 6 of 12 patients In 2 of the 6 patients the blood-flow increased only in the calf muscles of one leg The duration of the transient improvement was such that it might well have been missed by our tests

It seems possible, then, that the subjective improvement claimed by some patients receiving dilatal may have been real But the transient nature and short duration of this improvement indicate that more detailed information is required about the blood-levels of dilatal if a satisfactory dose frequency is to be worked out The fact that only some patients tested in the acute clinical experiments responded to dilatal may be due either to the fact that not all patients absorb dilatal equally efficiently or to the fact that the blood-vessels of some patients respond to dilatal by dilatation whereas those of others do not These factors require fuller investigation before the true value of dilatal can be assessed

It has been shown, then, that dilatal can bring about a transient increase in resting muscle blood-flow in some patients This does not necessarily mean that any increased tolerance to exercise—i e, ability to do more work before being stopped by claudication pain—will follow It was thought worth while to examine the relationship between the improvement in resting blood-flow and exercise tolerance in our patients to find whether an improvement in the blood-flow was reflected by a corresponding improvement in exercise tolerance Such was not invariably the case, since in many patients the resting blood-flow improved without any improvement in exercise tolerance Statistically there was no significant correlation between improvement in resting blood-flow and change in exercise tolerance ($r = 0\ 022$)

Summary

A clinical trial was made of the effectiveness of dilatal in the treatment of intermittent claudication 50 patients completed the trial, 24 being controls

There was a statistically significant subjective improvement in the treated patients, but this improvement could not be confirmed by objective tests of blood-flow

Acute clinical experiments showed that dilatal produced a transient increased resting blood flow in the calf muscles of some patients It therefore seems to be necessary to determine by individual clinical test which patients will respond to dilatal

The 'Dilatal' (now known as 'Perdilatal') was supplied by Messrs Smith & Nephew

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REVERSAL OF PULMONARY HYPERTROPHIC OSTEOARTHROPATHY BY VAGOTOMY

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IN an exhaustive review of osteoarthropathy Mendlowitz (1942) grouped the ætiological factors under the headings "pulmonary," "cardiac," "hepatic," "gastro intestinal," and "miscellaneous", and these factors covered a very wide range including roundworm infestation, cirrhosis of the liver, myxoid tumour of the right auricle, and thyroidectomy Mendlowitz also discussed the theories of causation under the titles "trophic," "circulatory," "toxic-infective," "mechanical," "toxic mechanical," "anoxic," and "miscellaneous" His conclusions were not very different from those of Hippocrates, who first described the condition in the 5th century B C As West said in 1897, "clubbing is one of those phenomena with which we are all so familiar that we appear to know more about it than we really do"

Hypertrophic osteoarthropathy has been described in association with many conditions, but it is found most typically as a secondary manifestation of chronic pulmonary or cardiac disorder, such as severe emphysema, bronchiectasis, or congenital heart disease, and yet it is extremely rare in chronic pulmonary tuberculosis Its connection with bronchial carcinoma is well recognised, and clubbing of the fingers and toes, with or without pains and sometimes effusions in the wrists, elbows, ankles, and knees, may long precede pulmonary symptoms The patient is often treated for "rheumatism" or "arthritis" for as long as twelve months before a neoplasm is revealed by radiographic examination of the chest Such growths, though sometimes very small, may be accompanied by rarefaction of the shafts of the long bones, deposition of new subperiosteal bone at the muscular insertions into the shafts and at the diaphyseal ends, and quite substantial effusions into the related joints, as well as clubbing All these changes are due to increased vascularity, in particular an increase in the terminal arterioles, and, Mendlowitz (1942) holds, "an increase in blood flow per unit of tissue caused chiefly [in the case of simple clubbing] by increased digital arterial pressure" The pain to which these pathological changes subject the patient is commonly not only the first symptom but also much the worst, robbing him of sleep for long periods Since such bone changes are hardly ever associated with tuberculous lesions their presence may virtually end all doubt as to whether an isolated abnormal opacity in a chest radiograph is due to a neoplasm

Alvarez (1948) estimated that as many as 50% of resectable bronchial carcinomas were accompanied by arthropathy, and suggested that articular symptoms were as common as respiratory Hansen (1952) reviewed 100 cases of bronchial carcinoma and found 12 (excluding 5 with bone metastases) with joint pain, and such pain was the presenting symptom in 4 In my own experience I would place the prevalence of joint pain in bronchial carcinoma as 5–10%, and in these cases careful inquiry usually shows that arthralgia was the first abnormality noted (Flavell 1953)

It has long been known that resection of the growth is followed instantly by cessation of all pain, no matter how long this has been present, and that secondary changes such as clubbing of the nails and redness and swelling of the nail-bed at once resolve, the shape of the nails returning to normal as the nails grow out This remarkable fact has led to much speculation but no conclusion, and hitherto no explanation of the mechanism involved has proved satisfactory It is, for example, The platelet retraction factor ("retractin") is, thus, clearly distinguishable from other constituents of platelets It can be also isolated from brain tissue, and in lesser amounts from spleen and liver, but not from erythrocytes It is resistant at 56°C for at least two hours and stable indefinitely at $-20°C$ Studies for the identification of the factor, very likely a lipoid substance are in progress

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SERGIO I MAGALINI
MARIO STEFANINI

ELECTRON-MICROSCOPY OF ATHEROMA

SIR,—Dr Loveno (Jan 14) asks me what reason I have for assuming that the material shown in my letter of Dec 31 is really collagen

Collagen is characterised chemically by a specific high content of the amino acid hydroxyproline (13 6%[1]) The hydroxyproline content of other proteins is low, in fibrin we found 0 12%

In whole cornea we found a hydroxyproline content of 7 1%,[2] so the collagen content is $\frac{100}{13\ 6} \times 7\ 1 = 52\ 2\%$

Examination of corneal connective tissue by means of the electron microscope shows that it contains—besides cells and ground substance—exclusively fibrils as shown in my letter, the fibrils are uniformly thin (300-350Å) and have a cross banding of about 220Å Considering this we may safely assume that the fibrils in question are in fact collagenous

We have made hydroxyproline determinations in aortic atheroma in two cases and found values of 4 25 and 4 26% (signifying a collagen content of 31 2 and 31 3%) In an unaffected part of one of the aorta under investigation we found 2 9% hydroxyproline in the intima and 2 66% in the whole wall (corresponding to 21 3 and 19 8% collagen)

Thus collagen is a substantial component of the aortic wall, probably the development of atheroma is accompanied by an increase of collagen in the form of unusual thin fibrils

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A VAN DEN HOOFF

PROTOPHRENIA

SIR,—May I thank your correspondents for encouraging and helpful criticism Also, I need a few lines to answer Dr Gellner (Jan 7), this I do reluctantly and only because her strictures, which anyone could refute reading the work freshly, were separated by five weeks from my paper (Dec 3)

Actually in the paper I discussed in detail, which I shall not re state, the only valid objection Dr Gellner raises This was that, unlike the cases with demonstrable organic pathology, the "residual" group among the defective children in my series might not have been a reliable sample of such cases in general Dr Gellner, however, advances this with two strange assertions

One is that only feckless parents would seek hospital care for an imbecile child if he looks anatomically normal Plainly from this, she knows nothing of the burden such a misfortune may bring to a working-class home A chat with an urban doctor, or simply with the parents of children just like this at her hospital, might be enlightening for her

Her second assertion, which is no less extravagant, is that the proportion of my "residual" cases was unduly small In outpatients, she says, "residual" cases outweigh the organic Which outpatients, I wonder? Anyone with experience of children so very severely defective as these, all with I Q s below 50, is aware that the great majority present obvious organic disease In fact, I quoted other work to show that my proportions tallied with modern findings

Oddly enough, most of Dr Gellner's long letter is devoted to her own theories, which directly contradict this statement of hers Clinical signs of organic disease of the nervous system exist, she declares, in all cases of mental defect, "residual" or otherwise, though they are only to be found by the esoteric methods of neurological examination prescribed in her unpublished papers I am ignorant of these, but having read other letters to the medical press from Dr Gellner I can see why she dismisses my data about emotional adversity being one possible cause of mental defect

A single child's case[1] was enough to convince her that defect arises not from inadequacy of the higher cerebral centres but from the midbrain Subsequently,[2 3] she satisfied herself that this was indeed so and, in particular, that the vital lesions lay constantly in the corpora quadrigemina and the lateral geniculate bodies

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HAROLD BOURNE

HOMOSEXUALITY

SIR,—It seems to me that Dr. Comfort's article (Jan 21) is a classical example of pseudo scientific myopia and that he has not the ability to see the picture whole

A moral code is a human device for curbing animal passions so that man can live in communities and has to be learnt by each individual painfully, a fact from which Kinsey profited, but did not spot, we are all potential thieves, homosexuals, liars, and gluttons A code is the most important single factor in the natural history of man as a gregarious animal It dominated his psyche long before time was recorded in words It has tremendous survival value and a society without a code disintegrates, a modern example of which is not far distant To anyone who is interested in the method of disintegration in times of crisis I recommend Sir Edward Spears's *Assignment to Catastrophe*

Although these codes were formed over the centuries to meet man's biological needs and necessities, they have become integers which have to be accepted whole or not at all The fictitious Raffles, a professional thief but a perfect gentleman in other respects, is a psychological impossibility From what was said in Parliament recently the case of the missing diplomats affords an example of homosexuals who were unreliable in every way, which is not to say that homosexuals may not have great ability, especially artistic ability Dr Comfort gibes at the emotional words, phrases, and sentiments in the B M A report, but emotion is the very essence of a moral code, if people did not feel emotionally about it it would cease to dominate and combine I wonder whether, if somebody stole Dr Comfort's personal possessions, he would be so nonchalant about that breach of the moral code as he appears to be about homosexuality

Dr Comfort adduces the homosexual behaviour of his laboratory animals as in some way palliating homosexual behaviour in man He does not mention that throughout the mammalian world the young learn largely by imitating adult behaviour When he sees no harm in adult males indulging in private in mutual masturbation, intercrural intercourse, sodomy, and/or fellatio, the unholy quartet which constitute the euphemism homosexuality, has he not thought that this behaviour is bound to be imitated by many of the young?

A very able Departmental Committee have been hearing evidence on this subject for nearly a year and will soon be reporting Personally I very much hope that they will not recommend any changes in the laws governing homosexuality, although I think these laws might be implemented with more humanity and common sense I should have thought that it would have been better to await their report and not start shouting through the keyhole of their retiring-room, but as you have allowed Dr Comfort to do so I hope you will let me effusions In the last three the hila were not disturbed but the vagus on the side affected (right in case 3 and 5, left in case 4) was isolated as far away as possible and cut Equally dramatic relief and disappearance of joint swelling followed

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[1] Jackson D S Nature and Structure of Collagen London 1953

[2] Hooghwinkel, G J M, van den Hooff, A (In the press)

[1] Gellner, L *Lancet* 1950 i 881

[2] Gellner L *Brit med J* 1953 i 936

[3] Gellner L *Ibid*, ii 392

It would seem therefore that the manifestations of pulmonary hypertrophic osteoarthropathy are caused by a neural reflex passing from the affected lung in the fibres of the vagus nerve, and can be terminated by severing the vagus even when the related growth is irremovable

This finding casts an interesting light on the function of the vagus and the nature of osteoarthropathy, and it affords a certain method of relieving the persistent and distressing pain of osteoarthropathy

Summary

In cases of bronchial carcinoma associated with hyper trophic osteoarthropathy, severing the vagus nerve on the side of the affected lung has promptly dispelled the symptoms and signs of osteoarthropathy

Case 1 was referred by Dr S Locket, case 2 by Sir Horace Evans, case 3 by Dr A E Clark-Kennedy, and cases 4 and 5 by Dr J M Gray

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A NEW WAY OF TREATING FLAT FEET IN CHILDREN

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Two kinds of flat feet are found in children Congenital pes planus is the rarer of the two because most children with flat foot acquire it by everting the heel of an otherwise normal mobile foot (fig 1)

The normal foot bears weight chiefly at three points the heel and the heads of the first and fifth metatarsals (fig 2) This three-point weight-bearing is converted into a tripod by the longitudinal and transverse arches If the foot is flat or everted, the child bears weight as well along the inner border of the foot, which is not suitable for weight bearing The gait therefore becomes awkward The child may try to compensate by walking "pigeon-toed," and some who walk in this way and start with a mildly everted heel manage to reform the foot If the foot cannot compete with the eversion, the child walks with the feet splayed outwards—"Charlie Chaplin" gait In either case there is a tendency to tread down the stiffening of the outer wall of the heel seat of the shoe and to wear down the outer side of the heel of the shoe (fig 3)

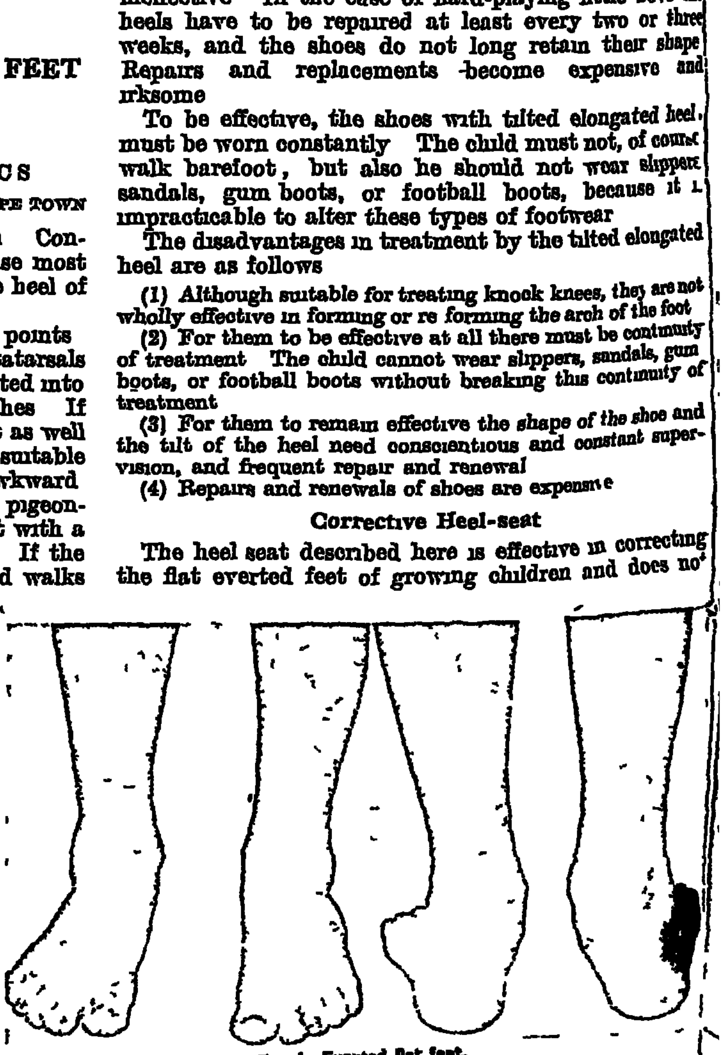

Fig 1—Everted flat feet.

Established Methods

Some pædiatricians believe that flat feet in children correct themselves spontaneously a visit to any orthopædic department dealing with adults or, more especially, to any military recruiting depot or orthopædic unit will rapidly dispel such an illusion

There are two established approaches to the problem

Arch-supports

For many years Continental schools have prescribed rigid arch supports These do raise the arch, but only by persisting with the fourth and unnatural weight bearing area (fig The consequence is that the arch does not devel strength and collapses once more when the supp is removed Because of this method of treat flat feet in children rigid arch-supports were standard issue in the German army of the 1939- war

In other words, once a child is used to arch supp it cannot do without them *Ordering arch supports fo* child is more than a prescription—it may be a li sentence

Tilted Elongated Heel

The second method, which is almost universal English-speaking countries, is to correct eversion the Thomas heel—i e, by tilting and elongating heel of the shoe on the inner side If the heel snugly, the tilt does correct the eversion Unfortunate to protect the welt one has to elongate the heel on inner side, and so the forefoot is also inverted slight Consequently, however long the child wears these alte shoes, the foot and heel relapse in some degree afterward

The tilted elongated heel has other disadvantages, the main one being that it is difficult to preserve the sn fit of the shoe round the child's heel The foot tends slip down the slope to the outer side of the shoe, deformin the outer wall of the heel-seat and wearing the heel dow along the outer border (fig 3)

Once the grip on the heel is lost, the shoe must b repaired or renewed, otherwise the method become ineffective In the case of hard-playing little boys the heels have to be repaired at least every two or three weeks, and the shoes do not long retain their shape Repairs and replacements become expensive and irksome

To be effective, the shoes with tilted elongated heel must be worn constantly The child must not, of cours walk barefoot, but also he should not wear slipper sandals, gum boots, or football boots, because it impracticable to alter these types of footwear

The disadvantages in treatment by the tilted elongated heel are as follows

(1) Although suitable for treating knock knees, they are not wholly effective in forming or re forming the arch of the foot

(2) For them to be effective at all there must be continuity of treatment The child cannot wear slippers, sandals, gum boots, or football boots without breaking this continuity of treatment

(3) For them to remain effective the shape of the shoe and the tilt of the heel need conscientious and constant supervision, and frequent repair and renewal

(4) Repairs and renewals of shoes are expensive

Corrective Heel-seat

The heel seat described here is effective in correcting the flat everted feet of growing children and does no eg supports The abdominal and vaginal surgeons do his part of the operation together, and it is only when the abdominal dissection is sufficiently advanced that the vaginal surgeon takes his station below, his part of the operation merely occupies the last half-hour of the combined proceeding In this way, the expert assistance of the vaginal surgeon is available both above and below The accompanying figure shows the amount of parametrium and paracolpos that we are now removing

I do not propose to enter into the controversial subject of radiation versus surgery as each case must be assessed and treated on its merits

Finally, I propose to publish in the near future a survey of my first fifty cases which will, I hope be of some encouragement to those surgeons who have performed or are contemplating this operation

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PRODUCTION OF CODEINE

SIR,—I suggest to Dr Williams that before he really believes what he wrote about codeine (Jan 21) he asks some chronic sufferers from such conditions as osteoarthritis or rheumatoid arthritis which they prefer for their pain—tab codein co or aspirin Also I would advise him if he should have a bad cough at night to take a dose of linctus codeine co *N.F* for each bout of coughing

Luton D R SNELLGROVE

CŒLIAC DISEASE

SIR,—In his admirable article[1] Dr Sheldon has cited a case of selective absence of lipase as unique May I correct this statement, and draw attention to the cases I have observed[2–4] and also to those reported by McDougall[5]

Indeed, the condition must be fairly common It is well known that the pancreas is a most sensitive organ and that its enzymes may be absent from duodenal juice in quite a number of pathological conditions It is also known that the dysfunction is mostly transitory although in some cases it apparently persists for long periods or even for life. According to common belief the three pancreatic enzymes are equally involved in the dysfunction In contrast with this, it has been found that, while in health a strict parallelism exists in the secretion of the three enzymes,[6 7] in pathological conditions associated with pancreatic dysfunction there is no parallelism, either in rate or in time, between the involvement of the single enzymes Lipase appears to be the most vulnerable of the three This enzyme has usually been the first to disappear and the last to return to normal, whether in infectious fevers, gastro-intestinal disease,[4] the acute toxic form of infantile diarrhœa,[8] or even protein deficiency disease[9 10], and among the reported cases of temporary selective deficiency of one enzyme, that of lipase appears to be the most usual, especially in scarlet fever,[3] but also in other conditions[4 5]

Permanent absence of trypsin[11] and (as Dr Sheldon remarks) of amylase[12] has been reported Of McDougall's[5] 16 cases with reduced activity of lipase alone, 1 took fifteen months to recover after the deficiency, probably of long standing, had led to symptoms of cœliac disease It may be assumed that permanent lipase deficiency may arise in consequence of some condition injurious to the pancreas, whether before birth[13] or subsequently

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ANTICOAGULANTS IN A HOT CLIMATE

SIR,—We have been analysing our figures for patients on long-term anticoagulant therapy to see whether we could confirm Dr Tawfic's claim[14] that patients receiving phenylindanedione may bleed more easily during hot weather We had not noticed this tendency and an examination of our records does not reveal it Since such an effect might have been masked by our using a smaller dose of the drug ('Dindevan') we have calculated the maintenance dose required by 10 randomly selected patients

We aim at a prothrombin index of 40–60% The results (see accompanying table) show no consistent alteration in relation to the mean average daily temperature The Egyptian summer is warmer than our own but from our observations it would appear that moderate heat does not affect the dose of phenylindanedione which is required for "long-term" maintenance anticoagulant therapy

AVERAGE DAILY DOSES (MG) OF PHENYLINDANEDIONE AND MEAN DAILY ENVIRONMENTAL TEMPERATURES (°C)

	Jan , Feb	March April	May, June	July, Aug	Sept , Oct	Nov , Dec
Temp.(°C)*	21 4	19 0	14 6	12 4	14 8	18 7
Case no						
1	125	130	135	135	130	125
2	105	70	72 5	67 5	67 5	67 5
3	150	112 5	137 5	145	147 5	150
4	55	50	50	50	45	45
5	70	70	70	70	67 5	70
6	155	155	155	150	152 5	152 5
7	95	95	80	87 5	92 5	97 5
8	135	130	130	130	130	130
9	115	115	115	115	120	125
10	120	115	115	115	115	115

* Shade readings calculated from figures midway between maximum and minimum in the twenty four hours

Department of Medicine C MERSKEY
University of Cape Town ELIZABETH SCHOLTZ

CORONARY-ARTERY DISEASE

SIR,—It is difficult to assess the real weight of the arguments of Dr Bronte-Stewart and his associates at Cape Town University (Jan 14) before fuller details are known of their very interesting, and apparently most valuable, findings

It will be particularly important to know (*a*) the age of the volunteers, and (*b*) the time-lag between the ingestion of the experimental foods and the testing of the cholesterol content of the blood Regarding (*a*) it is well known that the susceptibility of the cholesterol content of the blood to dietetic factors varies with age, being very low during the first three decades of life, and then increasing with each further decade Regarding (*b*), we know that cholesterol in the human body is rapidly broken down and easily synthesised within quite a short time

But even after clearing up these points, there would still be no absolute proof that it is, as they assert, the high content of unsaturated fatty acid contained in the germ of wheat and maize, and not the vitamin E, which is the decisive factor operating against coronary-artery disease, because all chemically untreated vegetable oils do contain in varying degrees natural tocopherols—i e, vitamin E—with their known biological activity. Nothing but complete elimination of the tocopherols from the vegetable oils before ingestion could substantiate their view Their finding that ground-nut oil fed in hydrogenated form produced a prompt rise in the serum-cholesterol level not only fails to support that

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Comments

The heel seats have to be made individually of plastic material from plaster-of-paris moulds of the child's feet and are therefore expensive I hope it will soon be possible to arrange for manufacture of the heel seats in a light, cheap, and durable form and in a wide range of sizes It takes from six to nine months before the average child grows out of any one size Only one pair of heel seats is required at a time, for they can be transferred as shoes are changed

For ordinary flat foot these heel-seats could be prescribed by family and school doctors and dispensed by appliance makers, or by trained employees in any good shoe store If the heel-seat fits the child's heel it is the right heel-seat So prescribed it would relieve some of the congestion in hospital orthopædic departments It may also be used prophylactically in convalescence if the child's feet are weakened by illness or recumbency

I am now convinced that the heel-seat gives us a sure, simple, and economical method of correcting flat, and developing strong, feet in children When we can use a plastic—e g , laminated fibre glass—a thin layer of which can stand big weights, we may be able to use the heel seat also for the flat feet of adults

ELECTRO-ENCEPHALOGRAPHY IN CHILDREN WITH RECURRENT ABDOMINAL PAIN

JOHN APLEY
M D Lond , M R C P
CONSULTANT PÆDIATRICIAN

JUNE K LLOYD
M B Brist , M R C P
REGISTRAR

UNITED BRISTOL HOSPITALS

CHRISTOPHER TURTON
M D , M Sc Lond , M R C P , D P M
CONSULTANT PSYCHIATRIST, BARROW HOSPITAL, BRISTOL

IN 1912, Still suggested that "masked epilepsy" could account for attacks of sudden abdominal pain in children From the few details provided, the diagnosis is open to criticism on several counts and indeed the suggestion has found few proponents until recently Lately, however, the diagnosis has won some adherents abroad (Klingman et al 1941, Moore 1944, Livingston 1951, Blumberg 1954), and a few in this country In Conway's (1951) series abdominal epilepsy was diagnosed once in 243 cases, and Mac Keith and O'Neill (1951) state that as the sole manifestation of epilepsy abdominal pain is rare , but it has been affirmed (Wallis 1955) that "the more commonly it [abdominal epilepsy] is sought the more commonly it appears" Some of these are only single case reports, and the sum total of recorded cases is small The absence of any control series should also be mentioned

The diagnosis of "abdominal epilepsy" is based on some such criteria as the following (Livingston 1951) (1) attacks of abdominal pain followed by exhaustion and sleep , (2) a favourable clinical response to treatment with anticonvulsants , (3) electro-encephalographic (E E G) records considered characteristic of epilepsy

Because of the small number of reported cases and the lack of normal controls, we consider that criteria of diagnosis have not been established and, as part of a wider investigation into the nosology of recurrent abdominal pains in children, they have been under review for some time In view of the recent interest (*Lancet* 1954, 1955) we felt that an account of the E E G findings would be of value

Material

The children were between 3 and 14 years of age We included those who complained of abdominal pains, recurring over a period of at least three months, severe enough to cause some interference with normal activities, and in whom no evidence of organic disease was found The only omission in the series with abdominal pain, as in the control series, was a very small number of children who were suffering from fits but who also had abdominal pain, either as an aura or unrelated to the fits

TABLE I—E E G ABNORMALITIES IN 133 CHILDREN WITH AND 133 CHILDREN WITHOUT RECURRENT ABDOMINAL PAIN

—	With pain	Without pain
Resting record		
Normal	121	120
All abnormalities*	12	13
Resting and evoked		
All abnormalities*	18	13

* Including "focal spikes" (6 in abdominal pain cases and 3 in control series), which may migrate, change site, or disappear (Gibbs et al 1954, Kellaway 1953), and "localised slow activity" (2 in abdominal pain cases and 1 in control series) In neither of these is there definite evidence of an enhanced tendency to epilepsy

Hospital Series

With these provisos, all the children with abdominal pains referred to a hospital outpatient department during a limited period had E E G s taken Over the same period, E E G s were taken of other children of approximately the same ages, from the ordinary run of non acute hospital patients There were 96 children with abdominal pains as defined and 55 patients without abdominal pains

School Series

As part of an investigation of abdominal pains in an unselected school population (Apley and Naish 1956) E E G s were taken from children attending school clinics for routine examination A series of 37 children with abdominal pains was obtained, and 78 of those without pains were used as controls in corresponding age groups

To avoid any possible bias, requests for E E G s were made with no information other than the heading of "hospital series" or "school series," so that all reports were made without knowledge of whether the patient had or had not abdominal pains One of us (C T) made all the reports, and those which appeared in any way abnormal were re examined and discussed

TABLE II—E E G "EPILEPTIFORM" ABNORMALITIES IN 133 CHILDREN WITH AND 133 CHILDREN WITHOUT RECURRENT ABDOMINAL PAIN

—	With pain	Without pain
Definite epileptic		
Resting record	2	5
Resting and evoked	14	14
Definite and borderline		
Resting record	4	9
Resting and evoked	22	22

Results

We found no significant differences between the hospital and school series of children with abdominal pains, and the two groups are therefore discussed together Similarly the hospital and school children without abdominal pains are grouped together for the purpose of discussion In assessing results the difficulty of defining an "epileptiform tracing" arises, and will be briefly discussed later

If all E E G abnormalities are grouped together it is seen (table I) that, comparing children with and without pains, there is almost complete identity on the resting records If, however, evoked responses (hyperpnœa and photic stimulation) are considered to be significant, and are therefore included, there is a slight preponderance

Notes and News

WORLD HEALTH ORGANISATION

THE 17th session of the Executive Board of the World Health Organisation opened at Geneva on Jan 17 under the chairmanship of Dr Sabeeh Al Wahbi, director of Karkh Hospital, Bagdad Iraq, who in his opening address quoted an Arab proverb 'there are two forgotten blessings, health and security,' and said that W.H.O had the duty of helping the world achieve these two blessings

Dr Nicolai Khmelev deputy minister of health of the Soviet Union, announced his country's decision to resume active participation in W.H.O, a decision which the board welcomed warmly The Soviet Union withdrew from W.H.O in 1949, but because the Organisation's constitution does not provide for a country's withdrawal, the Soviet Union and eight countries which took similar action were considered 'inactive members'

BRITISH JOURNAL OF TUBERCULOSIS AND DISEASES OF THE CHEST

To celebrate the 50th anniversary of this journal, Messrs Baillière, Tindall & Cox, the publishers, arranged a dinner which was held in London on Jan. 24 Sir Robert Young said that it had required great courage and vision on the part of the first editor, T N Kelynack, and the publishers to start a journal in a special field in 1906, when specialisation was at a very early stage of evolution But from the first number the journal was approved and supported by the chief specialists in tuberculosis and by the masters of medicine of the time After 27 years Kelynack was followed as editor by Lancelot Burrell whose early death was a great loss to the journal Clifford Hoyle, succeeding him, had recognised that its scope should be enlarged to include other diseases of the chest All these had maintained the critical and philosophical character of the publication and the writings of the present editor, Philip Ellman, showed a critical faculty and wide perspective, which, with his experience of chest diseases—clinical, pathological, and administrative—and his great enthusiasm and industry, contributed to the success of the journal As long ago as 1931 Dr Ellman had suggested the reorganisation of the tuberculosis dispensaries into chest clinics, enlarging their scope and usefulness, and these suggestions had been carried out 17 years later Dr Philip Ellman, responding from the chair, welcomed the guests who included Sir Russell Brain, P.R.C.P, Mr Charles Read P.R.C.O.G, Sir Clement Price Thomas (representing the Royal College of Surgeons), Dr G F Abercrombie (chairman of council of the College of General Practitioners), Dr W E Snell (president of the Tuberculosis Association), Dr J L Livingstone (president of the Thoracic Society), Dr Hugh Clegg (editor of the *British Medical Journal*) Sir Heneage Ogilvie (editor of the *Practitioner*) Dr J G Scadding and Mr Norman Barrett (editors of *Thorax*), and Lord Moran.

Sir John Charles (chief medical officer of the Ministry of Health), proposing the toast of Medical Journalism said that throughout the 50 years of the *British Journal of Tuberculosis* medical journalism had been the tried and trusted recording angel of the achievements of the profession it had given outstanding service in recording those facts as they appeared to the contemporary eye and understanding and in the production and propagation of ideas This constituted a responsibility, a charge, and a challenge which had been accepted with good humour and success The integrity of British medical journalism, the allegiance of its members to the highest ideals of the two professions, had been in accordance with the Hippocratic canon and a model to the world. Dr T F Fox (editor of *The Lancet*) compared medical journals to gardens, in which the workers might be many or few, whole-time, part-time, or jobbing He expressed admiration for the clinicians pathologists, and others who give so much of their time and of themselves, to such work. Their labours too often went unregarded or were taken for granted, but they were in fact the greater part of medical journalism Mr R F West (chairman of the publishers) said that the journal had had two parents—Dr Kelynack and Mr A. A Tindall, who was present at the dinner From Dr Hoyle who had borne the heat and burden of the day through the war, Dr Ellman had received a goodly heritage, but to an illustrious series of editors he had added lustre Never, surely had so much been accomplished in 50 years as in the world of medicine in the lifetime of the journal

DIDCOT RAILWAY DISASTER

AT a meeting of the Devon and Exeter Medico Chirurgical Society on Jan 19 Mr P M C Robbins spoke of the lessons learnt from the Didcot Railway Disaster 7 people were killed at once, 2 more died of multiple injuries soon after admission to hospital, and 1 man died on the way there, from a ruptured pancreas and spleen Of the 54 casualties admitted to the Radcliffe Infirmary, 20 had head injuries (5 major ones), 2 had severe chest injuries (1 with a fractured pelvis and the other with a dislocated hip), and 2 had moderate chest injuries One patient had a crushed leg, and several others also had compound fractures The remainder had minor fractures or lacerations There were no burns or abdominal injuries among them One woman died of a massive pulmonary embolus five weeks after the accident In the case of the patient with the crushed leg gangrene necessitated amputation Incidentally discovered during examination in hospital were 2 cases of pulmonary tuberculosis, 1 of diabetes mellitus, and 1 of leucoplakia of the cervix

Within an hour of the accident the first batch of 15 casualties was arriving at the hospital, where all possible patients had been discharged and admissions cancelled Reception space was found in the casualty department and outpatient hall When all 54 casualties had been admitted there were still 50 empty beds available Two theatres were immediately ready for use Almost the entire hospital staff reported for, or remained on, duty The organisation worked smoothly, and the emergency was all dealt with in twelve hours Mr Robbins had only one serious criticism owing to congestion. information was difficult to come by on the telephone A police radio-car at the site of the accident in direct communication with another car at the hospital would have provided a much more efficient information service

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University of London

The title of reader in anatomy has been conferred on Dr D H L Evans in respect of the post held by him at University College, and the title of reader in anatomy on Mr D A. Sholl, B SC, in respect of the post held by him at University College

Royal College of Obstetricians and Gynæcologists

A meeting of the council was held on Jan 28 with Mr Charles Read, the president, in the chair

L M Jacks was admitted to the membership in absentia The following were elected to the membership

E A Agius D G Bonham Reginald Bowman R. J M. Byrne J K Craig C A Cussen P P De Bond R P Elvidge, L A. J Evans Jack Evton Jones C O Fung-Kee-Fung J G Furber, P H Gelb Anne L M. Graham, Winifred J A Graham R G Harbison G F W Hossack, Anna R Kemp Edward Lacy J D Llewellyn Jones Margaret B Malloch John Mander M. D Manion, Brian Measday R W A Nel J P O Neill G M. Parkin H E Reiss L L Relf Freda M. Roberts S B Robertson, A W. Russell Jean M. Sharpe P F Venter, F C Wilkinson L M Wolf

Dr Rhoda Allison of Leeds has been awarded the Edgar Gentilli scholarship

Royal Appointment

Prof L G W Hill, has been appointed an honorary physician to the Queen in Scotland, in place of Dr A Greig Anderson, who has resigned

Royal Society of Health

On Wednesday, Feb 15, Dr Arnold Brown will speak on the Contribution of the Medical Officer of Health towards Industrial Health, and on Wednesday, March 14, Dr Kenneth Soddy will open a discussion on the Prevention of Break-up of Families Both meetings will be held at 2 30 P M at 90, Buckingham Palace Road London, S W.1

M O H for Bristol

Dr R C Wofinden has been appointed medical officer of health for Bristol in succession to Dr R H. Parry who has retired Since 1947 Dr Wofinden has served as deputy M O.H for the city and as lecturer in preventive medicine in the University

Dr Wofinden, who is 41, was educated at Rotherham Grammar School graduated M B Lond with honours in 1937 from St Mary s Hospital Medical School Two years later he took his M D in State medicine and the D.P H He has held posts in the public-health services of Rotherham and of Bradford For his investigation into problem families in Bristol he was made an honorary life fellow of the Eugenics Society In 1945 he was awarded the diploma of public administration of the University of London. Two years ago with a World Health Organisation travelling fellowship, he studied health and welfare services in Holland and Scandinavia tion (Daniels 1949) invaluable, and we have applied this method in 304 cases since the beginning of 1952

Technique

The operation should be done by an experienced surgeon, because vulnerable structures lie in the operation field

The biopsy is done on the more severely affected side, judged radiographically, or, if both sides are affected equally, on the right side After injection of local anæsthetic the skin and platysma muscle are incised for 3–4 cm parallel with, and 1–2 fingerbreadths above, the clavicle The superficial fascia is incised along the lateral border of the sternocleidomastoid muscle, which is retracted medially exposing the pad of fat on the anterior surface of the scalenus anterior muscle Care should be taken to avoid injuring the lymphatic duct on the right side and the phrenic nerve and the thoracic duct on the left side Sometimes the omohyoid muscle lies rather low, in which case the pad of fat is grasped above that muscle The pad is drawn forward and carefully examined In the pad lymph-nodes (which are part of the mediastinal system) may be visible or palpable, and these are removed, but, if no node is detected, as much as possible of the pad is removed The incision is then closed

The discomfort caused to the patient by this operation is very slight

Histological Findings

In sarcoidosis the lymph-node tissue is diffusely, and often densely, infiltrated by discrete, usually spherical, epithelioid-cell clusters of roughly uniform size Some of these clusters contain giant cells of the Langhans type in which we have occasionally found inclusions (either Schaumann or asteroid bodies) There may be slight central coagulation necrosis, chiefly fibrinoid, and also small areas of fresh caseous necrosis in occasional clusters of epithelioid cells Gross caseous necrosis is not found Collagen fibres, commonly hyalinised, appear first at the periphery of the epithelioid-cell clusters, which are gradually transformed into hyaline masses In advanced cases some epithelioid-cell clusters may not be hyalinised, whereas others are partly or fully hyalinised

Histological differentiation between sarcoidosis and other diseases, notably tuberculosis, is sometimes difficult This differentiation is based chiefly on the presence and degree of caseation, but if no acid fast bacilli are found it is often impossible to distinguish histologically between sarcoidosis and tuberculosis

Sarcoidosis should never be diagnosed on the basis of the histological findings alone

Results

The results of retroclavicular block dissection in 304 cases are shown in the accompanying table In only 4 cases were no lymph-nodes found In 130 cases histological examination showed healthy nodes or non specific lesions, but in 168 cases (55%) this examination helped to establish the diagnosis Of 237 patients with clinical and radiographic evidence of sarcoidosis, biopsy by this method supported the diagnosis in 148 (62%)

PRELIMINARY AND FINAL DIAGNOSES IN 304 CASES

Preliminary diagnosis	No of cases	Diagnosis after biopsy					No lymph nodes found	Lymph nodes healthy or lesion non specific
		Sarcoidosis	Pulmonary tuberculosis	Hodgkin's disease	Carcinoma of the lung	Uncertain (tuberculosis or sarcoidosis)		
Sarcoidosis	237	148	Nil	1	Nil	Nil	3	85
Pulmonary tuberculosis or sarcoidosis	24	5	7	Nil	Nil	1	Nil	11
Neoplasm or pulmonary tuberculosis	38	Nil	3	Nil	4	1	1	29
Unknown	5	Nil	Nil	Nil	Nil	Nil	Nil	5
Total	304	153	10	1	4	2	4	130

REFERENCE

Daniels, A C (1949) Dis Chest, 16, 360

CHRONIC PAROXYSMAL HYPOGLYCÆMIA
(WHIPPLE'S SYNDROME)
A FIFTEEN-YEAR CASE-REPORT

E H R ALTOUNYAN
M D Camb, F.R C S
DIRECTOR, ALTOUNYAN HOSPITAL, ALEPPO, SYRIA

THE second World War, the natural reluctance of the patient to submit to an operation hitherto unknown in this region, and the diffidence of the surgeon about operating on a patient who seemed perfectly normal for months at a time have given me the opportunity of *observing for fifteen years a patient* whose pancreas contained a solitary insulin tumour Removal of this has apparently arrested slowly progressive mental degeneration, restored the blood-sugar level to normal permanently, and enabled her to resume full time work on the hospital staff

Although several hundreds of such cases have by now been reported, I believe it is still worth while publishing each case verified by either operation or necropsy Moreover at operation the appearance of a "normal" pancreas may discourage the surgeon from proceeding with a blind partial excision and thus make him miss a radical cure

Case-report

A female hospital worker, aged 21, was found, on the morning of June 21, 1939, in coma on the floor by her bed Fortunately my first assistant, Dr A Hovnanian, found that her blood sugar level was 27 mg per 100 ml and the administration of glucose led to prompt recovery During the fifteen years that followed this first attack, until the day of her operation on Oct 1, 1954, despite every effort by diet and frequent meals to keep up her blood sugar level, she went into coma frequently, and thirty two blood sugar estimations were made, giving 27–64 mg per 100 ml and once 84 mg per 100 ml A glucose tolerance test in 1949 gave 39–155–38 mg per 100 ml, and in 1952 55–105–59 mg per 100 ml Gradually the patient became less and less able to work, and mental degeneration set in During her last attack, immediately before operation, she became maniacal and was given the choice of either submitting to operation or being transferred to a mental hospital

Operation (Oct 1, 1954)—Blood sugar levels were as follows 40 mg per 100 ml immediately before operation, *230–120–122 mg per 100 ml during operation,* when glucose was being continuously administered, and 169, 160, 175, 154, and 127 mg per 100 ml on successive days after operation Sixteen subsequent blood sugar estimates were within normal limits, and the patient made a good recovery and is now back on full work Her mental improvement was noticed immediately and has been maintained during the past year

Comments

The one point I wish to emphasise about the operation is that, the completely exposed pancreas appeared to be perfectly normal, without any reddish nodules or nodules of any kind palpable by the exploring finger on the anterior surface In view of the history it was decided to remove the tail and body of the pancreas, which was accordingly lifted clear of its bed and turned over On palpation of the head between finger and thumb a hard nodule, perfectly round and just over 1 cm in diameter, with a thin calcareous shell, was discovered embedded in the substance of the head This nodule was removed

CLINICAL CANCER RESEARCH*

D W SMITHERS
M D Camb, F R C.P, F F R

PROFESSOR OF RADIOTHERAPY IN THE INSTITUTE OF CANCER RESEARCH ROYAL CANCER HOSPITAL, AND DIRECTOR OF THE RADIOTHERAPY DEPARTMENT, ROYAL MARSDEN HOSPITAL

RESEARCH is sometimes used in a most practical attempt to find an immediate answer to a specific problem, but basic or fundamental research is more truly the expression of a state of mind It is an attitude, a curiosity about patterns, relationships and mechanisms, an urge to understand Its methods are observation, experiment, and contemplation It takes its inspiration from Nature and not from need, its proper reward is understanding, not practical application This seems to me to apply to cancer no less than to any other subject —and to some clinical cancer research no less than to non clinical I do not say that application is unimportant, merely that it should not be the primary concern of the basic research worker and that when it does become so his work is apt to suffer

Those of us whose lives are intimately bound up each day with urgent human problems sometimes have great difficulty in remembering that research departments, if they are to flourish, must protect their independence from those of us who wish to put their work to use, and that they must not allow themselves to become too concentrated on the solution of practical problems The business of making research effective is not primarily theirs and needs separate thought and organisation The links between basic research and clinical practice in cancer have to be most securely forged if the fundamental research workers are to maintain this desirable state of privileged independence of man's needs, and if their work is to advance the cause of prevention and healing as well as that of science Some medical research must itself have this same freedom to follow nature—in fact the basic clinical research worker is far too rare *amongst us* We could do with many more in the cancer field cloistered, academic, fundamental, and unhurried, on whom we should make no demands for practical results, but from whom, in time, we may hope for some increase in understanding from whatever unlikely direction their inquiry may have led them

Today the directors of large cancer research organisations have a terrific task It is essential that they *should* have complete control of how the research within their organisations is done, but so many special branches of science are involved that if they are to be knowledgeable enough to be effective they cannot, at the same time, possibly have more than the most superficial contact with the whole world of clinical medicine which is most intimately involved When limits have to be set to their endeavours it is a great deal to expect that they should always be relied on to decide wisely without some consultation on the best emphasis to be placed on the over all programme On the other side directors of clinical cancer research organisations are so rare as to be practically unheard of, and the anatomical specialisation within medicine has become so detailed and so widespread that there are few doctors attempting to survey the whole clinical cancer scene, let alone trying to keep contact with basic research as well There is, therefore, a sad lack of those with the interest and authority necessary for a proper discussion with the directors of the cancer research organisations to help them decide on the directions in which new effort might be made and from which unprofitable attempts might be withdrawn There seems to me to be an urgent need for more clinical cancer research workers, of a different class from those with complete academic freedom to follow their ideas who will concentrate on the neglected task of two way communication with the purpose of making research effective They are required to be familiar with the human problem so that the flow of ideas arising from it may reach the fundamental research workers and so that their discoveries may in turn have a channel to the ward It is of these middle men that I propose to speak—the links between basic cancer research and practice, the men with an insecure foot in both camps not always too well regarded by either but without whom freedom in fundamental research may become restricted with its viewpoint narrowed and the patient unlikely to reap the full benefit of the immense effort which is made

The Duties of the Middle-men

The first duty of these middle men is to be familiar with their subject, which is an extremely common disease process in man Sir Thomas Lewis said

> "When we investigate clinically some disease, or some manifestation of it, we may be seriously handicapped by circumstance, but we are possessed of the certain knowledge that what we study is precisely what we set out to study"

Their second duty is to find their way into research laboratories and staff rooms, to talk, to listen, to attend meetings, and to read review articles Their purpose here is to feel what is nowadays called the "climate of opinion" and to try to do two things The first is to feed in ideas gained in clinical practice, and the second to try to see the implications of new knowledge If they do this they will move amongst experts in every basic science and in every branch of medicine, each expert knowing so much more than they do about his own specialty that they may at times be in danger of feeling inferior instead of necessary If in some need of reassurance, they may repeat to themselves a few words spoken by Sir Francis Walshe which should give them comfort from both directions Sir Francis said

> "It is clear that experiment involves an even higher degree of abstraction than simple observation, for many more facts out of the total presenting are put in the discard, and this is why, perhaps, the experimental method, exclusively pursued, may prove somewhat narrowing to the mind, adverse to a philosophic generality of outlook, and to the free play of ideas ranging over the sum of presenting phenomena"

He also said in that same Harveian Oration

> "Some generality of understanding is the essence of civilised culture, and is a crying need in medicine and we must seek it earnestly if we are not to decline to the level of craftsmen and technicians"

Their third and main duty is to engage in research on their own account in the hospital ward—that laboratory nearest to their problems—in their own experimental laboratories, which do not need to be expensive or large, and in the collection, sorting, and analysis of detailed clinical observation, work which *does* need to be far more elaborately equipped and staffed than it has ever been before Their task here is to develop the ideas they will pass on to the basic research workers, to test hypotheses they have formed *from contact* with them, to clarify the problem to be tackled, and to assess the value of what is being *done about it* For my own part I would like to see a few outstanding physicians, clinical professors of medicine, engaged in this work, with their own beds and with access to those of their colleagues, and assisted by a sufficiency of clinical pathologists

A Middle-man's Point of View

Having stressed the need and said where I think the duties lie, I will try to sketch for you my view of the sort of philosophy which one of these middle-men might is thoughtful and thought provoking and should appeal to readers who are interested in methods of scientific inquiry and proof A chapter on medical and lay opinion illustrates amusingly the range of conclusions that may be drawn from the same evidence, but the general reader will probably be more interested to know the author's own verdict, which is "not proven"

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* An address to the Plymouth Medical Society on Friday Dec 2, 1955

This is a good-tempered book by one who holds that "most smokers are not addicts, the pleasure of smoking is real " But it leaves an impression that the only serious objection to the present vast world consumption of tobacco is its possible relevance to cancer of the lung, and it does not therefore fulfil its claim to summarise present medical opinion and also to discuss the social implications of smoking

Infant Nutrition in the Tropics and Subtropics

D B JELLIFFE, M D, M R C P, D C H, D T M & H World Health Organisation Monograph Series no 29 Geneva 1955 Pp 237 25s

THE author, who is a W H O visiting professor of pædiatrics in Calcutta, has a wide experience of his subject, obtained in West Africa, Jamaica, and now in India He emphasises the importance of social anthropology as a background to pædiatric practice, and the need to learn the attitudes of mothers both to disease and feeding habits He is concerned with methods of instruction suitable for primitive or illiterate persons, and there is a good chapter on nutrition instruction in the maternal and child-health centre A large part of the monograph is taken up with an account, country by country, of infant-feeding practices

Dr Jelliffe is most interesting when writing from his experience he is far less apt with the literature, and the text is too frequently encumbered with long quotations from his 812 references The 24 figures and two coloured plates are of the high quality we have come to expect in United Nations publications The photographs taken in homes and hospitals leave a vivid impression of the tragedies of disease in childhood

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Medical Research Mid Century Survey —This report of the American Foundation on Medical Research in the United States, which was discussed in a leader in our issue of Jan 7 (p 29), is published in this country by Messrs J & A Churchill, of London, at 5 guineas for the two volumes

An Atlas of Bone-Marrow Pathology (2nd ed London Heinemann 1955 Pp 85 30s)—That a second edition of Dr M C G Israëls's atlas has been called for shows that it has secured its place among the standard hæmatological works The text has undergone minor changes transitional or intermediate megaloblasts are now described and the plate illustrating the cytogenetics of erythroblasts is correspondingly modified, myeloid reticulosis and acute reticulum celled leukæmia are also described, and there is an illustration of metastatic cells from a gastric carcinoma All these are illustrated on a plate containing six new paintings The colour reproduction is excellent The atlas will be particularly useful to those who have to teach themselves hæmatology and who cannot refer continually to actual slides

Comparative Physiology of Reproduction (London Cambridge University Press 1955 Pp 253 50s)—No 4 of the memoirs of the Society of Endocrinology is based on a symposium held in July, 1954, at the University of Liverpool on the comparative endocrinology of vertebrates The memoir, which has been edited by Mr I Chester-Jones, PH.D and Dr Peter Eckstein, reviews reproductive patterns in fish, amphibia, reptiles, and mammals and goes on to describe the effects of sex hormones in groups of vertebrates Memoir no 5 (Pp 124 25s), on hormonal control of water and salt electrolyte metabolism in vertebrates, completes the record of the symposium

United States Dispensatory (25th ed Philadelphia J B Lippincott London Pitman Medical Publishing Co 1956 Pp 2139 £10) —The gestation period of elephants is lengthy, and it is not to be wondered that new editions of this enormous work of reference appear only every ten years The latest is the "biggest ever," and in preparing it Prof Arthur Osol, PH G, and Prof George Farrar, F A C P, have drawn information from the *British Pharmacopœia*, the *International Formulary*, *New and Non official Remedies*, and 25,000 issues of medical, pharmaceutical, biological, and chemical journals The book is bound in heavy buckram which looks as though it will stand up well to constant wear during the next ten years

Porphyrin Biosynthesis and Metabolism (London J & A Churchill 1955 Pp 308 30s) —The papers given at the symposium on this subject held by the Ciba Foundation in London in February, 1955, under the chairmanship of Prof C Rimington, F R S, have now been published The editors of the volume are Dr G E W Wolstenholme and Miss Elaine Millar, A H W C

New Inventions

DIATHERMY HÆMOSTATS FOR PROSTATECTOMY

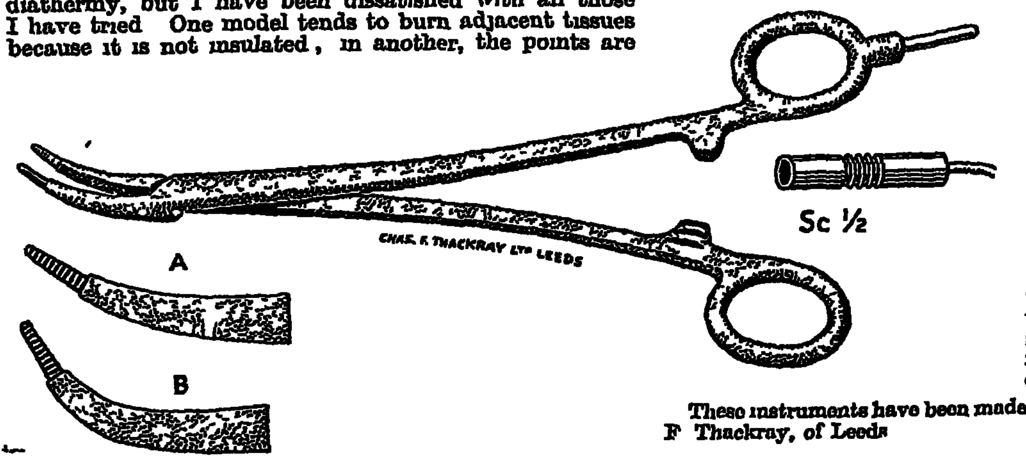
ESPECIALLY in those forms of prostatectomy in which the bladder is closed without drainage—e g, Millin's retropubic operation and the Wilson Hey procedure—efficient hæmostasis is essential Various artery forceps have been designed to obtain hæmostasis by diathermy, but I have been dissatisfied with all those I have tried One model tends to burn adjacent tissues because it is not insulated, in another, the points are too broad and blunt and the bite is therefore unnecessarily large Straight forceps are always difficult to use because the bleeding points in the prostatic bed are usually not on the floor but on the posterior and lateral walls

The hæmostats which I designed some time ago to overcome these difficulties have proved so satisfactory that they may be of interest to others—although I must emphasise that I claim no originality for them Their salient features are

1 The insulation is carried to within $^1/_4$ in of the extremity

2 The non insulated part is slender and "fines" down to a slightly blunted extremity

3 Two pairs are provided, both 9 in long The one in general use has only a slight curve The other, with its more pronounced curve, is used for bleeding points on the lateral wall of the prostatic cavity on the side of the operator, thus making it unnecessary for the surgeon to move to the opposite side during the operation



These instruments have been made for me by Messrs Charles F Thackray, of Leeds

J COSBIE ROSS
CH.M Lpool, F R C S

Liverpool, 1

echanisms, may at times be partly responsible for isorganised growth The long time that many of the citing factors take to act, the fact that promoting actors may shorten this time (one of the two perhaps y weakening local control) and that the shortest latent eriods are found with viruses—the only suspects which irectly introduce a new source of self-reproducing rotein into the cell—all seem to him to fit quite reason- bly into the picture Whether the control is overcome rom within the cell or from without, by increased eproductive activity or by relaxation of those influences hich hold its reproductive urge at bay, or through some ombination of the two, the result in terms of changed ehaviour pattern or of the cancer process is likely to e the same No special intracellular evil seems necessary o explain this process, though several different ones ay each play their part at times, when such intra- ellular changes and weakening of extracellular controls ccur together they are likely to be more effective than ither is alone This view limits but does not deny he *findings of research workers who have adhered to the* irus theory, the mutation theory, or other intracellular iews, indeed, it seems to make possible the reconciliation of much of their work which appeared to be in onflict

Perhaps then, thinks this man of ours upon his bridge, the idea of a special evil always present within every cancer cell, so diligently sought on the one side and so relentlessly pursued on the other, may be a myth Since belief in its existence has dominated cancer thought for so long without much profit to the patient he wonders what would happen if more people seriously considered once again the possibility that there may be substance in the hypothesis that the cancer cell is basically normal and that what goes wrong is essentially due to interference with organisation It is organisation which appears to be the unstable marvel of human existence——not disorganisation, which is merely its inevitable accompaniment A similar permissive view of cancer has been held by many, but there would seem to be more reason for holding it today than ever before Sir William Savory, in the third Bradshaw Lecture in 1884, said

> "Before we shall ever be able to answer the question, why or how do tumours form? it seems to me we must be able to solve the problem of normal growth and development and to answer the question why or how it is that these continue up to a certain point and then suddenly cease"

The great questions of orderly development and maintenance are better understood than they were then but still seem no less fundamental to the problems of disorderly development and decay The wonder is not that we should be faced with disorganised growth or cancer, but that organised growth should occur at all and that disorganisation should often be so delayed that many people are preserved long after they have ceased to be biologically useful

In multicellular organisms with sexual reproduction, only those cells which achieve physiological isolation after fertilisation but before differentiation and which are situated in a favourable environment are able to produce whole adult organisms whether as twins or other multiples Those which become isolated after some differentiation has occurred though no longer both totipotential and suitably placed, may still be pleuripotential and able to establish some imperfect organisation of their own in their attempt to fulfil their inheritance If already specialised and type specific they may, when isolated and dedifferentiated, produce a mass of primitive cells only faintly resembling their tissue of origin, being more like the cells from which that tissue was derived Undifferentiated tumours arising in many different tissues are notoriously alike The only cells which never seem to escape from control are those fixed postmitotic cells which have differentiated away their whole inheritance, leaving themselves no other possibility of self expression—one example of which is to be found in the lens of the eye

Seen in this light, cancer appears as a name applied loosely to the most disorganised end of an ill defined group of disorders of growth which are due to an inevitable breakdown of some part of that complicated organisation of the body which is able to build it up and to maintain it for a while as a functioning whole The cancer cell is then seen as a normal cell which, through physiological isolation, has partially escaped from the body's control mechanisms, undergone some dedifferentiation, and is trying under more or less difficult circumstances to express its natural potentialities The manifestations of cancer depend on the one hand on the degree to which control is overcome, the amount of dedifferentiation achieved and the possibilities for developmental expression remaining to the cells affected, and on the other on the sites at which loss of control *has occurred and their extent, the favourability of the* environment in these regions for growth, the distribution throughout the body of the cells affected, and the opportunities for dissemination The causes of cancer appear as any of those many conditions which lead to the physiological isolation of cells from their fellows in any complicated organism These multiple causes are seen to be in two main groups those raising cell activity above that of its control and those lowering the controls The first group contains most of the irritant, inciting, carcinogenic factors, all those injuries which demand repeated attempts at regeneration, recurrent local hormone stimulation, and any of the intracellular changes which may increase cellular growth potential The second contains the poorly understood process of ageing, those nervous and metabolic gradients which largely determine and maintain our growth and form, perhaps some of the cancer-promoting agents which may affect these local control mechanisms, and the general hormone system of diffusable control of homologous tissues and of tissues related in some common function throughout the body

"The cure of cancer" becomes a meaningless phrase while the cure of individual patients with cancers at special sites has long been an established fact The future is seen to lie with more efficient prevention or postponement of tissue disorganisation, with better removal or destruction of some disorganised tissues, and with renewed attempts at re establishment of control, knowing that these may all be successful in individual tissues of individual patients but not in any generality A final, complete solution of this problem is seen to be impossible, since it is part of the nature of complicated organisms that they cannot maintain their organisation indefinitely Only an isolated unicellular organism in a boundless, favourable environment is immortal and eternally expressing its inherent ability for endless self-reproduction Evolution is not compatible with immortality, it requires complexity and organisation for expression and death for progress

Fundamental Cancer Research

Having considered his point of view, the middle man may then look towards the basic research workers Individually they seem much like scientists in any field, but collectively they appear to differ from most other groups in that their work is not centred around a single basic discipline but around an ill-defined disease process of which most of them have no first hand knowledge in the human patient at all They are clearly not inhibited into inaction by a long acquaintance with the march of this illusive disease, they have been trained in their respective scientific fields to expect to be able to find answers to most questions if they work long and hard enough, and for the most part they seem eager and

Heat, Salt, and Water

As "payment" for the advantages of a highly developed heat-regulating mechanism, man must constantly make good the salt and water lost in the sweat In the laboratory, sweat losses up to 8 litres in four hours have been recorded, but the high temperatures and work-rates involved cannot be long sustained, and the total lost in twenty-four hours in hot countries is probably rarely more than 10 litres The salt content of sweat is so variable that the range of salt loss is hard to estimate Moreover, there is considerable variation in the response of the individual exposed repeatedly or continuously to heat, and it has often been shown that a degree of acclimatisation develops The features of acclimatisation are (1) an increase in the rate of sweating, (2) a lower pulse-rate, and (3) a lower body-temperature, as compared with the initial response to hot conditions, and these changes are accompanied by an increasing sense of well-being Different workers have given different times for the development of acclimatisation, but five to fifteen days covers most estimates, provided the subjects are exposed to fairly severe conditions and also do physical work of moderate intensity[1 2] The corollary to these findings is that the tolerance-time for severe conditions increases steadily during acclimatisation These changes in sweat-rate, body-temperature, and heart-rate do not continue indefinitely, after about fifteen days there is little further change, except that the sweat-rate may gradually decline over a period of weeks or months[3]

These findings form the basis for assessing water and salt requirement in conditions of heat ADOLPH[4] has shown that man cannot adapt himself to a diminished water-supply Furthermore, with one possible exception (the "free circulating water" of LADELL[5]), man cannot carry a reserve of water in the body the drinking of extra water, before exposure to conditions of water loss, is useless because the excess water simply induces a diuresis ADOLPH has also pointed out that thirst is a poor guide to water requirements, and severe dehydration can develop with an adequate water-supply available, when intakes of about 10 litres per day are needed It might seem that with a diminished water intake a high sweat-rate would fall, and so lead to a rise in body-temperature, but it has been claimed that moderate water deficiency does not significantly alter the sweat-rate[6 7] This problem has been re-examined by LADELL,[5] who has analysed data from experiments carried out some ten years ago by the Medical Research Council team at the National Hospital for Nervous Diseases, Queen Square, London During short exposures to severe heat he found that abstention from water had no effect on the sweat-rate until the water debt exceeded 2 5 litres This point has considerable academic as well as practical importance The effects of acclimatisation and the considerable differences from person to person make the design of climatic experiments far from simple In conducting climatic experiments in hot environments, when the subjects are sweating freely, should they be allowed to drink at will, or should water be replaced strictly according to the sweat loss? Or should there be a fixed ration for them all? Clearly, it would be easier to plan experiments of this kind if water intake had in fact no influence on sweat-rate The problem was carefully investigated by ELLIS and his colleagues in the M R C team at the Royal Naval Tropical Research Unit at Singapore[8] They showed, quite clearly, that the amount of sweat secreted varied with the amount of water drunk It seems that the reason for the disagreement between these and earlier results was that ELLIS and his co-workers were able, thanks to the work at Queen Square and the experience of the research-workers there, to control more exactly the conditions for their experiments

LADELL[5] has also put forward the view that there is a volume of "free circulating water" which is approximately 2–2 5 litres, and that until this volume has been lost bodily function continues unimpaired This view is in accordance with his studies of water deprivation in temperate surroundings, where he found little change in the volume of urine secreted until twenty-four hours after water intake ceased In acclimatisation to heat this "free-water volume" may increase BASS et al,[9] after a very detailed study of acclimatisation in man, conclude that an important feature was an expansion of the extracellular fluid volume in the first few days of exposure to heat They believe that this expansion (in which the blood-plasma was included) was largely responsible for the greater cardiovascular efficiency which they regard as the essential feature of adaptation to heat We may provisionally conclude that water intake has a small but definite effect on the sweat rate, although further work is needed on a wider range of environments and water intakes

The question of salt requirement is equally important At present we know that the salt content of the sweat is determined by the salt intake, by the degree of acclimatisation, and by the severity and the duration of the exposure to heat MCCANCE[10] and others have shown that the commonly observed decline in the salt content of sweat with continued exposure to heat can be due to inadequate salt intake The studies of BASS et al, however, indicate that with adequate salt replacement salt is retained during the first few days of heat exposure, and, in their view, the retained salt is needed for the increase in the extracellular fluid volume Once this has been achieved, the kidneys excrete more or less salt, as required to maintain a balance Calculations of sodium-chloride balances depend for their accuracy on the techniques used to take a sample of sweat A convenient and widely used method is to collect sweat in an arm bag By this method, LADELL has produced a chart from which intracellular fluid volume can be calculated from the salt and water balances

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1 Robinson S Turrell, E S, Gerking, S D *Amer J Physiol* 1944 143 21

2 Ladell, W S S *J Physiol* 1951, 115 296

3 Adam J M, Ellis F P, John R T, Lee T S, Macpherson R K. Report (R N P 53/750) to Royal Naval Personnel Research Committee Medical Research Council, London 1953

4 Adolph, E F Physiology of Man in the Desert New York 1947

5 Ladell, W S S *J Physiol* 1955 127, 11

6 Robinson S *In* Physiology of Heat Regulation Philadelphia, 1949

7 Ladell, W S S *J Physiol* 1949, 108, 440

8 Ellis, F P, Ferres, H M, Lind, A R *Ibid*, 1954, 125, 61P

9 Bass D E Kleeman, C R, Quinn, M, Henschel, A, Hegnauer, A H *Medicine, Baltimore* 1955, 34 323

10 McCance, R A *J Physiol* 1938, 92, 208

having posed their question they can only go on doing their best until some magic answer arrives It seems that this is a situation which needs breaking up, and that nothing is so likely to do it as to persuade doctors to take a new and controversial view of the basic assumptions they have made

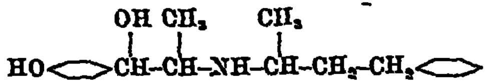
The effects on physicians of holding this common, simple, and perhaps unfounded view have been many One tendency has been that whenever they get into difficulties with classification they are apt to adjust their definition So wedded are they to fatality that a patient who lives, especially if treated by a method they do not themselves practise, is readily accepted as having had some other disease until he dies, but then cancer is still likely to be written on his death certificate however long he may have been symptom-free When to this attitude is added a knowledge of the overriding importance of the nature of the tumour to any result which can be obtained by any treatment, a hopeless view of excellent work may further depress enthusiasm Eagerness and confidence too easily pass to the thoughtless and the quacks To many, however, a growing knowledge of the variety of behaviour exhibited by tumours under different circumstances is bringing healthy doubt as to the validity of the old simple thesis while the obvious advances in diagnosis, and in surgery and radiotherapy, bring new enthusiasm and hope The growing interest in organisation and control that has followed the demonstration that the whole course of the disease can be influenced by alteration in hormone balance is adding impetus to this changing conception The growing recognition of the importance of biological predeterminism in human cancer, whereby the stage is set for the behaviour pattern which is to follow by the degree of dedifferentiation and the mitotic-rate established, is helping in the better selection of treatment method and leading to a sounder understanding both of what is possible and of what has really been achieved The slow penetration of this view through the general body of medicine seems to be due chiefly to the fact that so few people are primarily concerned, and to the combination of fatalistic and miraculous frames of mind which have flourished amongst doctors far too long What the middle-man wants from clinicians are ideas born of long experience, minds receptive to implications derived from basic research, and an unbiased attitude which makes all possible forms of aid available to every patient according to his need and not according to the skills of the first specialist he sees

As the man on the bridge looks into the future he wonders if any real appreciation of the cancer problem as a natural phenomenon, stripped of shame, to be accepted, coped with, but never conquered, will come easily It may well be the general public that is most ready to accept it and to find in it relief from fear The medical effort may become more firmly concentrated on prevention and postponement of disorganisation The initiative may pass into their hands once more so that they see this problem again as primarily their own job and not as somebody else's, as a job not really any more difficult because it can never be finally disposed of one of great importance in medicine and very well worth doing So much of value is already being done, its worth is underestimated only because it does not seem to provide a simple answer in terms of survival to all the impossible questions put A doctor's job is to continue to learn, to comfort, encourage, relieve, and to cure when he can, it is no part of his business to become a mere disinterested spectator waiting for a miracle to occur against the whole force of Nature The cancer problem is ours, and we must see to it that more people actively engage in the clinical research work so necessary if the sensible and possible advances are to flow from the application of new knowledge

DILATAL IN THE TREATMENT OF INTERMITTENT CLAUDICATION IN THE CALF MUSCLES

D N WALDER
M D Brist, F R C S, F R C S E
SENIOR LECTURER IN EXPERIMENTAL SURGERY IN THE UNIVERSITY OF DURHAM

'DILATAL' is a recently introduced drug which is claimed to increase muscle circulation It was synthesised by Kulz and Schneider (1950) from an adrenaline-like basal substance, parahydroxy ephedrine, to which by substitution a lengthy side chain had been added to give phenyl-iso butyl nor-parahydroxy ephedrine



$$\mathrm{HO{-}C_6H_4{-}CH(OH){-}CH(CH_3){-}NH{-}CH(CH_3){-}CH_2{-}CH_2{-}C_6H_5}$$

It is known that adrenaline given by continuous infusion intravenously to man increases the resting muscle blood-flow (Allen et al 1946) Kulz and Schneider were looking for a substance which would have this effect without the side effects of adrenaline and would be active when given by mouth

Wiemers (1951) showed that dilatal 0 1 mg per kg of body-weight given intravenously to anæsthetised dogs and cats lowered the blood-pressure and moderately raised the pulse and respiration rates The coronary circulation was increased, but there was only a slight change in cardiac output Plethysmography of the hind limbs of dogs showed an increase in blood flow of 200–300%, which lasted for 10–15 minutes The vasodilator effect was shown to be greater in the muscle vessels than in the skin vessels

If such an effect could be paralleled in man, dilatal might be of value in treating those forms of peripheral vascular disease affecting muscle blood-flow and associated with intermittent claudication

Dilatal has been extensively used clinically in Germany for many conditions, but few of the trials reported included a critical examination of its effect on muscle blood-flow Ostwald (1950) states that "vigorous stimulation of muscle circulation was observed" but gives no figures Hensel et al (1955), in America, using the calorimetersende to measure muscle blood flow, state that in 8 of 10 healthy persons the blood flow increased up to 250% of the resting value, and the increase lasted for 50 minutes when dilatal was infused intravenously for 10 minutes In England Riddell et al (1954) studied the effect of dilatal 5 mg per kg of body-weight given by mouth to healthy adults and noted, among other changes, a transient increase in flow, measured by plethysmography in the calf and foot, to twice its normal resting value for about 10 minutes and a slightly greater increase in the blood flow of the hand From these observations they concluded that the main effect of dilatal was on the skin vessels rather than the muscle vessels It is doubtful whether their results are statistically significant

The published evidence does not provide a satisfactory answer to the questions whether muscle blood-flow in man is enhanced to any significant extent by dilatal or whether patients with intermittent claudication can benefit from it It was therefore decided to submit it to a trial by clinical experiment

Clinical Trial

After consultation with the makers it was decided to give a dose of 2 5 mg (one tablet) every 2 hours (preferably after meals) during the day, starting at 8 A M and finishing at 6 P M A course of tablets lasting 8–9 weeks was given

52 patients were collected from the hospital outpatient department The criteria used in their selection was that

And how do people spend their leisure? There is very little information, though plenty of baseless belief, on what different sorts of people of different ages do with their time, and how this is changing with the coming of television, for instance On this, as on a great deal of work psychology and sociology, the labour of research is waiting to be done But the doctor's task, as champion of the individual's welfare, is above all to remind the planners of the new industrial age of the diversity of individuals Automation will not bring happiness with its riches unless it is planned for men

Annotations

TUBERCULOSIS THEN AND NOW

THREE medical journals in this country are concerned exclusively with diseases of the chest and tuberculosis The youngest of them, *Thorax*, was founded in 1946, *Tubercle* started 27 years earlier, in 1919, and the oldest, the *British Journal of Tuberculosis and Diseases of the Chest*, published its first number 49 years ago, in January, 1907 The special number marking its golden jubilee has a series of articles under the general title "Fifty Years On—Then and Now," and its impressive record of progress is summed up in an editorial which wisely draws attention to the present need to define the limits of the specialty in radically altered and rapidly changing conditions "The attainment of a comprehensive chest service which will include respiratory tuberculosis and all other chest disease *integrated with other branches of medicine* must surely," the journal says, "be our aim, with prevention, diagnosis, treatment and after care, including rehabilitation, coordinated as one continuous process"

At first sight few will dispute this policy, but it would perhaps be wise to examine its implications more fully before they become accepted as self evident The study of diseases of the chest is an established specialty and it should continue to be one the subject, even without pulmonary tuberculosis, is quite large enough to justify a special compartment But it cannot be assumed from this alone that a "comprehensive chest service" is desirable Neurology is an accepted specialty, but a comprehensive neurology service has, as far as we know, not been suggested Is there a place for a comprehensive heart service or skin service? The idea of a chest service does not appear incongruous, because it develops from an established and familiar institution—the tuberculosis service But it is hard to believe that diseases of the respiratory system, other than tuberculosis, differ so much in social significance that they need a service that cannot be provided by the general hospital If, as is hoped, the prevalence of tuberculosis decreases to such an extent that the resources of the chest clinics and chest hospitals become inadequately employed, it may be expedient to use them for purposes other than the prevention and treatment of tuberculosis But it may not necessarily be right to do so Before considering how chest clinics can best be employed, it might be profitable, though unpopular, to ask whether they should continue to exist at all, and whether the administrative stroke that attempted to turn 'tuberculosis dispensaries" into "chest clinics" and "tuberculosis officers" into "chest physicians" was indeed a wise decision The experience of the past fifty years has demonstrated the value of a comprehensive tuberculosis service, but those who advocate an equally comprehensive chest service must do more than rest their case on tuberculosis then and now

PENICILLIN V

VARIOUS penicillins with different properties have been produced by changing the strain of the fungus, the conditions of growth, and the composition of the medium So far, penicillin G has been the most widely used A new type of penicillin, penicillin V, or phenoxymethyl penicillin, has been produced by biosynthesis by growing *Penicillium chrysogenum* Q176 in a culture medium containing a special type of nutrient[1] Being an acid and acid resistant, penicillin V passes through the stomach unchanged, unlike penicillin G, which is partially inactivated by acid, and is largely destroyed by the acid gastric juice if taken by mouth[2,3] Oral absorption of penicillin G is variable and much larger doses must be given by mouth than by injection Penicillin V is stable as the free acid, and, unlike the other penicillins, need not be prepared as a metallic or organic salt It is dissolved and absorbed unchanged in the alkaline medium of the small intestine, and is therefore eminently suitable for oral administration Broadly speaking, its antibacterial spectrum is identical with that of penicillin G, but it is said to be 60% more active than the latter against *Staphylococcus aureus*[3] The two penicillins also differ slightly in their activity against *Micrococcus pyogenes* Because of slight quantitative differences in their action on the test organisms in biological assay, the dose of penicillin V is best assessed by weight in mg and not in units 60 mg of penicillin V is equivalent to 100,000 units of penicillin G by chemical assay

After penicillin V has been given by mouth, the blood levels are higher and more sustained than those produced by an equivalent dose of penicillin G[1] An oral dose of 120 mg (200,000 units) of penicillin V gives detectable blood levels six hours after administration, although the level declines after four hours[5] If this quantity of penicillin G is given orally, the blood level is approaching zero after six hours[6] The recommended dose of penicillin V is 120–240 mg every four hours round the clock, but for convenience the last night dose can be doubled to avoid awakening the patient in the night About 25% of an oral dose of penicillin V is excreted in the urine[7] It is more sensitive to penicillinase than penicillin G, and therefore any that is unabsorbed when taken by mouth is destroyed in the lower part of the gut by organisms producing penicillinase Like penicillin G, penicillin V does not readily penetrate the blood-brain barrier in normal subjects It is possible, however, that it may traverse it if the meninges are inflamed, just as penicillin G does Therapeutically effective amounts of penicillin V have been found to diffuse into the pleural and peritoneal cavities, and to be excreted into the bile[8]

In the treatment of mild to moderate infections due to susceptible organisms, 120–240 mg of penicillin V every four hours has been found effective If the infection is severe, it may be necessary to use a higher dosage (e g, 480 mg), and to give it more frequently[6] Reactions and sensitivity seem just as likely with this new penicillin as with penicillin G Gastro intestinal irritation with loose stools, no doubt due to altering the balance of the intestinal flora, has been reported[6,9] Preliminary reports with penicillin V in this country have been encourag

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[1] Brandl E Margreiter H *Österr Chem Z* 1954, 55, 11

[2] Parker G Cox, R J, Richards D *J Pharm, Lond* 1955 7 683

[3] Brandl, E *Wien med Wschr* 1953 103, 602

[4] Martin W J Nichols D R Heilman, F R *Proc Mayo Clin* 1955 30 467

[5] Proceedings of 3rd Annual Symposium on Antibiotics November 1955 Washington D C To be published

[6] Jones, W F, Finland M *New Engl J Med* 1955, 253 754

[7] Wright, W W, Kirshbaum A, Arret B, Putnam L F, Welch H *Antibiot Med* 1955 1 490

[8] Martin, W J Nichols D R, Heilman, F R *Proc Mayo Clin* 1955 30 521

[9] Hausmann E, Zischinsky H *Wien med Wschr* 1953, 103, 725

The work done during the exercise was calculated in the llowing way The patient did the exercise of raising mself up and down on his toes standing with a light ard resting on his head This board was arranged that it was pushed vertically up by the patient's head ery time he raised himself on his toes The board llowed the downward movement of the patient's head he lowered himself The movements of the board were corded on a kymograph smoked paper This provided permanent record of the height to which the patient used himself each time he went up on his toes By ultiplying the patient's weight (in lb) by the total f all the individual heights to which he raised himself in ft) the total work done can be calculated (ft -lb)

ABLE I—PATIENT'S OWN ESTIMATE OF IMPROVEMENT AFTER TREATMENT

Improvement in walking distance (yards)	Patients taking dilatal	Patients taking placebo
>300	7	2
151–300	3	1
0–150	8	8
N C	8	12
−0–150	0	1
Total	26	24

t = 2·71 P = <0·01

Results of Clinical Trial

Patient's Estimate of Improvement after Treatment

Table I shows that, of those patients who felt they had derived some benefit from the course of tablets, more came from the group who had been on dilatal than from the group who had been on the placebo A statistical analysis based on the patient's estimate of his increased walking distance after his course of tablets showed a sig[illegible]cant improvement in those who had taken dilatal [illegible]ared with those who had been given the placebo [illegible] 2·71 P < 0·01)

Measured Improvement Following Treatment

(1) The amount of work possible (ft -lb)
(2) The duration of work possible (min)

In neither of these factors did the patients who had dilatal for 8 weeks improve to such an extent as to make the results significantly different from those of the patients who received placebo tablets When the two factors are plotted as a scattergram—one for those patients who received dilatal and one for those patients who received placebo tablets—there is a remarkable similarity in the distribution of the points (figs 2 and 3)

(3) The rate of doing work (ft -lb per min)
(4) The resting blood-flow (ml per 100 g per min)
(5) The greatest post exercise blood-flow (ml per 100 g per min)

There was no significant difference between the results obtained after treatment by the patients on dilatal and those on placebo tablets either in the improvement of the rate of doing work (t = 0·66, P > 0·5), improvement of resting blood-flow (t = 0·95, P > 0·3), or improvement in greatest post-exercise blood flow (t = 0·33, P > 0·9)

(6) Duration of post-exercise hyperæmia

If dilatal produces a more efficient circulation in the calf muscles, it might be expected that the post-exercise hyperæmia would not last so long in the patients on dilatal as in those receiving placebo tablets In fact, there was no significant statistical evidence to indicate that dilatal had materially affected this factor (t = 0·21, P = > 0·8)

TABLE II—INFLUENCE OF PREVIOUS TREATMENT
Patient's own estimate of improvement

Previous treatment	Patients taking dilatal		Patients taking placebo	
	Total	Improved	Total	Improved
None	5	5	4	2
Sympathectomy	14	10	13	5
Tolazoline	7	3	7	4

TABLE III—INFLUENCE OF PREVIOUS TREATMENT
(Number of legs showing improvement (amount of work possible) after treatment

Previous treatment	Patients taking dilatal		Patients taking placebo	
	Total	Improved	Total	Improved
None	9	6	8	2
Sympathectomy	28	14	26	18
Tolazoline	14	6	14	7

(7) The influence of the previous treatment

When the results are examined from the point of view of the patients' treatment previous to the trial (tables II and III), it is seen that the best results with dilatal were obtained in those patients who had received no previous treatment The patients who had been treated by sympathectomy benefited more than those who had received a previous course of tolazoline No statistical analysis of these results has been attempted because the number of individuals in each group is so small

TABLE IV—EFFECT OF DILATAL ON RESTING BLOOD FLOW OF RIGHT AND LEFT CALVES OF PATIENTS WITH INTERMITTENT CLAUDICATION

Case no	Resting blood flow before dilatal (ml per 100 g per min)	Dose of dilatal (mg)	Peak resting blood flow after dilatal (ml per 100 g per min)	Increase (%)	Duration of blood flow above pre-dilatal level (min)
1	R 0·6	2·5 (oral)	R 2·8	350	50
	L 1·0		L 1·7	70	15
2	R 1·4	„	R 1·1	0	0
	L 1·2		L 1·3	8	0
3	R 3·7	„	R 3·7	0	0
	L 2·7		L 2·7	0	0
4	P 0·8	„	R 1·1	40	30
	L 2·4		L 6·6	170	[illegible]
5	R 0·5		R 0·5	0	0
	L 1·7		L 1·7	0	0
6	R 0·8		R 1·2	50	30
	L 1·1		L 1·8	60	20
7	R 0·6	5 (oral)	R 0·8	30	60
	L 0·8		L 1·4	70	40
8	R 2·3	„	R 1·8	0	0
	L 1·2		L 0·9	0	0
9	R 0·6		R 0·6	0	0
	L 6·9		L 5·6	0	0
10	P 0·7	5 (I M)	R 0·7	0	0
	L 1·0		L 0·8	0	0
11	R 0·9		R 0·5	0	0
	L 1·2		L 2·1	75	25
12	R 2·0		R 1·6	0	0
	L 1·2		L 1·1	0	0

Results of Acute Experiments

Some patients showed a transient improvement in resting blood flow when given dilatal The peak improvement in one case was 350% Many patients, however, showed no increase in blood-flow after a course of dilatal (table IV)

Discussion

Perhaps one of the most interesting points brought out by this trial is the spontaneous improvement of some patients on the placebo tablets Figs 2 and 3 show that 22 of 48 (45%) of the legs of the patients receiving placebo tablets were improved at the end of their course in that the patients were able to do more work in the same time or for a longer time, whereas 22 of 51 (43%) of the legs of patients taking dilatal were improved This observation emphasises the importance of having a control series of patients when clinically testing drugs of this type in a condition such as intermittent claudicafull anticonvulsant potency after the mice had undergone bilateral nephrectomy The anticonvulsant property of the sulphonamides seemed to be related to carbonic anhydrase inhibition, but it was evidently not dependent on the production of metabolic acidosis In fact further experiments showed that when acidosis was induced in mice by administration of ammonium chloride, *only a very slight degree of protection against* convulsions was conferred Millichap et al next turned their attention to carbonic anhydrase in the brain They found that after administration of equivalent amounts of the two drugs sulphanilamide was present in the brain in a concentration fifty times greater than that of acetazolamide Since acetazolamide was one hundred times more powerful an inhibitor of carbonic anhydrase, it was evident that after equal doses acetazolamide would exert twice the degree of enzyme inhibition This corresponded with the observation that acetazolamide was twice as effective as sulphanilamide in the prevention of seizures Moreover, the two drugs had their strongest anticonvulsant action at a time when the inhibition of carbonic anhydrase was greatest

It is not yet clear in what way inhibition of carbonic anhydrase in the brain prevents convulsions Not all anticonvulsant drugs act in this way, since phenobarbitone, phenytoin, and troxidone do not inhibit carbonic anhydrase[27] Inhibition of carbonic anhydrase leads to the accumulation of carbon dioxide at the nerve cell membrane, and the resulting decrease in the velocity of conduction of impulses may be related to the lowered susceptibility to convulsions Further research is proceeding on this subject, and meanwhile it has again been demonstrated that acetazolamide is a valuable tool in the study of fundamental cellular mechanisms

SALMONELLÆ OFF THEIR BEAT

DURING a period of three months salmonella infections were acquired by 5 hospital patients Investigating these cases, Kunz and Ouchterlony[28] found the source of the organisms in a previously unsuspected food product —namely, dried brewers' yeast Each of the 5 patients had been fed by stomach-tube In the wards and diet kitchens concerned, none of the staff were carriers of salmonellæ, and attention was turned to the tube-feeds At the time of the infections the preparation of the tube-feeds did not include boiling or heating of the ingredients or of the finished product Dried yeast and spray dried milk powder were common to all the feeds given to the infected patients, and (rather unexpectedly) the yeast it was that showed the presence of salmonellæ on culture

To culture salmonellæ from the yeast it was necessary to examine large samples, each of from 50 to 100 g, and to leave them in contact with 200 ml of water, saline, or broth for from six to twenty-four hours at 30–37°C before culturing Several 1 or 2 ml aliquots of the suspension, each in 10 ml of selenite and of tetrathionate broth, were taken for culture and thereafter the ordinary procedure was followed Examination of small samples without preliminary "hydration" gave negative cultures from batches of yeast subsequently proved to contain salmonellæ The way in which the yeast became infected during manufacture was of interest because yeast is only one of many dried foods all of which may be subject to the same hazards Salmonellæ were not found either in the equipment or in yeast from the culture tanks, separators, holding tanks, drying drums, or intermediate conveyors It was only during the final stages of milling, screening, and packing that salmonellæ were occasionally found Finally, it was established that the bacteria were being introduced into the factory through a ventilating duct, and when the incoming air was filtered the contamination ceased It is very likely, although not proven, that the ultimate source of the salmonellæ was the excreta of animal This speculation is of particular interest in view of the report by Rohde[29] of an outbreak of salmonella infection in *Hamburg, in 1954,* which was traced to pastry, the original source of the infection being apparently wheaten flour from a mill heavily infested with rats and mice

A third unexpected vehicle for the transmission of salmonellæ was recently discovered in Melbourne by Wilson and Mackenzie[30] who, investigating an outbreak of typhoid fever, found a variety of salmonella species, including *Salmonella typhi*, in desiccated coconut produced under very primitive conditions in Papua and imported into Australia

Knowledge of these unexpected sources of salmonellæ may help and even stimulate day-to day inquiries into food-poisoning incidents But the main burden of the problem of food-poisoning lies in discovering how to control the familiar sources of infection One useful lead in this connection is the evidence produced by Anderson and Stone[31] that spray dried milk manufactured in warm weather, especially near the end of a day when the equipment needs cleaning, may actually contain not only abundant staphylococci but, in all probability, their pre formed toxin also, which is well preserved by drying

A useful and comprehensive survey of many other and more familiar problems of food-poisoning was given by a group of distinguished contributors to a symposium on Food Microbiology and Public Health which was held at Cambridge last July by the Society for Applied Bacteriology[32]

THE USE OF AN AMBULANCE

IT is reported[33] that an ambulance service refused to carry a doctor, a nurse, and drugs to help a patient who had collapsed in his home The reason given was that an ambulance is provided, according to the regulations, "to convey patients where necessary," and that it is not the duty of the ambulance service to convey doctors and drugs A neighbouring ambulance service undertook the task, apparently on the principle that it is better to do what appears necessary, and to make inquiries afterwards It may well be that a private car or a taxi could have been used, and this was pointed out at the time, but many people will be left with the feeling that regulations were interpreted too strictly on this occasion Of course the organisation which sticks most carefully to its regulations is most likely to seem efficient in the eyes of authority, but it will rarely be able to react quickly to the unexpected situation for which no regulations provide Those who declined to respond to this call for an ambulance may say that "urgent" calls are often exaggerated and sometimes unnecessary, and that speed is seldom as important under these circumstances as many people believe Certainly this particular patient died in a few hours, and there was probably nothing more that could have been done to save him But that is hardly the point there should be no doubt in anybody's mind that the utmost has been done for a patient, and the facts reported in this case will not dispel all doubts ifficult to conceive that a circulating toxin or metabolite should cease to function with amputation of the lung.

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[28] Kunz L J, Ouchterlony, O T G *New Engl J Med* 1955 253 701

[29] Rohde, R *Arch f Hyg u Bakt* 1955, 139, 148

[30] Wilson, M M, Mackenzie, E F *J Appl Bact* 1955, 18 510

[31] Anderson P H R Stone D M *J Hyg Camb* 1955, 53 387, see annotation *Lancet* Feb 4, 1956 p 240

[32] *J Appl Bact* 1955, 18 162

[33] *Liverpool Echo* Jan 16, 1956

Wyburn Mason (1948), however, stated that in two cases of hypertrophic osteoarthropathy that were known to him mere ligature of the pulmonary artery without removal of the lung had the same immediate effect in relieving arthropathy as excision. This might be assumed to support the theory of a circulating toxin arising from the neoplasm. Hansen (1952) described the association of arthralgia with bronchial carcinoma in four cases of his own. In three of these resection led to complete relief of symptoms due to osteoarthropathy. In the fourth case the operation was abandoned after extensive dissection of the hilum. Although no vessels were tied the pain disappeared as in the other three cases, and he speculated as to whether hilar neurectomy had brought about this result.

It has long seemed evident to me that only a neural reflex could explain the abrupt and consistent cessation of pain; and in the cases mentioned by Wyburn Mason (1948) I believe that the arrest of symptoms was due, not to the ligature of the pulmonary artery, but to the fact that, as in Hansen's case, clearance of the hilum with severance of the nerve-fibres entering it, was first performed.

Operation

In the pursuance of this belief I have now performed a number of operations, mostly on patients with inoperable bronchial carcinomas accompanied by hypertrophic osteoarthropathy.

In several patients I performed as complete a hilar clearance as possible, dividing the pleural investment and all the fibres of the vagus or sympathetic entering the root of the lung. In these cases the joint pains were relieved as effectively as in other cases treated by pulmonary resection. In two patients who had clubbing and arthralgia exploratory thoracotomy alone had no effect.

As the vagus branches to the lung are easily recognised and isolated, I next tried division of these alone avoiding all interference with the rest of the hilum.

Case-reports

Case 1.—A man, aged 53, in February, 1953, noticed that his feet and legs had become swollen and painful, and he had to give up his work on this account. He was admitted to hospital where his knees also swelled and became painful. Pain also developed in arms and wrists and was so severe that it kept him awake at night.

Examination.—Clubbing of fingers and toes. Effusions in both knees and elbows with limitation of movement and swelling of interphalangeal joints. Tenderness of tibiæ and humeri. Radiography showed new subperiosteal bone formation on the right femur, and a mass at the right hilum.

Operation (May 11).—Right thoracotomy: an inoperable carcinoma was present at the hilum accompanied by numerous carcinomatous mediastinal glands. All the branches of the vagus entering the hilum were identified and cut. Biopsy showed polygonal cell bronchial carcinoma.

Postoperative Course.—Immediately after operation all joint pain was abolished and limb movements at once greatly improved. On Nov. 20 his doctor reported: "He is going downhill and losing weight, but the pains for which he had his neurectomy have never recurred." The patient died on Feb. 16, 1954, without having had any recurrence of his joint symptoms.

Case 2.—A man, aged 49, in January, 1953, first noticed swelling of ankles, wrists, and hands. February: onset of aching pain in knees and elbows which kept him awake; movement of these joints greatly limited. March: pains worse.

Examination.—Gross clubbing of fingers and toes. Swelling of wrists and ankles. Radiography showed typical and extensive hypertrophic pulmonary osteoarthropathy of long bones; carcinoma in the upper lobe of the left lung.

Operation (April 13).—Left thoracotomy: irremovable carcinoma arising in the upper lobe, extending into the hilum, and involving the arch of the aorta. The branches of the vagus entering the hilum were alone cut and the chest closed.

Postoperative Course.—All joint pains were dramatically relieved, and within twenty four hours the patient could flex his knees and ankles for the first time in weeks. On July 23 his doctor reported: "Going rapidly downhill, but no pain or swelling of joints."

Case 3.—A man, aged 68, was admitted to hospital on March 24, 1955, with cardiac infarction and was found to have an abnormal opacity in the lower lobe of his right lung. Squamous carcinoma cells present in sputum. Refused operation. In October he began to have rheumatism-like pains in elbows, wrists, ankles and knees, gradually becoming more severe and causing him considerable distress.

Examination.—Complaining bitterly of joint pains. Severe clubbing of fingers. Some swelling of affected joints. Radiography showed new subperiosteal bone on shafts of long bones, characteristic of hypertrophic osteoarthropathy.

Operation (Sept. 19).—Right thoracotomy: mass of neoplasm in right lower lobe; secondary deposits on surface of upper and middle lobes and on parietal pleura. The hilum of the lung was not touched but the right vagus was picked up high on the mediastinum above the vena azygos and cut.

Postoperative Course.—The following day all joint pains had vanished and they have never recurred. The swelling of joints subsided within a day or two. The patient was completely relieved of skeletal symptoms.

Case 4.—A man, aged 45, in August, 1955, began to have swelling and later pain in the ankles. A month later the knees were swollen and painful; and after a further month the wrists were swollen and elbows and fingers were stiff and painful.

Examination.—Gross clubbing of fingers and toes. Gross effusions in both elbows, knees, and ankles. Radiography showed typical hypertrophic osteoarthropathy of all the long bones; small opacity in the upper lobe of the left lung. Squamous cells were present in the sputum. The patient agreed to a two stage operation.

First Operation (Nov. 23).—A left intercostal incision was made and the presence of an operable carcinoma in the upper lobe of the left lung confirmed. Without disturbing any of the hilar structures the left vagus was picked up just distal to its recurrent laryngeal branch and cut; the chest was closed.

Postoperative Course.—The following morning the patient was asked if he felt any different. "Goodness me, yes," he said, "all my pains are gone; and look—I can bend my knees for the first time in weeks!" Within forty eight hours the effusions in his knees and ankles had almost disappeared, and neither these nor the joint pains have recurred.

Second Operation (Nov. 30).—The wound was reopened and a left upper lobectomy carried out. The tumour was a squamous cell carcinoma and there was no spread to regional glands. The second operation made no difference to the patient, all of whose joint symptoms had already disappeared in the week after vagotomy and before resection of the lung.

Case 5.—A man, aged 59, six months before admission, began to have aching pain in his knees and ankles and later in the wrists and elbows. The pains persisted until operation and were sufficiently severe to keep him awake at night. Some time after their onset he began to cough and to lose weight.

On examination his fingers were clubbed and there were small effusions in both knees. Radiographs of the chest showed collapse of the middle and lower lobes of the right lung, and bronchoscopy confirmed the presence of an inoperable squamous celled carcinoma of the bronchus. There was well marked new subperiosteal bone formation down the shafts of radius, ulna, tibia, and fibula on both sides of the body.

Operation.—A 6 in. long thoracotomy was performed just below the angle of the right scapula, and the fifth intercostal space was incised sufficiently to enable a retractor and a Nelson malleable light to be inserted. The upper lobe of the lung was drawn downwards to expose the superior mediastinum, and the vagus nerve picked up with a hook as it passed down a few inches below the thoracic inlet, and cut with long scissors. The incision was closed after the lung had been fully inflated; the whole operation lasted less than a quarter of an hour. The patient's pains were completely abolished for the first time in six months.

Discussion

In two of these five cases the branches of the vagus entering the hilum on the affected side (right in case 1, left in case 2), were cut; and this led to immediate and complete relief of joint symptoms and resolution of admitted to hospital suffer emotional upset Much depends on the constitution of the child Some have a more robust make-up than others, and can thereby withstand emotional deprivation with less adverse effect Their reaction depends, too, on the quality of their previous relationship with parents or guardians Moreover, if an earlier separation has been mishandled the child will naturally tend to react more violently to a second separation, because he is pre-judging it in terms of the last time

We need some means of sorting out these various types of case—the long-term from the short term emotional disturbance, the stable from the unstable, those likely, from their past experience, to settle down readily from those in whom we can expect a turbulent reaction Having screened them in this way, we need the administrative means to place each child according to his particular emotional requirements We need, in fact, a reception centre in each area The success of such a centre will depend on the understanding and insight with which the staff handle these children, and the staff must therefore be carefully selected and specially trained

It is not only the difficult child who may be emotionally disturbed Deprived children are too often judged by their nuisance value If they create no disturbance socially in their environment, it may be falsely assumed that they have settled down Yet some children who suffer serious emotional disorder, because of their personality make up, are unable to express their feelings outwardly Instead, they "bottle up" their emotions within themselves, and so tend to withdraw into a state of dreamy detachment and apparent apathy, which may readily be mistaken for evidence that they have equably accepted their substitute home Such children "take it out" of themselves instead of "taking it out" of their environment Because they abstain from provocative behaviour and appear quiescent, it does not follow that they are less disturbed than their more aggressive fellows

REAL PARENTS AND FOSTER PARENTS

We are familiar with the economic and social conditions which contribute to the disruption of the family unit—unemployment, overcrowded houses, ill health, the death of a parent, and so forth It is perhaps not so widely recognised that the stability of family life may be seriously undermined by emotional factors, especially adverse emotional experiences in the early childhood of the parents A father or mother who has been deprived in childhood may lack the security and maturity to foster lasting family ties Unwittingly such parents perpetuate in their own children the faulty attitudes of which they originally were victims as children Emotional deprivation, which we recognise as an effect of family breakdown, may also be one of its causes If we are to prevent the dissolution of family ties, we must give as much attention to this cause as to the more obvious social factors We must try to rehabilitate these problem parents to avoid another generation of problem children

Much has been said and written about the paramount importance of keeping the family together, but in my experience far too many children are removed from their homes because of material conditions If it is true that adverse emotional factors can disrupt the solidarity of the home, it is equally true that positive emotional factors can do much to offset material degradation No matter how deplorable the physical conditions, and how severe the material privations, where there is strong family affection and close emotional bonds we should never break up that family with the sole object of improving its living conditions Children will tolerate incredible conditions of material deprivation so long as their emotional ties remain intact Conversely, they will fret and become emotionally disturbed, no matter how much we improve their physical surroundings, if in the process they are emotionally deprived By all means let us try to upgrade their living conditions, but always on the foundation of preserving the family unit

If a child has to be taken into care our aim should be to maintain constancy throughout the period, and to avoid disturbing changes in his surroundings and in his new relationships To this end, it is important to make one officer responsible for the child Whatever decisions are taken for the child's welfare, this officer should carry out these procedures direct with the child, and interpret to him the decisions taken on behalf of the department

Similarly we should, as far as possible, avoid moving children from one home to another Once they are placed in an environment, chosen to meet their particular needs, every effort should be made to keep them there, so that they learn to achieve the sense of belonging which is so vital to their well-being

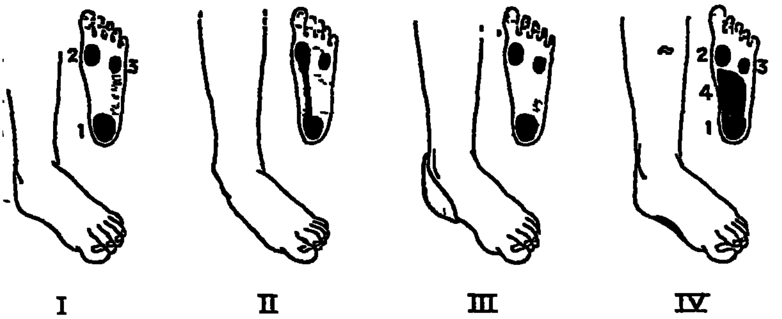
To avoid distressing change we must prepare the ground carefully with prospective foster parents, before asking them to accept the care of a potentially difficult child It is not enough to be satisfied that the foster mother is a stable and kindly soul, that she has warm maternal instincts and personal integrity, and that she maintains a good standard of hygiene and cleanliness in her home These qualities are necessary, but it is equally important to make sure that she has the capacity to understand the child's emotional difficulties and to tolerate his provocative behaviour, should it develop It is vital to find the right foster parents for a particular child Having found them, it is as important to stand by them with encouragement and support, in order to help them to surmount the initial period of adjustment, because at this stage the child may begin to test them It is unfair to them and the child to leave them to cope unaided without regular guidance and technical advice

In my hospital department I bring together a group of these foster-mothers, who are each having to contend with similar problems We meet regularly, and we thrash out together the difficulties which have arisen in the day-to day conduct of the children in their charge There is no doubt that it helps them enormously to discuss their individual problems in a group They take fresh heart at finding that other people have to face similar problems, equally provoking, and by discussion, with my prompting, they come to a deeper understanding of these deprived children, and they learn how to modify their own attitudes.

CONCLUSION

When deprived children present problems in their behaviour, or in their failure to conform within a given environment, we must interpret their conduct in terms of their past experience and emotional make up We must remember the emotional stresses to which they may have been subject, and we must not judge them by our standards, because we are looking in on them from the outside, as secure and well adjusted observers, while they are looking out at us from the inside, from a private world very different to ours—a world fraught with insecurity and doubt

When they resort to provocative behaviour in their efforts to test their new relations, we must remember that they are prompted, not by reason or by cold logical thinking, but by deep seated emotions of which they may be only dimly aware, and certainly not able to control without our help If we fail to provide for them the emotional haven which they need, the consequences may well be far reaching for society and for the child If we succeed, our reward is the child's return to the ranks of well adjusted society



g 2—Manner of weight bearing I, in normal foot (weight is borne on heads of first and fifth metatarsals and on heel), II in flat foot (unnatural weight bearing along inner border of foot), III with corrective heel-seat (normal tripod weight bearing is resumed), IV, with arch-support (a fourth and abnormal weight bearing surface is added)

uffer the disadvantages of the tilted elongated heel It s the first method which in a positive manner, forms and evelops a normally arched foot

The idea of the corrective heel seat is based on two remises

(1) With the forefoot held flat on the floor, inversion of the eel produces an arch, and the greater the inversion the igher is the arch In other words, with the heads of the first nd fifth metatarsals bearing weight normally in the shoe, orrection of the eversion of the heel corrects the flat foot A vertical heel gives the flat foot a normal arch

(2) The growing foot develops and functions in the shape n which it is held—i e, if the growing foot is held and allowed to function in the normal shape it will "set" in the normal shape An extreme example of this was provided by the now discarded Chinese practice of constantly binding the feet of baby girls into a "club" shape With growth they developed fixed club feet Similarly, if we allow children's feet to function with a normal arch, they develop normally shaped feet Moreover, if the foot is so held without arch supports—as the heel seat acts—it will develop a strong arch and strong foot

The heel seat shown in figs 4 and 5 is so constructed that it fits snugly into the back of the shoe, boot, sandal with heels, or even slipper, so long as the stiffening of the heel of the shoe, boot, slipper, or sandal is strong enough to maintain it in position When snug in the back of a shoe the inner surface of the heel-seat is in the shape of a normal heel in the normal vertical position As soon as the child puts on the shoe with a heel-seat, any eversion of the heel is corrected, and it is a virtue of the appliance that the child does not feel any discomfort

Results

Fig 5 shows the immediate effect of the heel seat on the shape of the foot Fig 2 shows the manner of weight bearing

I, in the normal foot

II, in the flat foot with unnatural weight bearing along the inner border of the foot

III, with a corrective heel seat (there is restoration of normal tripod weight bearing)

IV, with an arch support (there is still an abnormal weight-bearing surface)

After heel seats have been inserted, the child's gait is almost immediately and immeasurably improved "Pigeon toed" or splay-feet gaits are corrected, and the child is more agile and less awkward The effect on gait can be assessed from the way in which the shoes wear down Whereas previously the heels of the shoes wore down quickly on the outer side and the heel-seat became deformed, with the corrective heel-seat the heel wears evenly and the shoe maintains its shape Moreover shoes last at least twice as long before they need repair

I have been using heel seats for more than seven years, during which I have prescribed them for about 500 children I find that the average time a child must wear the heel seats constantly before the arch is "set" is from two to two and a half years The arch is then strong and permanent, and no further treatment is required

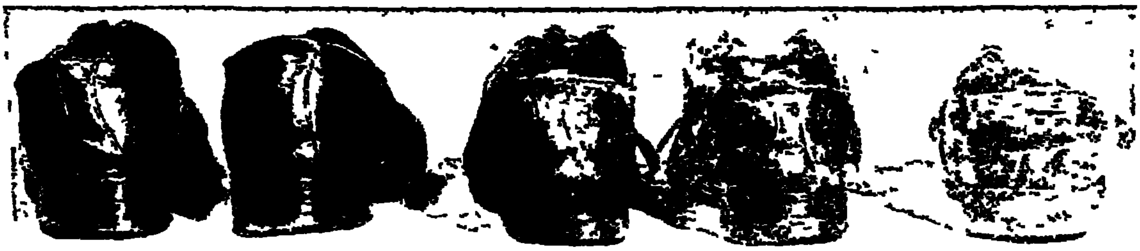


Fig 3—Stages in deformity of shoes of one schoolboy He not only wears down heels on outer side but also deforms heel-seats. When heels of shoes are purposely tilted deformity of heel-seats still results

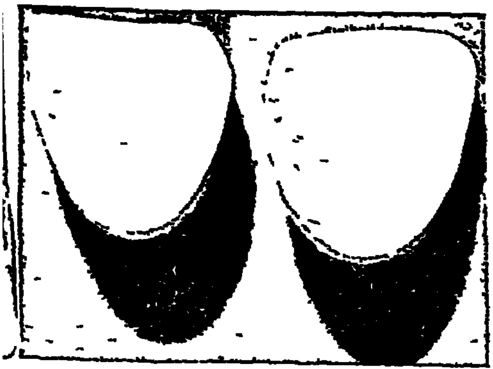


Fig 4—Corrective heel-seats

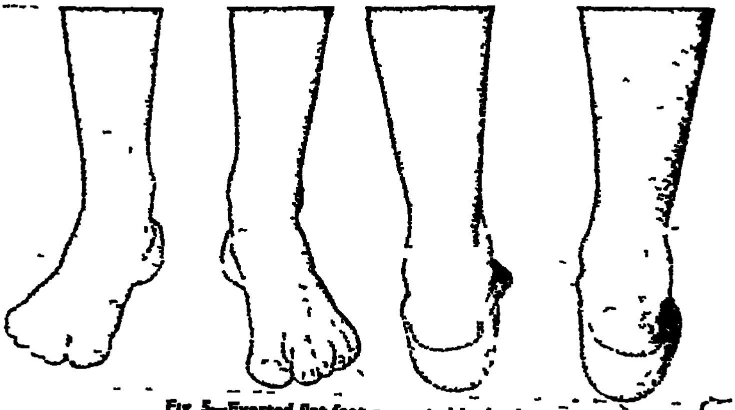


Fig 5—Everted flat feet corrected by heel-seats

In the Mental Hospital *

FACTORY IN A HOSPITAL

A A BAKER
M D Lond, D P M

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A POLICY of providing work, under factory conditions, for patients in mental hospitals would have far-reaching consequences In this article I shall offer some personal reflections based on experience at Banstead Hospital, where an experimental workshop established by a Medical Research Council unit now employs 40 women and 20 men

WORKING CONDITIONS

We needed to find floor space where a considerable number of patients could work under supervision, and we sought the advice of the local Factory Inspector, who visited the hospital to see the rooms available The most suitable site was a large ward, 80 × 30 ft, which had provided sleeping accommodation for 60 patients Following an active treatment, rehabilitation, and discharge policy, there were sufficient vacancies on other long stay wards to enable this dormitory to be cleared It had adequate lighting, and tables were provided from the hospital workshop by converting old bench-type tables which had been turned out of the wards when modern furniture was introduced

The men do piece work for a motor factory, and the women assemble cardboard boxes, and over a 25-hour working week they have been able to earn between 10s and £2 weekly This may seem a low scale of pay, but it is more than patients can earn by ordinary hospital work such as floor-scrubbing, laundry work, needle work, or ward chores, where pay ranges from 1s to 5s a week. This has led to immediate repercussions in that many of the better workers in the hospital departments have become discontented and wish to move to what is called "the box factory" We have therefore decided that the conditions on which a patient goes to the box factory shall be (1) that he has been an inpatient for several years, (2) that there is a reasonable possibility of his being discharged from hospital, and (3) he should have proved his stability and willingness to work by a period of useful service to the hospital departments It has been realised that patients doing hospital work have been paid too little and the upper level of pay for hospital work has been raised to 10s We hope that the deteriorated psychotic patients on the long-stay wards, who in the past may have spent years sitting in corners, can now be persuaded to do elementary chores in the ward under supervision When they have succeeded at this employment they may be tried outside the ward, with less supervision If this proves successful they can then move to one of the hospital utility departments, such as the laundry or linen room, and after a successful period of work there, can go to the box factory, from which the next step is to leave hospital for ordinary employment

The nurses have shown some ambivalence towards the project Many have been sceptical and felt that factory conditions could not be reproduced within hospital or would fail for lack of cooperation in the patients We are pleased to record that almost all patients have proved far more successful than expected Some ward sisters, understandably, were anxious lest their best ward workers would be taken away and given factory work Again this fear has been largely unjustified, for we have always found it possible to replace the ward workers who have gone to the factory by other patients within the ward There is no doubt that if a patient gets the reputation of being a good ward worker this may prove a disadvantage both to him (or more probably her) and to others on the ward She may unconsciously settle down to a routine where she receives a fair amount of reward and approval for her efforts and therefore be less likely to make the effort to get out of hospital The other patients have less incentive to work, since the work is done for them Thus removal of the good ward worker may lead to fresh progress among others who were previously considered unemployable

EARLY RESULTS

One problem which will soon have to be faced is that many patients working in the factory find that their way of life is highly satisfactory They receive all the benefits of hospital life—full privileges, board and lodging, clothing, television shows, social outings, and even summer holidays They are now able to work under pleasant conditions and receive considerable pocket money Many could well say to us that they cannot obtain such situations for themselves outside hospital and be reluctant to leave However, this has not happened so far Of the first 20 patients who went to our factory some four months ago, 3 have already left hospital The length of stay in hospital of these 3 patients was nineteen, twenty-four, and four years All have gone to full time employment under normal working condition

The improvement in the patients who have been working in the factory is obvious Apart from the 3 who have already left hospital to return to the community, several who were previously on disturbed wards have moved to better wards and others have earned more privileges Ward sisters spontaneously say that these patients take more pride in their appearance, have more self-confidence, and are showing a fresh interest not only in their life in the hospital but in the possibilities of leaving This is true of patients who were considered "institutionalised" and for whom the prognosis under ordinary hospital conditions had been very poor

NEW USES FOR OUR MENTAL HOSPITALS

There are eight other large mental hospitals within a few miles of Banstead Hospital, and I estimate that together the mental hospitals of the area contain several thousand potentially employable people In the present state of employment, when there are more jobs than people and when firms are willing to offer piece work, it is relatively easy to arrange work-therapy for the hospital patient If the hospital system were reorganised so that work-therapy replaced the traditional occupational therapy, there might be disastrous results should under employment cease, and we must not forget that the factory work introduced into some mental hospitals in the early 1930s was abandoned during the economic depression On the other hand, it is clear that the desire to create normal living and working conditions for mental patients is part of the general trend towards their more humane treatment, and on this if no other ground our work therapy policy should be continued

If many patients prove their ability to work at a level which will enable them to be self-supporting outside hospital, we shall have to face another social problem Only a third of these long stay patients have any known relative, friend, or contact outside hospital, and this means that when they are well enough to leave hospital it will be necessary to find for many of them accommodation as well as work Even with the improvement in housing in the past year or two it is still difficult for a healthy and active person to find satisfactory lodging, and for our long stay patients, whose initiative and drive is diminished, it will be an even harder task We feel,

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* A group of articles chiefly concerned with the value of active occupation and work for mental patients and the means whereby it is best provided

f E E G abnormalities in children with pains[1] Such a reponderance, small though it is, is however made up argely of focal spikes, which we do not consider to be ndicative of epilepsy

If "epileptiform" records alone are compared in the wo groups (table II), the children without pains show ather more abnormalities in the resting records, while f children with a normal resting record those with bdominal pains produce more "epileptic" responses ith hyperpnœa and photic stimulation

None of the differences between our two groups is tatistically significant at the 5% level of probability

Discussion

It is difficult to discuss "abdominal epilepsy" without lefining "epilepsy," the undefinable Our remarks are onfined to an alleged association between recurrent bdominal pain and epilepsy Our conclusions are based on the premise that a group of children with epilepsy shows a significantly higher proportion of characteristically abnormal E E G s than does a group of non-epileptics

In all four groups of children—hospital and school children, with or without recurrent abdominal pains—the distribution of abnormal E E G s was similar The comparative figures are substantially unaffected, whether resting and/or evoked records are considered The similarity between the four groups suggests that E E G abnormalities and recurrent abdominal pains are not associated or inherently related

We infer that the suggested causal relationship between abdominal pains and cerebral dysrhythmia may be based on (*a*) a failure to compare E E G s with those of apparently normal children of similar ages and attainments, and (*b*) a consequent acceptance of E E G variants as indicative of epilepsy

We realise that a small proportion of children with epilepsy also have recurrent abdominal pains Most, if not all, however, can be recognised if the history of fits, turns faints, spells, &c, is meticulously taken, as we attempted to do in our children with pains and in our control series As a sole manifestation of epilepsy, abdominal pain must be rare But even the overt association of the two is relatively unusual, from our figures, and if the few children suffering from fits had not been excluded from our series the results would have been affected only to an insignificant degree Our cases differ in many respects from the series of 33 children with "cyclical vomiting" and a remarkably high number of E E G abnormalities reported by Millichap et al (1955) In that series there was admittedly some selection of cases (14 children had a history of fits), vomiting was periodic in type and prolonged, and abdominal pains occurred in only about half the patients

Since an abnormal E E G is admittedly much commoner in epileptic than in non-epileptic patients, our findings suggest the corollary is also true and that *children with no symptoms other than recurrent abdominal pains* should no more be considered "epileptic" than children without them

Summary

Electro-encephalograms were taken from 133 children with recurrent abdominal pains but no demonstrable organic disease and from 133 children of corresponding ages without abdominal pains A very small number with a history of fits were excluded from both groups

In the two groups the proportion with epileptiform E E G s was almost identical

Since epileptiform E E G s are significantly commoner in epileptic than in non-epileptic patients these findings lend no support to the view that there is a relationship between epilepsy and recurrent abdominal pains in childhood

We are indebted to Dr Grey Walter and to Miss E H L Duncan, M A., B.SC., for helpful advice, and also to the three recordists, Mrs A B Spear, Miss J P Rockett, and Miss V D Heaven, whose patient work with the children was of special importance

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RETROCLAVICULAR BLOCK DISSECTION IN THE DIAGNOSIS OF SARCOIDOSIS OF THE LUNG

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Sarcoidosis of the lung is less uncommon, and less benign, than was formerly supposed Increased knowledge of the disease, and more widespread use of tuberculin tests and mass radiography have been largely responsible for this disease being diagnosed more frequently.

At Solliden Sanatorium, which serves a population of 145 000 about 300 cases of sarcoidosis of the lung have been detected in the past five years

Criteria for Diagnosis

Unequivocal diagnosis of sarcoidosis of the lung is impossible We have adopted the following criteria

(1) The patient should have the typical history and signs and/or radiographic evidence The relative paucity of symptoms contrasts sharply with the extent of the lesions, which are widespread Hyperglobulinæmia should be sought

(2) Other diseases (e g, tuberculosis, pneumoconiosis, Hodgkin's disease, neoplasm, and the mycoses) should be excluded

(3) Corroborative histological evidence should be obtained by biopsy of lymph-nodes and by Kveim's test

Sarcoidosis can be diagnosed when only criteria (1) and (2) are satisfied, provided that lesions are found in at least three organs, but we are never fully satisfied without positive evidence from biopsy Most cases of suspected sarcoidosis of the lung are discovered by radiography, and in such cases there are commonly no enlarged superficial lymph-nodes or cutaneous lesions In such cases we have found retrocl

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[1] Walter (1950) has shown that so called diagnostic epileptic patterns can be evoked from normal resting records in some "normal" persons, a finding confirmed by Jewesbury (1952) Gastaut (1953) suggests that these evoked responses are probably better regarded as a measure of the convulsive threshold rather than as diagnostic of epilepsy

Disease He believes in local government and in a real, everyday, practical, partnership of local authorities with family doctors in the care of the sick which is why Bristol can show so interesting a group of clinics and potential health centres—the latest (the fifth to be built since the war) opened only the other day He has stood always for the integration of medical work and has often been able to make it a reality Long ago, as professor of preventive medicine and M O H, he was offering chemical and bacteriological services to practitioners, he coordinated the school services with those for maternity and child welfare, and under his inspiration the city was developing its hospitals with consultants and specialists drawn from the voluntary hospitals Latterly he has tended to think of the future M O H as increasingly an epidemiologist in the wide sense, and characteristically has acted on this thought by arranging for a medical statistical section to be set up as a joint venture of the city and university During the war [illegible] again in 1951 he visited America, and in 1949—the [illegible]r of his presidency of the Society of Medical Officers [illegible] Health—he spent four months in Greece as expert [illegible]viser to the American Mission *Looking at Pairy*, [illegible]e sees that public health is the career for excitement

Influenza

Laboratory confirmation has been received of virus-A influenza in the Stowmarket area There is similar confirmation in cases in the Camberley area, in a school outbreak at Otley, Yorkshire, and in an army unit at Caterham Influenza-like outbreaks continue to be reported from other areas Among these are outbreaks in two public schools—one in Berkshire and one in Lancashire There are indications of an increasing spread of virus-A influenza in many parts of the country but, on the whole, cases have been clinically mild, and the weekly claims for sickness benefit have not been much affected

Third Quarter in England and Wales

The Registrar-General has already published some preliminary figures for the September quarter of 1955[1] A more detailed analysis[2] has now appeared There were 3493 notifications of poliomyelitis in the quarter and the death-rate was 9 per million population In the corresponding quarter of 1954 there were 880 notifications, with a death-rate of 4 per million population Tuberculosis notifications in England and Wales totalled 9239 compared with 10,204 in the same period of 1954 The tuberculosis death-rate was 116 per million population, as against 146 per million the year before

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[1] See *Lancet*, 1955, ii 922

[2] Registrar General's Return for England and Wales for the quarter ended Sept 30, 1955 H M Stationery Office Pp 20 1s 6*d*

Infectious Diseases in England and Wales

Disease	Week ended January			
	7	14	21	28*
Diphtheria	9	4	10	4
Dysentery	696	687	890	867
Encephalitis				
Infective		1	3	5
Postinfectious	1	3	3	
Food poisoning	122	124	293	92
Measles, excluding rubella	3230	2308	1960	2130
Meningococcal infection	27	33	29	31
Ophthalmia neonatorum	23	26	31	35
Paratyphoid fever	8	9	10	4
Pneumonia primary or influenzal	850	897	796	836
Poliomyelitis				
Paralytic	41	35	23	21
Non paralytic	18	24	16	10
Puerperal pyrexia	259	209	245	263
Scarlet fever	740	714	1035	964
Smallpox				
Tuberculosis				
Respiratory	517	574	668	700
Meninges and C N S	8	9	11	19
Other	72	67	65	83
Typhoid fever	1		2	2
Whooping cough	1130	1269	1422	1537

* Not including late returns

Parliament

Hospital Farms

Replying to a short debate in the House of Commons on Jan 30, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the basis on which farming at mental hospitals had been conducted had always been accepted as the need for a green belt to provide security and privacy, and outdoor occupation for suitable patients There was no question of cutting down that type of farming The third basis was the value of the farm and garden produce in the diet of patients, particularly where large supplies of milk and vegetables were not always available As long ago as 1948 it was apparent that farming in many hospitals had developed into a large-scale venture undertaken for its own sake A circular was then sent to hospital authorities pointing out that the criteria for farming should fall into the three categories which she had mentioned Not much action was taken after this warning People who had prize farms tended to hang on to them A departmental committee was set up in 1952 to investigate the farming activities of these hospitals It reached the conclusion that Government's criteria were not always being observed It found that few patients were being employed on farm work as a form of occupational therapy Only 3 3% of male patients were employed on farming and 3 2% in gardening, and only 0 3% of female patients were employed The complexity of modern farming tended to make it less easy to use patients and there had been a steady increase of outside staff on these farms The legal position was that hospital management committees had no authority to run a farm except in so far as it provided occupation or food for patients The present position was that at Oct 31 last decisions had been reached about 126 farms Of these 47 were to cease, and 38 had to reduce their activities A further 81 farms had been surveyed, about which decisions had not been made

QUESTION TIME

Social Services and the Family

Replying to questions, Major GWILYM LLOYD GEORGE, the Home Secretary, said he had considered with care and sympathy the proposals made by Mrs Fisher's deputation in July last year, for a general inquiry into the social services concerned with the family, and by a deputation from the Magistrates' Association in November that the suggested inquiry should be coupled with a review of the working of the juvenile court system in England and Wales Mrs Fisher's deputation had drawn attention to the need for better coordination of the services in question This matter had already received much attention in the departments concerned, and the Government proposed to follow up, by departmental study and administrative action, the steps already taken to improve coördination of the local services at all levels and to secure a combined approach to a family's problems As regards the proposals of the Magistrates' Association for a review of the work of the juvenile courts and the treatment of children coming before them, he had come to the conclusion that the time was ripe for a new study of this subject, and he proposed to set up a committee to consider and make recommendations on the working of the relevant provisions of the Children and Young Persons Act, 1933, as amended

Both deputations had also drawn attention to the need to pay more attention to preventive work, and the committee's terms of reference would include consideration of the powers and duties of local authorities under the Children Act for preventing the suffering of children neglected in their own homes The membership and exact terms of reference of the committee would be announced in due course In order that interested organisations might have time to consider what evidence to submit, he contemplated that the committee should not start work before the autumn The Government believed that the action which he had announced would meet the situation and be of more practical value than a wide ranging general inquiry at the present time

Remand Centres

Replying to a question, Major LLOYD GEORGE said that he regretted that the need to restrict expenditure on Government parately from the main excised portion. Two large rainage tubes were inserted down to the bed of the xcised portion of the pancreas, discharged freely for a onth and were removed six weeks later. Biopsy owed an insulin tumour strangled by fibrous tissue.

The patient weighed 10 st. $11\frac{3}{4}$ lb. on Sept. 20, 1952 nd 9 st. $10\frac{1}{2}$ lb. on June 20, 1955.

Numerous tests applied to this patient excluded other ossible causes of her condition. Serial sections of the xcised portion of the pancreas have not yet been xamined; but, in view of the pathological report on he nodule, it is perhaps just as well that the more xtensive operation was done.

Reviews of Books

Clinical Neurology

A. B. BAKER, M.D., professor of neurology, University of Minnesota. New York: Hoeber. London: Cassell. 1955. Vols. I, II, and III. Pp. 2021. 20 guineas the set.

IN a book remarkable for the quality of the printing and illustration the thoughts of 64 American neurologists have been gathered. The mention of a few names will indicate the happiness of the editor's choices: Jasper (electro-encephalography), Woltmann and Kernohan (peripheral nerves), Breutsch (symptomatology and pathology of neurosyphilis), Kunkle and Wolff (headache), and Courville (cerebral anoxia). The book is a success and deserves a place in the reference library or on the bookshelf of the expert.

There are, however, some notable omissions: the effect of occlusion of the basilar and vertebral arteries is not considered in the chapter on vascular disease; there is no mention of peripheral neuropathies or cerebellar degeneration in association with neoplasia; some of the more recent evidence on the metabolic disorder in Wilson's disease has not been included; and the neurological effects of cervical spondylosis receive no notice.

Dr. Baker's aim was to present in encyclopædic form current knowledge of neurological diseases both common and rare, and to give an account of the many extensions of neurology into other branches of medicine. The first part of the first volume illustrates his attempt to systematise this amorphous subject. Thus, there are sections on history-taking and the technique of examination (admirably presented), followed by a fairly lengthy exposition of the accessory diagnostic methods. Later chapters deal with basic subjects, such as cerebral localisation, agnosia and aphasia, and cerebral anoxia. It is these basic chapters that first deviate from the editorial aim; for, although the radiology and the electro-encephalography are presented very lucidly, the consideration of the diagnostic implications of ophthalmology tails off into some untidy guerrilla warfare relating to angiomatosis retinæ, Wilson's disease, dystrophia myotonica, and other matters.

After the basic principles, there are essays, rather than chapters, on the various aspects of neurology. The very brevity of some of the contributions carries dogmatism at times too far. Moreover, some writers, in their attempts to give an authoritative verdict, have introduced contradictions; thus, the concept of narcolepsy on p. 1920 is totally at variance with that expressed on p. 1204.

In so large and complex an undertaking, such faults are inevitable, and the good easily outweighs the bad. Dr. Baker and his team have made a definite contribution to medical literature and their work will undoubtedly gain in value as it moves through further editions.

Whys and Wherefores in Tuberculosis

GEORGE DAY, M.D. London: National Association for the Prevention of Tuberculosis. 1955. Pp. 44. 3s. 6d.

A DELIGHTFULLY written booklet for patients by a physician of exceptional experience in the psychological aspects of tuberculosis. A short historical review is followed by concise common-sense epidemiological information, easily appreciated by patients. The factors affecting resistance are briefly examined and the different aspects of treatment simply and clearly discussed. While some medical readers may question one or two statements (e.g., "B.C.G. or vole bacillus vaccination will probably become accepted as a routine for new-born babies") every reader will be stimulated by this brief and intelligent review.

Anatomie radiographique du massif facial

M. BOUCHET, otorhinolaryngologiste des Hôpitaux de Paris; G. DULAC, electro radiologiste, ancien chef de service de la Fondation Curie; with the collaboration of R. PAILLEP. Paris: Masson. 1955. Pp. 187. Fr. 2800.

THE interpretation of radiographs of the classical projections of the nose, nasal sinus, and adjacent structures of the face depends on a sound knowledge of the detailed radiological anatomy of this region. The authors carefully define each projection and then describe its features with the aid of simple diagrams in the first instance, followed by more complicated "schemas" as extra details are added.

Nine of the commonly used projections are thus dealt with, and then follows a brief section on tomography in the anteroposterior plane, treated in the same way. The second part of the book is devoted to illustrations of radiographs, with fully annotated diagrams. The radiographs are designed as an exercise in interpretation of the standard projections and of some of their variants.

The authors hope to improve the standard of interpretation of "sinus" films, since they regard the reports "sinuses clear" and "sinuses opaque" as often very inadequate. To anyone who takes the trouble to work conscientiously through the "schemas," interpretation should be relatively easy, for the basic anatomy should then present no difficulty. The book is well produced and easy to understand by anyone with an elementary knowledge of French.

Psychosomatics

MAX HAMILTON, M.D., senior lecturer, department of psychiatry, University of Leeds School of Medicine. London: Chapman & Hall. 1955. Pp. 225. 21s.

DR. HAMILTON has covered the subject in an admirable way, avoiding diffuse theoretical discussion for mainly factual and experimental findings. His book is a readable and successful attempt to present, from a scientific point of view, emotional and environmental factors in disease.

The first chapter discusses the physiology of the emotions, with many references to fundamental work, such as that of Cannon; and later chapters describe such conditions as asthma, peptic ulcer, hypertension, urticaria, and many others.

Throughout, there is an unusually balanced presentation of the subject. The main points of evidence are given, and certain extremist points of view are criticised.

Smoking and its Effects

With Special Reference to Lung Cancer. SIDNEY RUSS, C.B.E., D.SC., emeritus professor, University of London. London: Hutchinson's Scientific and Technical Publications. 1955. Pp. 141. 8s. 6d.

PROFESSOR RUSS is here writing for the general reader, and sets out to cover the history and practice of smoking, including opium and hemp as well as tobacco.

Nine-tenths of his book, however, is concerned with tobacco-smoking, and nearly half of it with the special problem of smoking and lung cancer. To succeed in summarising the history, methods, and implications of smoking in so small a space would indeed be a feat; and though the style is easy and readable the arrangement of material is uneven and sometimes haphazard. The early chapters contain interesting information, but their general effect is sketchy, and the arguments put forward are open to question. The author says: "Smoking is a very deep rooted habit in the peoples of the world. Let us not try to stop it by methods which are almost bound to fail, but supplant the poppy and hemp by the tobacco plant." Though many would agree with him, even this small book contains evidence to suggest that the answer is not quite as simple as that.

Having spent most of his life directing and working in a laboratory for cancer research, Professor Russ gets into his stride when he comes to his main theme—the relation between tobacco-smoking and bronchial carcinoma. This

His Lordship thought that some such provision should be made, as the £750 belonging to the son would not last for ever. Maintenance ought not to be limited to the mere provision of food, clothing, and shelter, but should be extended to what were known as "comforts" in institutions of the kind in which the plaintiff now was. His Lordship did not think that the beneficiaries would consider it unfair on them if he altered the provisions of the will of the mother so that the son would be provided with 10s. a week, and he would order that the son should receive that sum out of the estate of the mother as from her death for his life or until cesser of his disability or until further order.

In re Pringle, Deceased.—*Chancery Division.* Vaisey, *J.* Feb. 1, 1956. B. S. Tatham (Crossman, Block & Co. for McKenzie Bell & Sons, Sunderland); K. W. Rubin (Bentleys, Stokes & Lowless r Criddle, Ord & Mickle, Newcastle upon Tyne) and Raymond alton (Speechly, Mumford & Craig for Saul & Lightfoot, Carlisle).

IRVINE G. R. MOSES
Barrister-at-Law

The Doctor's Bag

The director of a company of photographic printers d free-lance photographers was carrying photographic uipment in a shooting-brake for the purpose of his isiness. The car was licensed as a private car and he as charged with the offence of unlawfully using the car ithout the proper rate of duty—namely, the higher rate pplicable to goods vehicles—having been paid. The ustices dismissed the charge on the ground that the hooting-brake was not constructed or adapted for the arriage of goods, because they considered that "if the est is the nature of the 'goods' irrespective of the type f vehicle, then the carriage of a doctor's professional nstruments or a lawyer's text-books in a private car ight result in these offences." The prosecutor appealed o the Divisional Court, and counsel on his behalf agreed hat a doctor carrying his bag in a shooting-brake would e liable to the higher rate of duty, but not if he were sing a private saloon car.

Lord GODDARD, C.J., said that a shooting-brake was onstructed or adapted for the carriage of goods and if was used for that purpose the higher rate of duty had o be paid. However, if such a vehicle was not used n the carriage of goods, for hire or reward, or in connection with a trade or business it was not liable to the igher duty. It was not necessary for the court to ecide in the present case whether a doctor using a hooting-brake and carrying his bag of instruments with im would be liable, but his Lordship was far from saying hat it might not be so. The director of the photographic ompany was therefore liable to pay the higher duty. he case would go back to the justices with a direction hat an offence had been committed.

Taylor v. Thompson.—*Queen's Bench Division (Divisional Court).* ord Goddard, *C.J.*, Hilbery and Stable, *JJ.* Jan. 26, 1956. ounsel and solicitors: Rodger Winn (Treasury Solicitor).

C. J. ELLIS
Barrister-at-Law

Legislation on Sexual Crimes

The Government have decided[1] to introduce a Bill to onsolidate the statute law relating to sexual crimes, nd to the abduction, procuration, and prostitution of omen, and some kindred offences.

The proposed corrections and minor improvements include larification of drafting and removal of anomalies. Thus, he maximum punishment for attempted incest in the case f a man is two years, but in the case of a woman seven years. he reason is that the punishment for a man was originally wo years' hard labour—regarded as heavier punishment than even years' imprisonment—but in 1948 hard labour was abolished without any adjustment of sentences. The Government now propose to reduce the maximum penalty for this offence by a woman to two years.

The Government's decision to consolidate the existing law is not necessarily an indication that they have decided against major reforms. The proposed Bill will be introduced under the Consolidation of Enactments (Procedure) Act, 1949, which is designed to facilitate the consolidation from time to time of various portions of the statute law.

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[1] Consolidation of Enactments relating to Sexual Offences, etc. Memorandum. H.M. Stationery Office. 9d.

In England Now

A Running Commentary by Peripatetic Correspondents

HE got off his motor-bike and crossed the road towards me, but it was only as he reached the car that I recognised Kenneth. We felt awkward and shy with each other, and though I walked to the sidecar to meet his wife and baby daughter, my manner seemed false even to me. Normally, I am at ease with patients, but now I found myself over-hearty, embarrassed at the sudden reminder of a former intimacy.

Kenneth and I were intimate enough in the early months of 1947. I inherited him when—on my return from the war—a senior colleague handed me a block of his tuberculosis beds. Kenneth had collected several medals with the Commandos—also pulmonary tuberculosis, and, when I first saw him, after a right pneumonectomy in those pre-streptomycin days, he lay in bed emaciated and hectic. His bronchopleural fistula on the right side had led to mixed tuberculous and pyogenic empyema, and in his remaining lung a fresh focus was accompanied by a pleural effusion. By way of introduction, my colleague whispered his history to me at the foot of the bed, murmured of the hopelessness of any treatment, and moved on. Keen ears picked up the words and I saw Kenneth turn his face to the wall.

I came and sat by his bed late that night, and at first he tried hard to be indifferent. Without preliminaries, I sketched out a position that he might have found himself in as a Commando—retreat cut off, wounded, surrounded by a powerful, well-armed and invisible enemy. What, I asked, would he have done—surrendered? His reply confirmed my estimate of his quality. I reminded him of what he had overheard that morning, stressing that it was a sound opinion that none would dispute—was he still prepared to throw defiance at the enemy and fight back? Again, he left me in no doubt. I outlined his programme for the next two years—pointing out the pain, hardship, and boredom he must cheerfully accept—but as we shook hands I knew he would win.

When he left for industrial training in 1949, he was a little twisted in body—a 10-rib Schede does that—but his spirit was straight enough.

Driving away after that short, embarrassed meeting at my car-door, I could not help thinking how easy streptomycin and isoniazid had now made it all, but no-one could claim they had made it more interesting.

* * *

The county town lies some fifteen miles to the east of our village, and we can reach it by either of two roads—the old road or the new road. These run parallel and are nowhere more than a mile apart, but they are totally different in character. The new road has attracted to itself all the horrors of modern life, while the old road remains exactly as it has been for hundreds of years.

The new road passes through three villages, each with a charming name, and not so many years ago each was as beautiful as its name. Now the dominating feature in all three is the garage, guarded by rows of tall petrol pumps, littered about with cars in various stages of repair and innumerable advertisements. Half way along the road is a vast caravan site, where twenty years ago was a shady wood. Two miles further along is a sort of knacker's yard of old cars in every stage of disembowelment.

Then saddest of all we come to *Ye Olde Traveller's Rest*, a monument of imitation antique, its beams and panelling of plywood, its windows leaded with strips of black paper. Along the new road the trees and coppices are being gradually cut down, and little bungalows built in their stead.

How different is the old road. We feel we owe it an apology for being in a car; we ought to be in a wagonette, a stanhope, or at least a dog-cart. It passes through two villages; in the first is an ancient smithy, where once many horses put on their shoes and where the one remaining horse is still shod. As the blacksmith says, four hooves give him a little shoeing practice. In the second village is a wheelwright, who does better than the blacksmith, for there are more tractor-drawn farm carts needing wheels than farm horses needing shoes. Leaving

THE LANCET
LONDON   SATURDAY, FEB 11, 1956

Treatment of Infective Hepatitis

As we have no specific drug with which to attack agent causing infective hepatitis, treatment must irected to providing the best conditions for natural very In general this means regulation of diet and ision of rest The practical questions which arise what kind of food should be given and for how long patient should be confined to bed Different views e been expressed on these points,[1–5] but the wers can best be sought by carrying out a large and refully controlled therapeutic trial, as has recently been done by an American team working in the Far East [6] In a series of studies, patients suffering from infective hepatitis were allotted at random to different treatment groups The design of the experiment was arranged so that the doctor deciding to admit a patient to the investigation did not know what treatment the patient was to receive Careful checks were made to ensure that the treatment ordered was actually carried out The first inquiry into the effect of diet showed that patients forced to eat an abundance of calories, protein, and vitamins throughout their stay in hospital improved more rapidly than those patients eating only what they chose from a normally nutritious diet, but when they were examined a year later no difference was discernible between the two groups In a second investigation, diets containing either 3000 or 4000 calories (of which 19% were supplied as protein) were compared with ones of the same calorie values but containing only 11% as protein The diets with the higher protein content were associated with shorter illnesses At a follow-up examination the patients who had received the high-protein high-calorie diet showed a slightly higher incidence of mild residual abnormalities compared with the other three groups

A study of the effect of rest was more surprising acutely ill patients improved just as rapidly when they were allowed up and about the ward at will as when they were strictly confined to bed The duration of the acute illness, defined as the time from admission the finding of a serum-bilirubin level of 1 5 mg per 0 ml or less and a bromsulphalein retention of 5% or less in forty-five minutes, was similar with the two regimens There was no evidence that enforced bed rest led to a more rapid disappearance of hepatic tenderness or enlargement The recurrence of symptoms after discharge to duty was equal in the two groups, and at examination after a year no significant difference was noted In a further study, patients were subjected to severe exercise at a physical reconditioning centre, while others were kept in hospital and allowed to rest at will The strenuous activity began as soon as the acute stage of the illness (as previously defined) had subsided Those in the early-exercise group later showed significantly more minor abnormalities, such as rises in serum-bilirubin and bromsulphalein retention, as well as more recurrences of symptoms and hepatomegaly, but these features disappeared in spite of continued exercise When seen later, this group had more complaints of right-upper-quadrant pain and significantly more tender livers Chalmers et al believe, however, that these findings were associated with little clinical disability and that no definitely harmful effects were caused by this strenuous exertion during convalescence

It is important to emphasise that these experiments were carried out on previously well-fed healthy males *during military service It would be unjustifiable to* transfer the conclusions to the treatment of all cases of infective hepatitis Furthermore, as all the patients were transferred to a special centre, the various treatments were begun on the average about ten days after the onset of symptoms The results therefore do not apply to the initial stage of the disease, when strict rest may be of greater importance The results of a *high-protein diet have often in the past been conflicting,*[7–10] and from the clinical viewpoint the reduction in the duration of the illness, which is apparently sometimes achieved by diet, is generally not great In this recent trial the significance of some of the mild residual clinical features which appeared in those exercised early or forced to eat large high-protein diets is difficult to determine Hence, a doctor should hesitate before adding to a patient's discomfort by forcing on him a diet much greater than he feels inclined to eat Nevertheless, in treating patients of military age, Chalmers et al make certain recommendations as a result of these studies The daily diet for a patient with infective hepatitis should contain about 3000 calories, with approximately 150 g each of protein and fat During the stage of severe anorexia *the patient should be encouraged to take frequent* small feeds Although the high-protein diet was shown on the average to hasten recovery, critically ill patients with severe liver damage may be harmed by excess protein and they clearly require special treatment with only a maintenance amount of protein Chalmers et al believe that patients should stay in bed as long as acute symptoms persist, but as soon as they begin to feel well they should be allowed to get up regardless of the degree of jaundice Rest in bed for one hour after each meal should be enforced, but otherwise they should be permitted the freedom of the ward This moderate activity avoids the usual delay in overcoming the effects of long rest in bed and appreciably shortens the stay in hospital

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7 Hardwick C *Quart J Med* 1945 14, 223
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10 Capps R B, Barker, M H *Ann intern Med* 1947, 26, 405

satisfactory, and if there is lack of response this should be *a signal, not automatically* to start ringing the changes of other newer and more powerful antibiotics, but to reassess the case and reconsider the diagnosis The real indications for the tetracyclines need to be more clearly defined, there must be very few absolute primary indications for their use

These and other points related to the use of antibiotics need further study, for surely there are few other fields of medicine at present where *muddled thinking so abounds*

There was much to be said for the arrangements, before the tetracyclines were generally released in April of last year, by which these drugs were available through hospitals for prescribed conditions While I do not advocate a reversal *to this system in its entirety,* it did at least make one think twice before using the drugs It was a pity that similar restrictions did not apply to the young hospital residents, who were perhaps much more liberal with the tetracyclines than the general practitioners

he New Zealand government's bold step should lead our n Ministry of Health and all the leaders of our profession hink again how best to apply a rational policy on the use he antibiotics

Beckenham, Kent JOHN FRY

THE STRATEGY OF MEDICAL RESEARCH

SIR,—It is a pleasure to read your praise (Jan 7) of the ntly published volumes dealing with research in the ited States You rightly praise the unexpected finding ich leads to great results and deprecate the "local service tion" approach

You criticise the fact that a crutch will fetch more money han a hearing aid Any disease can have a crutch as a motto or sign You should praise the public relations of the friends of poliomyelitis and deprecate the tardiness of the friends of the *deaf There is much good will in the public toward* research, and all it needs is intelligent direction No one will have anything but praise for your support of fundamental research But practicality should not damn research either

There is a small factual error The Rockefeller Institute *is totally independent of the Rockefeller Foundation*

The last paragraph of your editorial causes the greatest alarm and I would like to make some comments These views of mine have developed over a period of years You state "this work should make us appreciate the value of our system by which grants to the universities and Medical Research Council are made through the Privy Council and are thus beyond any ill informed or undesirable political pressures" No doubt you mean governmental pressures and not medico political pressures The important point is to know how much money travels via the university or via non M R C channels to the research-worker and how much via the M R C Would it be fair to say that the M R C has a *virtual monopoly* of research monies? The basis of a democracy is a combination of independent and competing units, and research should be on the same sound basis If vitamin Q was being investigated by D A with M R C funds, would D B's request *for funds* to the M R C be well received if his views were divergent from those of the M R C 's advisers?

As the U S A was not considered to have a common law, the Congress formally enacted, in 1890, the "Sherman Anti trust Act" to declare illegal "every contract in restraint *of trade,"*[1] *to help* law abiding citizens who felt victimised Owing to continual vigilance this has been a useful statute The size of the groups involved is not important, and combinations which contribute to efficiency have not been destroyed

Whether the M R C acts in restraint of trade (in this case research) *depends on the activity* and strength of the competing agencies, which in this case would seem to be the local hospital committees and the universities The threatening aspect is the growth of the power of the M R C Concerted action is not monopoly, and the M R C has played a leading part in joint *clinical investigations* which deserves great praise

In discussing the Sherman Antitrust Act, Arnold[1] has said

> "Whether some of the largest and most exacting monopolies are directed by men with *criminal or benevolent* intentions is purely a matter of accident It is the results growing out of their operation which are significant for our purpose Actually the violation of antitrust laws by great industrial leaders does not usually fall in the class of *offences* which involve *moral turpitude* It is more like passing through a traffic light at high speed without the intention of *harming anyone This makes it less immoral* but not less dangerous"

Research *money with strings attached* is not dangerous if one can turn elsewhere, but research money given freely may be restrictive if no other source is available

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Iowa City,
Iowa, U S A J MACLEAN SMITH

EPIDEMIC KERATO-CONJUNCTIVITIS

SIR,—I was interested to read your annotation (Jan 28) which mentioned *an* outbreak of pharyngo conjunctival fever in America I have recently seen one or more cases of this condition in my own practice in South East London

On Jan 7 I saw A, aged 7, who had fallen ill the day before She complained of headache, a sore eye, loss of appetite, and general malaise She was pyrexial and had severe conjunctivitis in the right eye The pharynx was slightly injected and there were a few enlarged cervical *glands* The patient was treated with penicillin eye ointment, and later with sulphacetamide drops Neither of these affected the conjunctivitis The pyrexia persisted until the ninth day of the disease, when the temperature dropped to normal and the eye *condition began to clear* The *next day* the child was perfectly well Since the clinical picture conformed to the description of pharyngo conjunctival fever,[1] blood was sent for serological examination On the thirteenth day of the illness complement fixation tests, kindly carried out for me by the *Virus* Reference Laboratory, showed evidence of recent infection with the A P C group of viruses Six or seven days before she fell ill, this child was in contact with another child, who was reported to have had a similar illness This history fitted in with the incubation period of pharyngo conjunctival fever, but I later learned from the *family* doctor concerned that the second child had had a simple upper respiratory infection without conjunctivitis

On Jan 10 two brothers, B and C, aged 6 and 3, living in a self contained flat above A, began to have a similar illness, which lasted only four days B had conjunctivitis *in one eye,* but C had no eye involvement No serological investigations were made in these two cases

On Jan 14 A's mother had an attack of influenza, which lasted three days, and on Jan 13 the mother of B and C developed chickenpox

In view of the mild clinical course of pharyngo conjunctival fever, this *condition may* be *not* uncommon in this country

London, S E 26 R N JACKSON

BLOOD-TRANSFUSION

SIR,—Your leader (Dec 31) *and* subsequent *correspondence* reveal some ignorance of the scope and quantity of emergency work done at smaller provincial hospitals

The suggestion that the pathologist should be got out to perform every emergency cross match has already been dealt with If this proposal were *logically* extended, "the most expert available" surgeon and "the most expert available" anæsthetist should also be called out of bed to every emergency, and I have yet to hear that this is done

The suggestion that hospitals which have no resident clinical pathologist should not undertake *work for* which transfusion is often needed is obviously absurd At this hospital with some 350 beds (and there must be hundreds of a similar size and type), which has large orthopædic and maternity departments, as well as acute medical and surgical beds, emergencies requiring transfusion at *night are frequent* in one department or another Is it seriously suggested that all these emergencies should be sent to the nearest hospital with a resident pathologist, probably 25 miles away? Far from having a resident pathologist, we have but one registrar, in orthopædics, *and no resident* surgical officer, and a high proportion of the resident staff are in the pre registration stage

Lastly, as regards the practice of using *technicians for* emergency grouping and cross matching, I would point out that of the staff of seven in *this laboratory four* are either students or junior technicians, and I assume it is not suggested

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[1] Arnold T et al The Sherman Antitrust Act and its Enforcement Law and Contemporary Problems vol 7, Durham North Carolina

[1] Ryan R W O Rourke J I Iser G *Arch Ophthal, Chicago,* 1955, 54 211

VAN HEYNINGEN and WEINER,[11] however, have demonstrated that the composition of arm-bag sweat is always more concentrated than general body sweat, and therefore calculations of balances based on the arm-bag method will exaggerate salt loss. Since much of the published work on sodium-chloride balances depends on arm-bag sweat analyses, it may be that salt requirements in the heat have been overestimated. It is interesting that Nigerians are said to have an intake of only 7 g. of salt a day or even less, and it has also been reported that their sweat is more dilute than that of fully acclimatised Europeans.[12]

So far, most physiological work on the effect of long-continued exposure to heat has been concerned with the initial stages of acclimatisation, and until these were worked out it was not possible to distinguish clearly the more remote effects. The importance of studying these is evident; for, until the demands of the environment are understood, the complications introduced by disease will be much harder to comprehend. Future work should include not only the young men who have hitherto been the main subjects of climatic physiologists, but women and children as well. Normal physiological values should be established for tropical countries, since textbook figures are often applicable only to temperate zones. For example, the average daily urine output is usually given as 1500 ml., but in Singapore ADAM[13] has shown that the daily urinary output averages 1200 ml., and LADELL et al.[14] found that in Shaiba, before the extreme hot weather, the output was about 1000 ml., while in extremely hot conditions it fell to 700 ml. Until considerably more work has been done in the tropics, much of the advice given on salt and water requirements must remain empirical.

The Future of Work

AUTOMATION is a new word. The control of machines by machines is not a new idea, but the war-time development of electronics and of machines which can sum up a situation and adjust a process is making it a frequent idea in practice, and the automatic factory seems to lie ahead. It is part of the 20th-century material revolution which began with wireless, the automobile, and aspirin, and is now whirling through plastics, antibiotics, and atomic energy. Every invention, every new scientific application, in time transforms the conditions of human life, but it needs the shock of a new word to make people suddenly stop and consider where they are heading. Living from year to year and without a natural sense for recent history we quickly take for granted daily television, fresh foods out of season, the world's crises in the evening paper, and women at work in industry and the professions—as if they had been always so. Prof. LESLIE BANKS, in the paper on Industrialisation and Community Living, which we published on Feb. 4, said that Britain now has nearly a quarter of a million nurses and almost as many women teachers, and that the employment of men and women as clerks and in the distributive trades, in engineering and in chemicals, has greatly expanded in the last twenty years, while fewer are engaged in basic work like agriculture or coal-mining. "Two hundred years ago," the *Manchester Guardian*[1] remarks, "it took the efforts of every able bodied man to maintain a standard of living we would now call poverty. The Industrial Revolution changed that by making possible an enormous increase of individual productivity. . . . If instead of having 700,000 men dig 220 million tons of coal a year we generated the same amount of energy in nuclear power stations of the first crude design, less than 100,000 men would be needed."

Technological progress has been abolishing jobs for at least a couple of centuries, and creating fresh kinds of work also. What is new today is the speed of change, measured in fractions of a working life-time, and the numbers of people affected, in a society too highly organised to give the individual a free choice of occupation. A subcommittee of the United States Congress which recently reported on Automation and Technological Change,[2] thought that industry should provide organised re-training for workers, as well as financial compensation for the change of skill, and possibly change of abode, which the new work required. It recommended the government to collect statistics of occupational mobility, and to awaken people to the problems besetting their future employment, including the trend to larger impersonal businesses, the training of the elderly, and the threatened shortage of technicians and teachers of science in schools. Certainly if these problems are not solved we may expect unemployment and labour unrest as well as individual physical or mental breakdown. Modern industrial society already finds it harder to offer satisfactory employment to the dull, who need as much as other men to feel a sense of purpose in the community and to have an outlet for their creative urges. Mental hospitals already receive patients whose practical trouble is failure to find a satisfactory niche in life because their personalities belong to one of the minority groups, while modern society is planned more and more to suit the majority who cluster round the mean. A society which creates misfits needs advice on mental hygiene.

Professor BANKS raises also the problem of increasing leisure. He suggests that people might prefer to work a 60 hour week with 13 weeks' annual holiday rather than a 40-hour week with a fortnight, and the immediate value of this idea is its challenge to the present conventions of off-time. After all, the plan of resting the seventh day of every week was an invention of Semitic races, not practised in classical Rome or in other ancient civilisations. The British country-house classes expanded it into the weekend which everyone now expects; but habits can be changed. If health and output were the sole consideration (which they are not) it might be better to have one day off in every four, in some kinds of work anyway, rather than two at the end of every week. But it is noteworthy that the Soviet Union, having tried such an arrangement, has returned to a weekly rhythm.

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[11] van Heyningen, R., Weiner, J. S. *Ibid*, 1952, 116, 395.
[12] Ladell, W. S. S. *Ibid* 1950, 112, 15P.
[13] Adam, J. M. Personal communication 1956.
[14] Ladell, W. S. S., Waterlow, J. C., Hudson, M. F. *Lancet*, 1944, ii, 491.

[1] *Manchester Guardian*, Jan. 24, 1956.
[2] Report of the Subcommittee on Economic Stabilisation of the Joint Committee on the Economic Report. United States Government Printing Office, Washington, 1955.

Since the new regulations were introduced in 1952 no clear definitive statement has been made on this point The problem of tuberculosis is still not receiving the immediate and earnest attention that it should If routine annual tuberculin testing of all school children, with the tracking down of the source case in tuberculin positive cases, radiographic examination of all hospital cases, both inpatients and outpatients, radiographic examination of immigrants, vagrants, and especially of selected age groups such as men over 45, were carried out there would be an appreciable rise in the notification rate, and also a slight rise in the mortality figures All this would suggest that we were gradually getting to know more about the level of tuberculous infection in the community and make us realise that not only is the problem great but we are still a long way off the solution

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KENNETH MARSH

ACUTE MASTITIS

SIR,—With reference to Dr Mavis Gunther's article (Jan 28) I should like to make the following observations

> "Attempts to find an organism failed on the five occasions when blood was taken for culture as the temperature rose", but bacteriological examination of the secretion from the affected gland would be more logical, on account of the fairly effective milk-blood barrier
>
> Intramammary antibiotic therapy through the nipple or otherwise into the secretion may be very effective by providing a high concentration of the substance where it is most needed

In the cow there is little risk of mastitis with cessation of milking, provided a long acting antibiotic, such as procaine penicillin in oil (as little as 100,000 units every two days for a week), is introduced into the teat canal as a prophylactic There is abundant evidence that in the cow 100,000 units of sodium penicillin administered through the teat canal daily for four to five days will give excellent results in acute streptococcal mastitis, usually clinical cure results in twenty four hours, and bacteriological cure in three to four days Bovine staphylococcal mastitis is not so responsive, but unless intramammary antibiotic therapy is used the prognosis may be poor

Chwilog, Caernarvonshire

T HUGHES ELLIS

POLIOMYELITIS

SIR,—I have read Mr Daw's letter (Jan 21) with great interest

Last term my five year old daughter started going to the council infants' school After about three weeks she developed a cold, so I decided to take her but to have a word with her class mistress As it happened, I met the headmistress, and to my surprise she said she would much prefer the child not to come until the cold had cleared

Later that morning I received a visit from the sanitary inspector, who asked why my daughter was not at school I explained When he murmured something about polio which I did not hear correctly, I said, "Well I suppose it's possible although it looks like an ordinary cold, but why pick on us?" He looked astonished and said, "But didn't Miss—— tell you? A child in your daughter's class has polio That is why she asked you to keep her at home"

I decided not to send my daughter back to school for at least a week Meanwhile, I received a daily telephone call from the sanitary inspector's office to inquire about her health During the first of these telephone calls I asked whether this secrecy was council policy, but was assured that it was entirely a matter for the headmistress to decide

Later I visited the officer in charge of infants' education in the borough, which is in London It was perfectly clear from his reaction that it is the policy of this council to keep all knowledge of poliomyelitis as close a secret as possible He said that, had I asked the headmistress point blank if there was polio in the school, she would in all probability have said No He attempted to justify this extraordinary attitude by saying that parents would be frightened and keep their children away if they knew

Now, personally I find it reasonable to be frightened of poliomyelitis, and clearly I am not alone in this, because at the same time a reputable public school circularised the parents when they had one or more cases

Surely it is quite wrong to suppress a thing of this nature After all, one takes quite a different view of a cold if it is known that the child has been in contact with a case of poliomyelitis, then one can at least prevent it from making further contacts Secondly, it is folly to think that such things can be *kept secret* As Sir Winston Churchill well knew there is much less danger of panic if people are told bad news by authority than if they find it out through distorted rumours

M E C BLACKLAY

"MUNCHAUSEN'S SYNDROME"

SIR,—A man corresponding to the one described in previous letters[1] was seen in the casualty department on Feb 2 Clinical and radiographic findings were identical with those reported by Dr Baker (Jan 28) He complained of severe headache and giddiness and ataxia He denied ever having been a seaman and gave his occupation as vocalist and mental nurse On being offered analgesics and the services of a psychiatrist he left the hospital with some indignation His ataxia was observed to have disappeared when he reached the street This patient had previously been seen here on May 30, 1955, with a story that he had been admitted unconscious to Queen Adelaide Hospital, Dublin, five days previously and had undergone a radical mastoidectomy there At that time he had a right facial palsy

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A O ROBSON

THE EPIDEMIOLOGY OF LUNG CANCER IN NEW ZEALAND

SIR,—Dr Eastcott (Jan 7) is to be congratulated on a first class contribution to the study of the ætiology of lung cancer Dr Joules (Jan 21) is rather critical, but completely fails to present any evidence to justify such remarks as "Dr Eastcott has failed to note the scientific evidence from many parts of the world that there is a causal relationship between the number of cigarettes smoked and the incidence of this disease"

The death-rate from lung cancer among males aged 45-54 years is almost three times as high in this country as in New Zealand Are we to conclude, from what Dr Joules says, that this is due to the fact that the former group has smoked three times as many cigarettes, on the average, as the latter group? It seems rather unlikely But supposing it were so, it must follow that pipe smoking is a relatively harmless pastime, for the total consumption of tobacco per head is about the same in both countries, so that the inhabitants of New Zealand must have smoked three times as much pipe tobacco as the average Englishman Would Dr Joules agree with this view?

Dr Eastcott has not only demonstrated large differences in the incidence of lung cancer between native born New Zealanders and immigrants from the U K, he has also shown large differences in the latter group—between those who left the U K when under 30, and those who left after that age Perhaps Dr Joules could give some cogent reasons for expecting a difference in smoking habits between these two groups

It would be foolish to deny the existence of a relationship between smoking and lung cancer, but it seems equally foolish to insist that this is the only factor involved, especially in view of a recent paper by Stocks and Campbell[2] Some towns in England, for instance, have twice as much lung cancer as others It is unlikely that the inhabitants of the former towns smoke twice as much as the inhabitants of the latter These observations, it seems to me, are not at all incompatible with the idea of some sort of synergistic effect between smoking and air pollution

London N 7

J TORRANCE

SIR,—I should like to correct a misunderstanding by Dr Joules (Jan 21) of my article He says I have "failed to note the scientific evidence from many parts of the world that there is a causal relationship between the number of cigarettes smoked and the incidence of lung cancer" This is not true I have followed this work with the greatest admiration, and in particular I regard the work of Doll and Bradford Hill as a classical study that will stand out in history like that of such men as Snow, Budd, Ross, and ing[10, 11] and trials in Germany and Austria have shown its value by mouth, particularly in children[12, 13] It may be that many of the infections that have been treated with penicillin parenterally in the past may now be treated with penicillin V orally In conditions in which higher blood-levels are needed (bacterial endocarditis, for example) the simultaneous administration of probenecid is an advantage[8]

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[1] *Lancet*, Jan 14 1956 p 107 *Ibid*, Jan 21 1956, p 160 *Ibid* Jan 28 1956 p 207

[2] Stocks P Campbell J M *Brit med J* 1955, ii 923

At the Annual Symposium on Antibiotics held in Washington last November a speaker from Sweden said that 40% of the penicillin used in his country was now in the form of penicillin V tablets, and another speaker said that in Austria 30% of all the penicillin administered was given as oral penicillin V The drug has now been available in this country for several months

STAPHYLOCOCCAL INFECTIONS AFTER CARDIAC SURGERY

Postoperative sepsis is more common than is generally supposed, and, in spite of antibiotics, it may threaten the patient's life or at least his hope of a quick recovery In some branches of surgery particular attention has been given to the prevention of wound infection perhaps this is because the tissues concerned are especially liable to infection and because the results of sepsis after certain types of operation are unusually serious It is certainly true that the literature on this subject has been particularly concerned with intracranial, orthopædic, and plastic surgery and with the treatment of burns[14–17]

It seems that in the extending work of thoracic surgery similar problems are arising Operations on the lung are often complicated by staphylococcal infection of wounds and intrathoracic spaces[18] Fleming and Seal[19] now report 9 instances (5 of them fatal) of serious staphylococcal infection after operations on the heart or great vessels 7 of the operations were for mitral valvotomy and 2 for division of a patent ductus arteriosus An endocardial infection, demonstrated post mortem, was certainly responsible for 2 deaths and probably for 2 more Auricular fibrillation, associated with a myocardial abscess, was the cause of another death In the 4 surviving patients the clinical findings and positive blood-cultures suggested endocarditis Coagulase-positive *Staphylococcus aureus*, alone or in association with *Streptococcus viridans*, was the organism responsible in 6 cases It is particularly interesting that coagulase negative *Staph albus* was incriminated in the other 3 This organism was isolated from blood-cultures in each of these 3 patients, and in 1 it was also grown in pure culture from the mitral vegetations found at necropsy It was resistant to penicillin, and the patient's serum contained antibodies against it Fleming and Seal remark that failure to recognise the pathogenic rôle of *Staph albus* in this case led to inadequate treatment of the infection

Staph albus is a common contaminant and is often ignored when isolated from blood cultures There is good reason for the general belief that this organism is of lower pathogenicity than the related *Staph aureus* strains producing coagulase, but this is not to say that it cannot attack delicate tissues Bacteriologists who see a profuse and pure growth of *Staph albus* from cases of neonatal conjunctivitis may be easily convinced of this The susceptibility of the damaged endocardium to infection with *Strep viridans* suggests that this, too, is vulnerable to organisms of low virulence for other tissues, and it may well be that *Staph albus* can also cause endocarditis Fleming and Seal present good evidence, from their own work and from recent publications that this is so

They also discuss briefly the possible sources of infection in these 9 cases They believe that the chief risk was at the time of operation, although preoperative intravenous manipulations may have played a part They found that staphylococci were the main airborne organisms contaminating the surgeons' equipment and gloves, and these organisms may be introduced when a finger is put into the heart to dilate the mitral ring Another risk, not mentioned by Fleming and Seal, is that digital manipulations in a tight mitral valve probably cause extreme stretching of the glove rubber and may open minute holes through which organisms from the surgeon's skin can pass It has been shown that more than half the surgeons' gloves are punctured during lung operations,[18] and it would be interesting to know how often there is a puncture over the surgeon's finger after a mitral valvotomy With so many new materials about nowadays, something better than rubber could possibly be found for surgical gloves, but in the meantime thoracic surgeons might enclose the gloved finger in a freshly sterilised stall of some impervious plastic material immediately before putting it into the heart This might be preferable to Fleming and Seal's suggestion that prophylactic penicillin should be used to protect the patient against these infections

ANTICONVULSANT ACTION OF ACETAZOLAMIDE

Shortly after the introduction of the sulphonamides into clinical practice it was observed that sulphanilamide[20] and the dye 'Prontosil S'[21] were able to reduce the frequency of convulsions in some epileptic patients The sulphonamides are known to inhibit carbonic anhydrase[22] and thus produce acidosis, and it was thought that this acidosis was responsible for the anti-epileptic action, which was compared to the effect of the ketogenic diet Because of the toxicity of the earlier sulphonamides this observation was not widely explored Acetazolamide[23] provided a relatively non-toxic sulphonamide which was a powerful inhibitor of carbonic anhydrase, and it too has been used in the treatment of epilepsy in adults and children with, on the whole, favourable results[24–26] There may be side effects[24] and there are few cases in which acetazolamide is preferable to the standard anti-epileptic drugs On the other hand, one child whose epilepsy took the form of intense periods of hyperventilation was much relieved by acetazolamide[25]

Millichap and his co workers in the University of Utah[27] have studied the mechanism of the anticonvulsant action of acetazolamide in mice They confirmed that it prevented electrically induced seizures and was twice as effective in this way as sulphanilamide Acetazolamide was a hundred times more effective than sulphanilamide as an inhibitor of carbonic anhydrase Sulphathiazole, which does not inhibit carbonic anhydrase, did not prevent seizures in mice Millichap et al then found that both acetazolamide and sulphanilamide retained their

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10 Dove W L *Brit med J* 1955, ii, 1090
11 Bowerbank A G *Ibid* p 1029
12 Schindelmaisser, F *Wien med Wschr* 1953, 103 725
13 Simon A *Med Klin* 1954 49 2031
14 Cairns H *Lancet*, 1939 i 1193
15 Girdlestone G R, Bourdillon, R B McFarlan, A M *Ibid* 1951 i 597
16 Spooner E T C *J Hyg Camb* 1941, 41 320
17 Colebrook L Duncan J M., Butterfield, W J H *Lancet* 1947, i 321
18 Blowers R Mason G A Wallace K R, Walton M *Ibid* 1955 ii 786
19 Fleming H A Seal R M E *Thorax* 1955, 10 327

20 Yeoman J C *Brit med J* 1938 ii, 261
21 Cohen M E, Cobb S *Arch Neurol Psychiat*, *Chicago*, 1941, 46, 676
22 Mann T Keilin D *Nature, Lond* 1940, 146 164
23 See *Lancet*, 1955, i 706
24 Merlis S *Neurology*, 1954 4 863
25 Bergstrom W H Carroll, R F Lombroso C Davidson, D T Wallace W M *Amer J Dis Child* 1952 84, 771
26 Vivien P *Ann Méd* 1955, 56 95
27 Millichap J G, Woodbury D M Goodman, L S *J Pharmacol* 1955, 115 251

in his tortuous aorta, both on postero anterior and lateral views, completely consistent with atheroma

This finding, however, is not at all inconsistent with the theory that was proposed for the pathogenesis of atheroma formation, since the blood of hæmophiliacs obviously does clot, even if it takes longer than normal blood, and even though this patient did have a prolonged clotting-time (41 minutes), he had had 67 years to lay a little fibrin down on his aorta

I am grateful to Dr Benjamin Jacobson for allowing me to describe this case

Massachusetts General Hospital,
Boston 14, Mass, U S A JOHN R DAVID

INGUINAL HERNIORRHAPHY

SIR,—The "anatomical proof" by Mr Doran (Dec 24) of the inability of the conjoined tendon to act as a sphincter or shutter in relation to the inguinal canal seems to me to be built up on a false premise He takes a point on the linea alba below the umbilicus and claims that it cannot move in the long axis of the body so long as the sternum and pubis remain the same distance apart From this assumption he deduces that the conjoined tendon cannot shut down on the spermatic cord

The fallacy is that the linea alba is elastic, its length in the extended position of the trunk being at least 50% greater than that in the flexed position It is therefore illogical to claim that any point on it can be regarded as fixed, and it would be quite possible for points on its lower half to move towards the pubis on contraction of the abdominal muscles Much depends on the direction and power of the muscle fibres inserted into the linea alba, and it could be argued that since the pyramidalis muscles are the only ones which act almost parallel to the linea alba they will tend to pull down its lower part towards the pubis

Mr Doran may be correct in his claim regarding the absence of a shutter action, indeed, his own observations with radio opaque markers support this view But although he affirms that the lower fibres of the internal oblique muscle appear to run almost parallel to the inguinal ligament the anatomical insertion of the conjoined tendon is undoubtedly in part into the pubic crest and pectineal line, and fibres from the internal oblique and transversus abdominis arising from the inguinal ligament cannot reach such an insertion without arching over the spermatic cord Now, if the arched fibres of the conjoined tendon shorten when they are stimulated—and there seems to be no reason why they should not—their course must become straighter and this can only happen by their approximating more closely to the inguinal ligament

Manchester HERBERT HAXTON

DOMICILIARY CONSULTATION IN PSYCHIATRIC PRACTICE

SIR,—The problem of the community care of mentally disabled persons referred to by Dr Skottowe (Jan 28) has been partially solved in Holland by the establishment of sheltered workshops in some of the larger towns I recently visited one of these workshops in the Hague, and was most impressed by the way in which both mentally ill and mentally defective patients were gainfully employed This workshop has already been briefly described by Carstairs et al [1]

There are obvious disadvantages in mixing psychotic and defective patients, and plans have already been made for building new workshops where the two types of patient will be separated At present 290 patients (out of a total population of 600,000) are employed The staff consists of a works manager, 6 technical assistants, 7 nurses, and 3 clerks The whole enterprise is under the direct supervision of the city psychiatrist, Dr N Speyer The patients work a 48 hour week and are paid 40–80 cents per hour according to ability and output The "normal" factory worker is said to get 90 cents to 1 florin per hour (1 fl =2s approx)

Work is sent in from local factories, which also lend some of the necessary machinery and collect the finished products The work done includes making cardboard boxes, packing chocolates, machine riveting boxes, making articles of clothing with electric machines, assembling brake cables for mini motors, and book binding The patients live either in their own homes or in hostels and come to the factory by public transport, as the mentally ill patients improve they are found jobs in outside factories Psychiatric supervision is maintained by the department of mental health of the municipality of the Hague

If something of the same nature were to be started in this country there would be need for close collaboration between the local authorities and the regional hospital boards, but it would be a great pity if so potentially valuable a project were to be abandoned because of administrative difficulties By the use of such sheltered workshops not only could many patients be kept out of hospital but many of those now more or less permanently resident could be discharged with benefit to themselves, through prevention of deterioration and improvement in morale, as well as to the country as a whole by reducing the burden on the health service and helping in the production of goods

London, W 1 J C SAWLE THOMAS

"ESPRESSO WRIST"

SIR,—As far as I am aware no social medicine study has been made of the possible effects of the coffee bar epidemic which has swept London since the war A few visits will serve to convince an observer that there is much to discover both amongst those who serve and those who meet to drink Meanwhile, anyone who is contemplating such a survey is offered the information of an interesting orthopædic complication—"the espresso wrist"

de Quervain [1] described stenosing tendovaginitis at the radial styloid as long ago as 1895, and we are used to seeing cases amongst young mothers engaged in unaccustomed nappie wringing, seamstresses working overtime for the Christmas season, and high speed obsessional typists To these we can now add the espresso machine operator For each cup of coffee he has to carry out three to four strong movements of the wrist into full radial deviation, and in an average day may carry out several thousand similar manœuvres (Barmaids are no doubt immune because the beer is pulled with wrist held stiffly, the elbow being flexed)

Fortunately the acute condition responds readily to one or two well-placed injections of hydrocortisone and a slight change of technique, and the counter attack by the tea drinkers—we are told—is already well under way

London W 1 A W LIPMANN KESSEL

ECLAMPSIA

SIR,—I am grateful to Dr Schuurmans for his informative letters (Dec 17 and Jan 21) The information he supplies conforms with my ideas on eclampsia

In Holland, during the war, eclampsia almost disappeared with a low protein, low carbohydrate diet, which bordered on starvation In the Belgian Congo, among two million natives living on an "inadequate diet," also presumably of low protein and low carbohydrate content, not "a single case of toxæmia has ever occurred" (What a wonderfully thorough system of antenatal care they must have in the Congo to be able to report this!)

On the other hand, in Australia Hamlin has eradicated eclampsia with a high protein, low carbohydrate diet Clearly eclampsia disappears in spite of, and not because of, a high or low protein intake, but high protein intake is to be recommended because it helps to abate hunger when mothers are only eating little carbohydrate Equally clearly, in all three groups, it is the low carbohydrate intake which is the vital factor in preventing eclampsia and toxæmia

Coloured women in the Southern States of the U S A, eating relatively more carbohydrate, suffer, despite "the same antenatal care," much more commonly from severe toxæmia than do white women, who are eating more protein and (presumably) relatively less carbohydrate, in the Northern States But no antenatal care will prevent toxæmia if the diet is faulty—i e, if the carbohydrate is excessive The "care" merely observes the effects of the toxin on the mother and tries to palliate them, having waited for the toxin to be produced before it acts Production of toxin, as I said (Nov 5), can only be prevented reliably by controlling diet, appetite, and weight

If only the suicidal saying "eating for two" could be forgotten, and if a new motto, "eat starchy foods sparingly,"

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[1] Carstairs G M, Clark D H, O Connor N Lancet 1955 ii, 1023

[1] de Quervain, F Korresp Bl Schweiz Ärz 1895, 25, 389

Special Articles

UNDERSTANDING THE DEPRIVED CHILD*

PHILIP PINKERTON
M B Edin , D.P M
CONSULTANT PHYSICIAN IN PSYCHOLOGICAL MEDICINE,
ALDER HEY CHILDREN'S HOSPITAL, LIVERPOOL

MANY children who are deprived of a normal home life find it difficult to adjust to their altered circumstances They have to cope with new and perhaps frightening problems which have arisen from the breakdown of their family life, and they need help I am convinced that, however efficient the organisation for taking them into care, and however comprehensive our legislation to safeguard their welfare, we really begin to help them only when we get down to understanding the individual child and his problems

There is something oddly uniform in the manner and behaviour of these children As the following examples show

An 11 year old girl, who has been in care since the age of 2, is described as " sullen, reticent, and suspicious At times she is very destructive She has frequent outbursts of violent temper, and her behaviour in general is unpredictable "

A 9 year old boy, who has lived in several residential homes and for a time with foster parents, is described as " aloof and taciturn, solitary and resentful He had been caught stealing money from the foster home on several occasions and always lied blatantly about these thefts They had never succeeded in overcoming his aloofness He was always mistrustful and wore 'a chip on his shoulder ' If reprimanded, he would have a temper tantrum "

It is true that not all deprived children behave in this way, and it is equally true that by no means all children with such conduct disorders are technically deprived , but it is a recurring pattern among deprived children Why do they behave in this way ? Why are they so aloof and sullen and moody ? Why is it so difficult to get close to them ? Why are they so suspicious and unresponsive ?

BACKGROUND OF DEPRIVATION

During his formative years a child, whether deprived or not, has certain basic needs, including adequate nourishment, clothing, and shelter Equally vital is the child's need for constant affection, and for a feeling that he belongs securely within a family group. In the early years of life, this demand for affection is fundamental It is also highly selective, because it is the love of his mother that the child needs, or, in default of the mother, a substitute but constant mother figure

When young children are sent to hospital they are usually separated from their mothers, though only temporarily and usually for a short time While in hospital, they receive expert and kindly attention , yet, unless we take precautions some of them will so miss the indispensable relationship with their mothers that they will fret and show emotional upset Some fret openly and are inconsolable in their tears Others fret inwardly, becoming quiet and withdrawn, and morose

If normal young children can be adversely affected by a temporary loss of contact with maternal warmth and security, how much greater must be the effect on the deprived child whose loss is lengthy or permanent Consider how such a child must feel His security may already have been undermined by the disrupting influence of a broken home He may be struggling to overcome an engulfing wave of grief, from the death of a parent He may be confused, and bewildered in his loyalties, by the desertion of a feckless father or the defection of a deficient and selfish mother He may have been rejected and cast out at birth as an illegitimate and unwanted child, so that he has never known the warmth of maternal affection or the security of belonging within a family unit Often, such a child has suffered repeated rebuffs from parents or guardians, who have rejected him, sometimes shamelessly, or perhaps neglected him in ways more subtle but equally damaging When he comes into care, he appears withdrawn and unresponsive His feelings may have been hurt so many times that he has learnt to protect them by a taciturn and sullen mask

Many of these children have been let down again and again by unreliable parents, or misled repeatedly by false promises They feel suspicious and mistrustful of adults Our assurances, given in good faith, may have been heard before by the child, when they were not fulfilled How can he feel sure that this time he can accept them ? His suspicions and hostility, his withdrawal and moodiness, are surely understandable

Slowly, however, we overcome his suspicion and we think he is beginning to trust us and give his confidence to us Many of these boys and girls do respond in this way , but to our dismay—and even, let it be said, to our righteous indignation—there are some who bite the hand that feeds them, who repay kindness with aggression, and who take advantage of our tolerance by abusing privileges and by provoking disturbances How can we explain this phenomenon ?

When I am trying to pacify outraged foster parents, who complain bitterly about this sort of behaviour, I ask them to imagine that for years they have had to use a bridge to cross a dangerous river which separates their house from their shopping centre The bridge is solid and they have long since lost any qualms about committing their safety to it Then one day, during a violent storm, the bridge is struck by lightning while they are crossing and they are pitched into the water The experience is highly unpleasant When they have recovered, and resume their daily journey, they find a new bridge in place of the old one It looks unfamiliar, not as solid or secure as the original one, and they naturally feel some misgivings about committing their weight to it They could hardly be blamed if, as a precaution they were to test the stability of the bridge beforehand, by shaking it or perhaps kicking it, and only when they were satisfied that it could stand such punishment would they feel safe about crossing

These difficult children have been subjected to one upheaval after another and they have become understandably wary We, in our turn, set ourselves to convince them that they can safely open up their badly wounded feelings to us But the child must be sure of his support before he does so He is perhaps near the end of his emotional tether, and to be let down again might mean complete emotional breakdown Almost unconsciously, therefore, he is driven to test the support which is offered to him before he commits himself to it, and this is the basis of his provocative behaviour If he is loved while he remains cooperative and obedient, will he still be accepted when he is naughty and disobedient ? No child (or adult) likes to feel that he is loved, or that he is wanted, only on a selective basis We all like to feel that somewhere there is a place where we belong and where we will find unstinted affection, no matter how badly we behave

These children are groping blindly to achieve this aim And the only way they can allay their gnawing suspicions is deliberately to provoke adverse circumstances, so that they can judge the reaction of those who promise security If they are accepted when they are badly behaved, they can, they feel, safely put their trust in the security offered

NAUGHTY OR WITHDRAWN

As I have said, not all deprived children behave in this way For that matter, not all young children who are

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* Abstracted from an address to the annual conference of the Association of Children's Officers, Southport, Sept 29, 1955

Notes and News

WORLD HEALTH ORGANISATION

The Executive Board of the World Health Organisation, whose 17th session opened in Geneva on Jan 17, under the chairmanship of Dr Sabeeh Al-Wahbi (Iraq),[1] has recommended a budget of $11 million for the Organisation in 1957 This represents an increase of $800,000 over the current budget The board unanimously resolved that the time is ripe for large scale campaigns against leprosy in every country affected by the disease The board also decided that W H O should assume responsibility for coördinating and stimulating research into resistance to insecticides Dr M G Candau, director-general of W H O, declared "Should the degree of resistance in vectors of diseases such as malaria, yellow fever, plague, and typhus reach the point where control by the available insecticides is no longer possible, disastrous results from a health viewpoint will inevitably occur in many parts of the world" The board asked the director general to explore the possibility of organising centres for the histopathological examination of cancer tissues

WELLCOME TRUST

The Wellcome Trustees have announced two further awards They have made a grant of £80,000 to the Postgraduate Medical School of London, at Hammersmith, towards the cost of building and equipping laboratories for experimental research bearing upon problems of surgery The new laboratories will form part of the department of surgery, of which Prof Ian Aird is director Another grant goes to McGill University, Montreal, of $140,000 (approximately £50,000) to enable a Wellcome research professorship in anæsthesia to be created in the medical school The grant provides for the stipend of the chair and the research expenses of its department for five years, and for the initial equipment of its laboratories

PRESCRIPTIONS FOR POTASSIUM SALTS

Boots Pure Drug Co Ltd inform us that, with the more widespread use of cortisone and its allied steroids, doctors are prescribing potassium chloride in tablet form in order to combat hypokalæmia Prescriptions are being handed in at chemists' shops for tab pot chlor, but such an abbreviation is not used in the *British Pharmacopœia*, so there is some confusion as to whether potassium chlorate or potassium chloride is intended Messrs Boots have now asked their branches to be particularly careful over this point, and have suggested that it is the chloride which is more likely to be required than the chlorate The company remarks that, since internal administration of potassium chlorate may be dangerous, doctors should use the official terms—tab pot chlorid or tab pot chloras

A DEFENCE OF MASS RADIOGRAPHY

Prof A P Thomson, speaking to the Birmingham Regional Hospital Board on Jan 16, rebutted three criticisms of mass radiography—that it is expensive, that it leads to errors in diagnosis, and that it tends to make doctors neglect the clinical examination of their patients There could, he said, be no doubt about the value of the service in the Birmingham region the report of the Regional Director showed that in 1954, mass radiography revealed no fewer than 1357 patients with acute tuberculosis, 556 of whom had tubercle bacilli in their sputum Mass radiography was responsible for more than a third of all notifications of respiratory tuberculosis in Birmingham

The aim of mass radiography was not to make diagnoses but to discover abnormalities such as a "shadow" which required further investigation the diagnoses were made by physicians to whom the patients were referred Though sometimes a patient was told about a "shadow on the lung" which later was shown to be of no significance, any distress caused did not last long, and this small disadvantage was more than offset by the protection the service gave to the public, and to the reassurance it afforded those people who needlessly feared that they had tuberculosis

Among the patients in the Birmingham area examined by mass radiography in 1954, tuberculosis was found nearly seven times more frequently in those referred by general practitioners than in those in all the other groups The suggested that doctors did not neglect to examine the patients before referring them for radiography

Far from being expensive, the average cost of the mass radiography service for each person in the Birmingham region was 3d a year, which was cheap for a service which was in effect an important branch of preventive medicine Dr Thomson maintained that, at the present time, mass radiography afforded one of the best means of reducing the incidence of tuberculosis, by detecting it in its early stages and thus allowing infected patients to be isolated and treated promptly

OUTPATIENT DEPARTMENTS IN SCOTLAND

In 1954 hospital authorities in Scotland surveyed waiting times at outpatient departments On the basis of the information thus collected, and of other reports, the Secretary of State for Scotland has issued a memorandum[1] on the organisation of outpatient departments

Outpatient departments, says the memorandum, should be organised on the assumption that the present demand will be maintained or will increase Of 162 hospitals and clinics reported on, 93, with outpatient attendances estimated at 3,140,000 a year, had appointment systems for all attendances except casualties and self referred patients, 36, with 3,420,000 attendances, had appointment systems for more than half of their attendances, and 33, with 430,000 attendances, either had no appointment system at all or had one for less than half of their attendances Those hospitals or departments where an appointment system is in operation have much the lowest average waiting times It is clear that such systems are practicable in all specialties, and "where the operation of an appointment system is accompanied by a lengthy waiting period for appointments the fault is not the appointment system but the inadequacy of the department" Wherever possible a system of individual rather than block appointments should be used

COST OF INPATIENTS IN SCOTLAND

The average cost of maintaining a patient in hospital in Scotland, excluding the cost of the specialist service and overhead charges for empty beds, was £8 7s 3d a week in the year ended March 31, 1955, according to the annual analysis of the running costs of Scottish hospitals[2] This average was made up as follows

	£	s	d
Staff salaries and wages	4	5	2
Provisions	1	9	0
Drugs, dressings, patients clothing bedding &c		13	6
Domestic repairs laundry heat light, power &c	1	1	7
Overheads including maintenance of buildings and grounds		13	0
Board of management administration		6	0

The average weekly costs of maintaining and treating a patient in the different types of hospitals in 1954–55 were

		£	s	d
General	major teaching	12	8	1
”	over 300 beds	11	12	4
”	51–300 beds	12	0	10
”	1–50 beds	9	18	[illegible]
”	chronic sick	7	5	8
Convalescent hospitals and homes		8	8	7
Isolation hospitals		6	12	0
Sanatoria		9	3	0
Isolation and tuberculosis hospitals		10	0	2
Maternity hospitals and homes		15	11	1
Mental hospitals		5	0	10
Mental deficiency institutions		4	12	3
Other hospitals		9	10	0

The average cost of treating each outpatient was 5s per attendance

RESEARCH ON TRACHOMA IN THE MIDDLE EAST

A virus laboratory is being built in Jordan by the Order of the Hospital of St John of Jerusalem for research on the virus of trachoma, which, it is estimated, affects a quarter of the world's population and causes more visual disability and blindness than any other disease Sir Stewart Duke Elder, the hospitaller of the Order, said on Jan 30 that it was hoped that the laboratory would be working by the end of March under the direction of a research team consisting of a clinician a virologist, and a bacteriologist

Until recently, Sir Stewart said, trachoma was treated by cauterisation by copper and other metals—the kind of treatment used four thousand years ago Antibiotics have

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[1] See *Lancet* Feb 4 1956 p 251

[1] S H M 56/7

[2] H M Stationery Office 9s 6d

REMUNERATION OF DOCTORS

IN GENERAL PRACTICE AND IN HOSPITALS

We have received the following letter:

Sir,—The rise in the cost of living hits everyone in the country, but does not affect different classes of the community equally. Wages and many salaries have, by and large, fully kept pace with this rise. Some fortunate people have been able to offset the combined incidence of declining money values and high taxation by appreciation in capital values. Others have not been so fortunate. Amongst the worst sufferers are those whose incomes are determined and changed infrequently, and doctors, the great majority of whom are now remunerated almost entirely from public funds, fall into this group.

The cost of living has risen steeply since 1950 and the real value of the incomes of general practitioners and hospital medical staffs has declined. The medical profession during these difficult years has been reluctant, in view of the national situation, to draw attention to its own financial position. It is, however, now compelled to claim from the Government increased remuneration for both general practitioners and all grades of hospital medical staff. A detailed statement setting out the background of the case accompanies this letter.

When Parliament introduced a State provided National Health Service, it thereby assumed the responsibility for maintaining an adequate standard of living for the doctors who play an essential part in it. What we are now asking is not merely that the value of professional remuneration should be restored, but the recognition of this responsibility in principle and its embodiment in policy.

A. Talbot Rogers
Chairman
General Medical Services Committee

W. Russell Brain
Chairman
Joint Consultants Committee

Statement

So far as the medical profession is concerned, the basis of remuneration in the National Health Service has been, and still is, the two Spens reports which were accepted by the profession and the Government. The Spens Committees framed their recommendations in terms of 1939 values of money, and, to quote from the General Practitioner report, "left to others the problem of the necessary adjustment to present conditions, observing that such adjustment should have direct regard, not only to estimates of the change in the value of money, but to the increases which have in fact, taken place since 1939 in incomes in other professions." A similar safeguard was included in the Consultant Spens report.

In the field of general practice there has been no "adjustment" since 1950. It is true that since the Danckwerts award the method of calculating the Central Pool safeguards the level of income in so far as practice expenses and the number of doctors taking part in the Service are concerned, but this takes no account of variations subsequent to 1950 in the betterment factor, which is still assessed at the level of 100% over 1939. This level is certainly an unrealistic figure today.

In the hospital service, although medical staff are now remunerated under a later award of 1954, they are in the same position, as they too have received no increase in the betterment factor since 1950. During the negotiations which led up to the 1954 award, the Government refused to accept any claim based on betterment, and the settlement which was reached was on the ground that the Danckwerts award had disturbed the relativity between general practitioners and consultants (previously established by the two Spens Committees) and that an increase in consultant remuneration was necessary to safeguard recruitment to that branch of the profession.

Since the Danckwerts award established a betterment factor of 100% for general practitioners in 1950 and the consultant award of 1954 restored the balance between the two branches, it follows that the remuneration of both sections, in so far as the betterment factor is concerned, was stabilised as at 1950. To put it another way, general practitioners and hospital medical staff are now remunerated at rates which, so far as values of money are concerned, are related to the year 1950 and any adjustment to offset changes which have occurred since that date must apply to both branches of the profession.

In the past, negotiations in the field of remuneration have been carried out independently by the General Medical Services Committee of the British Medical Association, representing general practitioners, and by the Staff Side of Committee B of the Medical Whitley Council, representing hospital medical staff. This was perhaps inevitable because in previous claims the factors in dispute were not common to both fields. The present issue is, however, straightforward. It is that the existing rates of remuneration must be adjusted to meet the decline in the value of money since 1950. Since both branches are affected by this decline there is every advantage to be gained from a joint approach to the Government. Experience has shown that any claim submitted on behalf of one section of the profession would be examined by the Ministry not on its merits alone but also on its possible repercussions in other fields of practice.

These matters have been carefully considered by the General Medical Services Committee and the Joint Consultants Committee, and both feel that, with a continuing inflationary trend and in the light of the increases afforded to or claimed by other sections of the community, they have no option but to take immediate steps to remedy the disadvantageous position in which general practitioners and hospital medical staffs now find themselves.

Both committees are equally convinced that it is in the best interests of all that a joint claim should be made with the full weight of the profession behind it. This view has been endorsed by the council of the British Medical Association and by the Joint Consultants Committee.

In consequence the Minister of Health has been informed by the General Medical Services Committee of the British Medical Association, representing general practitioners, and the Joint Consultants Committee, acting on behalf of all grades of hospital medical staffs, of the intention to submit an early claim for an increase in the betterment factor.

The preparation of the joint claim is now under way and for this purpose a Joint Negotiating Committee of the two bodies has been set up under the joint chairmanship of the chairmen of the General Medical Services Committee and the Joint Consultants Committee. It will be assisted by Prof. R. G. D. Allen, D.SC., professor of statistics of the University of London, whose evidence played an invaluable part in the Danckwerts adjudication.

The Public Health Committee of the British Medical Association has been kept informed of these developments, and its chairman has been invited to be present at the meetings of the Joint Negotiating Committee referred to above.

It will be appreciated that the submission of a precise claim must depend largely upon the availability of accurate statistical information and we are advised that this will not be ready until the end of April. In the meantime all the necessary preparations are in hand.

Finally, it is wished to emphasise that this is not a claim for new money. Indeed, it is not a claim for anything more than the remuneration which the Spens reports laid down to be proper for the medical profession. The decline in the value of money has meant that the profession during the last five years has not received what was regarded as its due when the Spens reports were accepted by the Government at the inception of the National Health Service. What is asked is that this obvious injustice should now be made good.

A Medical High Commissioner

The Queen has appointed Mr Walter Elliot to be High Commissioner to the General Assembly of the Church of Scotland, *which meets in Edinburgh on May 22*

Society of Medical Officers of Health

Sir Selwyn Selwyn-Clarke has been appointed medical secretary of this society in succession to Dr Frederick Hall Sir Selwyn has held the posts of director of medical services, Hong-Kong, and chief health officer, Federated Malay States, and since his retirement from the governorship of the Seychelles he has been a principal medical officer at the Ministry of Health

Shortage of Mental Nurses in Lancashire

At the opening in Manchester of an exhibition intended to promote the recruitment of mental nurses, protests were made by the staff of local hospitals against their pay and conditions The *Times* (Jan 31) reports that 60 pickets paraded with sandwich-boards At the opening of the exhibition Mr N M Agnew, chairman of the Manchester Regional Hospital Board, said that, subject to the General Nursing Council's approval, his board was to introduce a four year course for student nurses to spend part of their training at a general hospital and part at a mental hospital

Changes in Industrial Injuries Benefits

The Minister of Pensions and National Insurance has accepted two recent recommendations by the Industrial Injuries Advisory Council (Cmd 9673 and 9674) The changes came into force on Feb 8

The conditions for payment of industrial injuries benefit for byssinosis are to be relaxed The period of qualifying employment in the cotton industry has been reduced from 20 years to 10 years, and the present condition that benefit cannot be paid unless the disablement is assessed at 50% or more has been removed

People whose occupations involve exposure to cadmium fumes are now to be insured under the Industrial Injuries Scheme against chronic as well as acute, cadmium poisoning

Special Times for Certificates ?

Doctors in large urban parishes in the Doncaster area are to be asked to consider a plan for reducing overcrowding in their surgeries Doncaster public health committee suggest that there would be more room for patients requiring treatment if special times were allocated to those wanting sickness certificates only , one proposal is that doctors might set aside half an hour at the beginning or the end of the normal surgery hours for dealing with certificates Dr R W L Ward, public-relations officer to the Doncaster division of the British Medical Association, is reported to have said that, in his opinion, most doctors would oppose any such distinction between patients

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Appointments

DISMORR P C, M R C S D P H appointed factory doctor Erith, Kent
FEARNLEY M E, D SC, M D Lond M R C P D PHYS MED part time consultant in physical medicine St George's Hospital London
JEFFERSON, K E M B Camb M R C P, F F R, D M R D part time consultant radiologist St George's Hospital, London
LANCASTER N P M D Manc D P M asst psychiatrist Deva *Hospital near Chester*
MAIR, MARJORIE, M B Brist B SC Wales asst M O H Bristol
WRIGHT, E W, M B Edin D P H deputy M O H and principal school M O Eastbourne
YOUNG S M L R C P F D P H deputy M O H and school M O Southport

East Anglian Regional Hospital Board

ALAM B M B Dacca registrar in E N T surgery, Ipswich and East Suffolk Hospital
DOWNES M M M B St And, M R C O G senior registrar in obstetrics and gynæcology, United Norwich Hospitals
KANE F P, M B Belf D C H registrar in psychiatry East Suffolk mental hospitals

South-Western Regional Hospital Board

BUTLER N G P, M B Lond F F A R C S, D A consultant anæsthetist Exeter clinical area
GUNATILLEKE, D E, M B Ceylon, F R C S registrar in obstetrics and gynæcology, Royal Devon and Exeter Hospital Exeter
MARTLEW, R H M D Lpool D P M consultant psychiatrist, Bristol clinical area
MUDREWICZ JULIAN M B Polish Sch of Med Edin registrar in obstetrics and gynæcology, Camborne-Redruth Miners and General Hospital, Redruth
WLYHAUSEN, E G, M B Dubl registrar in E N T surgery, South Devon and Cornwall Hospital Plymouth
WRIGHT D W, M B Brist medical registrar, Southmead Hospital Bristol

General Medical Council

An election for 11 members of the General Medical Co will be held shortly 8 members, of whom 1 must live in Wa will be elected to represent the doctors of England and Wa 2 to represent Scotland and 1 Ireland Nomination be sent in by Feb 29, and further particulars will be fo in our advertisement columns

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The 13th volume of the *Transactions of the Hunterian So* which has now been published covers the 1954–55 session includes the Hunterian lecture on pallor in the inflammatory syndrome which Dr Jack Adams-Ray of Stockholm was prevented by ill health from delivering and Dr Philip Hopkins's prize essay on the management of the climacteric in general practice

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Diary of the Week

FEB 12 TO 18

Monday, 13th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road W
4 P M Dr Brian Ackner Emotions and the Cardiovascular System

Tuesday, 14th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (The London School of Hygiene and Tropical Medicine Keppel Street W C 1) Dr T R R Mann, F R S Mammalian Semen
ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street, W 1
5 30 P M *Experimental Medicine* Dr L F Lamerton, D Mary Smith Dr M S R Hutt Clinical and Experimental Studies with Radioactive Iron
8 P M *Psychiatry* Prof E W Anderson, Dr W H Trethowan Mr J C Kenna An Experimental Approach to the Problem of Simulation in Mental Disorder
ROYAL ARMY MEDICAL COLLEGE Millbank S W 1
5 P M Sir Arthur Porritt Medicine and the Olympic Games
ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington, W 2
5 P M Dr A. Melvin Ramsay Post abortum Sepsis and Anuria
INSTITUTE OF DERMATOLOGY Lisle Street W C 2
5 30 P M Dr P J Hare Disorders of Pigmentation
CHELSEA CLINICAL SOCIETY
8 30 P M (Rembrandt Hotel, Thurloe Place, S W 7) Mr Green Armytage, Mr Reynold Boyd Civilisation and Sterilisation
MANCHESTER MEDICAL SOCIETY
8 P M (Medical School University of Manchester) *Surgery* Mr R T Johnson Surgical Principles in the Treatment of Intracranial Bleeding

Wednesday, 15th

ROYAL SOCIETY OF MEDICINE
8 15 P M *General Practice* Dr Guy Daynes Bread and Tears—Naughtiness Depression and Fits Due to Wheat Sensitivity
ST MARYLEBONE HOSPITAL FOR PSYCHIATRY AND CHILD GUIDANCE 48, Cosway Street N W 1
5 P M Dr Walter Schindler Group Psychotherapy
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S W 3
5 P M Dr R W Riddell Significance of Bacterial Resistance in Tuberculosis
INSTITUTE OF DERMATOLOGY
5 30 P M Dr H Haber Cellular Nævi and Melanomas
OXFORD UNIVERSITY
5 P M (Radcliffe Infirmary) Dr Rae Gilchrist *Clinical Aspects* of Coronary artery Disease
ROYAL FACULTY OF PHYSICIANS AND SURGEONS 242 St Vincent Street Glasgow C 2
5 P M Dr A L Goodall Hormones and Carcinoma of the Breast

Thursday, 16th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields W C 2
5 P M Mr F T Graves Anatomy of the Intrarenal Arteries in Health and Disease (Hunterian lecture)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine) Mr E S Horning D SC Anomalies in Endocrine Carcinogenesis
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W 1
7 30 P M Dr A C Allison Sicklæmia
MANCHESTER MEDICAL SOCIETY
8 P M *Anæsthetics* Dr John Gillies Hypotension and the Operative Risk

Friday, 17th

ROYAL SOCIETY OF MEDICINE
8 15 P M *Radiology and Ophthalmology* Mr A G Cross, Dr J W Cowie Dr M Lederman Orbital Tumours
POSTGRADUATE MEDICAL SCHOOL OF LONDON
NOON Sir Henry Cohen Systemic Lupus Erythematosus
FACULTY OF RADIOLOGISTS
5 P M (Royal College of Surgeons) *Radiotherapy* Mr F C W Capps Dr R A Kemp Harper Mr I G Williams Tumour of the Glomus Jugulare
BRITISH TUBERCULOSIS ASSOCIATION
5 P M (26 Portland Place, W 1) Sir Henry Cohen, Dr Philip Ellman Pulmonary Manifestations in the Systemic Collagen Diseases

herefore, that together with a work-therapy project, uch as we have started at Banstead, we shall also need o have hostel accommodation in our catchment area, ear to centres of industry, where patients who have left hospital can live

Even in the past year our increased interest in long stay patients and their problems, together with active treatment programmes for them, has shown that a considerable proportion can become well enough to leave hospital We feel that with the new techniques available we shall be able to discharge these patients much faster than was possible in the past, and that the large buildings and overcrowded wards which we have known for so many years will then become obsolete It would not seem impossible, in a hospital of this size, to discharge long stay patients at the rate of 100 a year, and this would mean that in twelve years the patient population at Banstead could be halved To build new hospital accommodation would seem unnecessary, and the old buildings we have, though unsatisfactory in so many ways, can be put to good use The large barn-like wards, which have been so seriously criticised of late, may find a fresh function Perhaps, in the future, they may be adapted from custodial care to factory floor space At present we have one ward out of forty which is working as a factory perhaps in twelve years we could have twenty wards for factory use and twenty left for ordinary treatment purposes Some ex-patients would then return to hospital in the daytime for the sheltered factory employment they need

Although the symbolic walls around our mental hospitals are being removed and the gates opened, there are still barriers in the minds of the community We may be willing to discharge our patients, but this does not mean that the community is willing to accept them Psychiatric treatment should not be concerned only with the immediate care of the patient but should also consider the major social influences in the community at large In many of our difficulties there is the same underlying, and as yet unanswered, question Does the community wish to keep its mentally sick, for whom there is no immediate active treatment, locked away, with someone else responsible for their care, and financially supported ? Or is the community prepared to accept the long-term patient in its midst, self supporting, but an occasional source of embarrassment ?

I wish to acknowledge the help and encouragement given by Dr E P H. Charlton, physician superintendent at the hospital I also want to acknowledge the work and coöperation of the nursing staff

Public Health

Poliomyelitis Vaccine

An "aide-memoire" prepared by the Ministry of Health for the information of medical officers of health gives some further details about the poliomyelitis vaccine to be used in this country

The Salk vaccine used in the United States of America is made from a mixture of pools of the three known types of poliomyelitis virus grown in a special tissue-culture medium (Connaught no 199 medium) containing monkey-kidney tissue Animal serum is added during the growing-out phase of the culture This medium also contains penicillin and streptomycin, which during subsequent processing are to a great extent inactivated The cultures are filtered and the virus inactivated by formaldehyde, this inactivating agent being added to a final concentration of 1 in 4000 Three tissue-culture tests are made to determine the rate of inactivation The pH of the mixture and the temperature of the inactivation process are also carefully controlled A bacteriostatic agent, merthiolate, together with 'Versene,' is added to the vaccine Filtration before and at stages during the inactivation process are considered important steps in ensuring a safe vaccine by the removal of particulate matter The strains of the three known types of poliomyelitis virus used in Salk vaccine are type I, Mahoney, type II, M E F 1, and type III, Saukett

The Salk-type vaccines of the two manufacturers in this country are similar but the component strains of poliomyelitis virus are different In the Glaxo vaccine the strains are type I, Enders modification of Brunhilde, type II, M E F 1, and type III, Saukett (The types II and III in this vaccine are the same as those used in the Salk vaccine) In the Burroughs Wellcome vaccine the strains are type I, Enders modification of Brunhilde, type II, attenuated Y-SK, and type III, attenuated Leon Final formal approval has not yet been given in respect of strains type II and III used in the Burroughs Wellcome vaccine

On the subject of safety tests, the aide-memoire says

"During and after inactivation each monovalent bulk strain pool is tested for active virus by tissue culture methods Not less than two tests are made during inactivation at 37°C on samples of 500 ml taken at intervals separated by at least three days The consistency with which manufacturers obtain negative results in tissue culture safety tests on strain pools is a major factor in determining safety

"The final vaccine, prepared by pooling monovalent bulk strain pools which have passed the prescribed tests, is again subjected to test A sample of at least 1500 ml is tested similarly by tissue culture methods In addition a monkey safety test is applied to a sample drawn from the final containers This safety test is made on healthy rhesus monkeys which have been treated with cortisone to make them more susceptible to infection with poliomyelitis virus Each monkey is injected intraspinally and intracerebrally and is observed for 28 days when it is killed and histological sections are examined from the central nervous system The number of monkey safety tests made is determined by the number of filling lots of the batch of the vaccine "

The vaccine is also tested for the absence of other pathogens for man (e g, *Mycobacterium tuberculosis*, virus B, and lymphocytic choriomeningitis virus)

Antigenicity tests are made on monkeys and on mice Other rodents such as guineapigs, hooded rats, and cotton rats are being tried for this purpose

Theoretically," the aide-memoire continues, "in view of the presence of monkey kidney protein in the vaccine, sensitisation to it and the production of Rh antibodies are possible but the extensive use of Salk vaccine in other countries indicates that these theoretical possibilities are of little practical importance "

The W H O group which met last November "considered that the amounts of penicillin and streptomycin in the poliomyelitis vaccine were so small that the danger of sensitisation to these antibiotics as a result of vaccination was very small Nevertheless the possible effects of sensitisation and of vaccination in a sensitised person must be kept in mind, although no reactions of this nature have been mentioned in reports from official sources in the United States, Canada, and other countries which have supplied information on their experience with poliomyelitis vaccine "

'Where advice is asked as to whether other immunising procedures should be undertaken simultaneously with vaccination against poliomyelitis, it is probably reasonable to suggest the postponement of smallpox vaccination and other immunisation for at least a fortnight "

Parry of Bristol

For more than a quarter of a century Robert Hughes Parry has been medical officer of health for Bristol, and now he has gone to be visiting professor in public health at Yale before becoming (so he says) a farmer at Criccieth He came to public health after three years in cancer research at the Middlesex Hospital and a further three years in general practice in North Wales with his wife, Dr Joan Parry From that time onwards, there has been nothing dull in his conception or his practice of preventive medicine, for he has believed in things and has said so strongly, vividly, humanly He believes that "if it is to fight disease effectively, the medical profession as a whole needs in fact to be more than interested in the social services that are fighting the other giants of the Beveridge report —Want, Ignorance, Squalor, and Idleness, as well as tion in the urine with the patient's degree of consciousness When a large dose of a short-acting barbiturate, such as pentobarbitone, is taken by mouth, the blood-level reaches about 5 mg per 100 ml twelve hours after ingestion of the drug The level then falls fairly steadily and nearly all the drug is cleared from the body within four days Consciousness is regained when the level falls to between 1 and 2 mg per 100 ml When the poisoning is fatal, the blood-level at death may not be significantly higher than the level found in some patients who recover With comparable doses of phenobarbitone, the blood-level may rise to 10 mg per 100 ml, and consciousness tends to return when the level reaches 5–6 mg The level falls slowly with this drug and the blood may still contain 4 mg per 100 ml seven days after ingestion Barbitone is also excreted very slowly blood levels approaching 20 mg per 100 ml have been found twenty four hours after ingestion, while ten days later the figure was still 2 mg per 100 ml There is, of course, variation from patient to patient in the degree of consciousness associated with different blood levels of the drugs WRIGHT found that 2 patients who had been subject to epilepsy for twenty years remained conscious when the phenobarbitone level was over 5 mg per 100 ml, but such tolerance was unusual, and no patient was free from symptoms or signs of intoxication with a blood-level of over 3 mg per 100 ml Dr WRIGHT and Mr BROUGHTON and his colleagues have done an important service in exploring this new biochemical technique the clinician will be glad of biochemical guidance about which barbiturate was taken, how much, and when, since he so often lacks this information when it is most needed

We have as yet no means of hastening the destruction or excretion of ingested barbiturate The use of analeptics in barbiturate poisoning, favoured by some workers and rejected by others, is designed to keep the patient conscious or nearly conscious until the barbiturate has been dissipated A more recent development is the introduction, by SHAW and SHULMAN and their associates in Melbourne,[5–7] of bemegride ('Megimide') as a specific barbiturate antagonist 41 patients, 9 of whom were classed as "serious," were treated with this drug, and only 1 died[6] It is said that bemegride quickly brings the comatose patient to a "safe state" of light unconsciousness from which he recovers to full consciousness some hours later, presumably when the blood barbiturate level has fallen spontaneously (SHULMAN also uses amiphenazole ['Daptazole'], which is thought to reduce the toxicity of bemegride and to potentiate its action) But, though favourable results have been obtained by others[8–14] in small numbers of cases, the value of bemegride has not yet been fully assessed WRIGHT,[15] while agreeing that it has an analeptic action in poisoning by short acting barbiturates, believes that the specificity of a barbiturate antagonist should be proved in poisoning by long acting barbiturates Calculating the expected time of recovery of consciousness in 7 of SHULMAN's patients who took phenobarbitone, he argues that only 2 of them recovered earlier than they would have done if bemegride had not been given Here, and when he questions the safety of the "safe state," his argument is an indirect one, and further work is awaited on the relation between the blood barbiturate level and the degree of consciousness in patients treated with bemegride a preliminary report by HOLTEN[9] records that after administration of bemegride a patient became conscious despite quite a high blood-barbiturate level. Another finding of WRIGHT[3] was that in patients seen within four hours of taking barbiturates, gastric lavage produced appreciable quantities of the ingested drug, but that after four hours only negligible amounts were recovered BROUGHTON et al report that up to 4% of the ingested dose can be recovered by gastric lavage provided this is undertaken within twelve hours of ingestion But the doctor in the casualty room seldom knows what time has elapsed since the drug was taken and the prospect of recovering at least some of the poison from the stomach or œsophagus will encourage him to wash out the stomach without delay THOMSON and ALSTEAD[16] have lately described the technique they recommend

In 1954, HUNTER and GREENBERG[17] described 3 cases in which the symptoms were originally attributed to islet cell tumour of the pancreas but were later found to be due to chronic barbiturate intoxication This clinical impersonation led HUNTER and his colleagues to inquire into the effects of the barbiturates on carbohydrate metabolism, and we have lately published their findings[18] 16 patients who were receiving large doses of barbiturates daily were given two doses of glucose, and the levels of glucose and of pyruvate in the blood were followed Abnormally high levels of both glucose and pyruvate were found, but these levels, especially that of pyruvate, could be restored towards normal by giving vitamin B complex for two weeks before the test The abnormal electro encephalogram of chronic barbiturate poisoning was improved, and the symptoms of barbiturate withdrawal diminished, by giving vitamin B complex These observations recall the findings of GOULD,[19] who treated delirium, psychoses, and coma due to drugs (very often barbiturates) by giving intravenously glucose, aneurine (thiamine), nicotinamide, pyridoxine, and ascorbic acid The extension of this line of research into the biochemical changes produced by barbiturates may well lead to important developments in the treatment of both chronic and acute intoxication by barbiturates

New Kidneys for Old

THE report[20] of the successful transplanting of a human kidney by MERRILL and his colleagues of Harvard brings hope to those ill with progressive bilateral renal disease Earlier attempts at renal transplantation in man had not been successful[21–23] MERRILL et al have earlier reported their previous experiences in detail[24] In 9 patients with severe bilateral renal disease in whom kidneys were transplanted, permanent function was not maintained although in 1 patient—a doctor with chronic glomerulonephritis—adequate renal function persisted in the transplanted kidney for 5½ months

The knowledge that skin homografts between identical twins have survived permanently[25] and the recent report of a successful kidney transplant between dizygotic cattle twins[20] led the Boston workers to transplant a kidney from a healthy young man into his twin brother who had advanced and diffuse chronic glomerulonephritis Later, both diseased kidneys were removed The function of the transplanted kidney was excellent 12 months after the operation, and the patient has made a remarkable recovery Before the transplant he was very

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5 Shaw, F H Simon S E Cass N M, Shulman A Austee, J R, Nelson E R *Nature Lond* 1954 173 102
6 Shulman A, Shaw F H Cass, N M, Whyte H M *Brit med J* 1955 i 1238
7 See *Lancet* 1954 ii 746
8 Montuschi E Wickenden P D *Ibid* 1955 i 632
9 Holten C *Ibid*, 1955 ii 619
10 Perinpanayagam, M S *Ibid* p 620
11 Rogerson C A *Ibid* p 873
12 Bingle J P, Whitteram J G *Brit med J* 1955 i 1340
13 Webb, J W S *Ibid*, 1955 ii, 56
14 Buckman J *Ibid* p 203
15 Wright J T *Lancet* 1955 i 1339
16 Thomson T J, Alstead S *Brit med J* 1955, i 1023
17 Hunter R A, Greenberg H P *Lancet* 1954, ii 58
18 Hunter, R A, Merivale, W H H, Smith, A J *Ibid* 195 ii, 1353
19 Gould, J *Ibid* 1953 i 570
20 Merrill, J P Murray J E Harrison, J H Guild, W *J Amer med Ass* 1956 160 277
21 Lawler R H et al *Ibid* 1951, 147 45
22 Kuss R Teinturier, J Milliez P *Mem Acad Chir* 1951 77 755
23 Michon L et al *Pr méd* 1953 61 1419
24 Hume D M Merrill J P Miller B F Thorn G W *J clin Invest* 1955 34 327
25 Brown J B *Surgery* 1937 1, 558

building made it impossible for him to say when he would be able to provide remand centres

Quarantine for Poliomyelitis

Replying to a question, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the Minister was advised that quarantine measures for poliomyelitis contacts, if they should be necessary, should depend on local and individual circumstances as assessed by the medical officer of health General advice was issued to all local authorities in July, 1954, and a form of notice suggested which might be addressed to contacts

Statistical Branch of Ministry of Health

Replying to a question, Mr R H TURTON, Minister of Health, said that a statistician was appointed in July, 1955, to advise on the collection, analysis, and interpretation of statistical information for the Ministry of Health The present staff of the statistical unit consisted of 15 executive and clerical staff and 6 trained machine operating staff

Medicine and the Law

Surgeon Cleared of Assault and Negligence

ON Dec 11, 1947, Miss A. H Baker performed an operation for hysterectomy on a patient, a doctor, then aged 43 The patient now sued Miss Baker for damages for alleged assault and negligence; among other things alleging that the operation had, and would continue to have, a bad effect upon her health, that it had been performed without her consent, and that it was totally unnecessary The patient gave evidence that although on entering the hospital she had signed a form of consent for the operation, agreeing to leave its nature and extent to the surgeon, she had thought that the operation to be performed was a curettage, and that anything that was done beyond that was done without her consent, she also alleged that, from the moment of her first examination, the surgeon had decided to perform a hysterectomy and had never communicated that decision to her Miss Baker's evidence was that she had specifically raised with the patient the question whether, if anything was found requiring hysterectomy, the patient would like her to continue at once while the patient was still under the anæsthetic, and that the patient had agreed Miss Baker said that when carrying out the curettage she found symptoms consistent with chronic fibrosis, and was able positively to diagnose that condition by the feel and sound of the curette, that she knew from her experience that the curetting would do no good in such a case, and that, having formed the view that the proper course was to remove the uterus, she performed the operation. Evidence was given that for upwards of three and a half years after December, 1947, the patient suffered from a severe mental and nervous disturbance, there was also evidence that, before the patient went into hospital, there had been matrimonial difficulties between her and her husband.

Mr JUSTICE BARRY said that the primary cause of the patient's breakdown was the domestic trouble but at a later stage it was substantially contributed to by worries in connection with the operation, primarily due to her fear of carcinoma which at that time she felt might have existed and which she feared had been kept from her knowledge, later that fear developed into anxiety as to whether the operation had been necessary There were two issues, the first—was the operation in fact performed with the patient's consent ?—resolved itself into a direct conflict of evidence and he had no hesitation whatsoever in accepting Miss Baker's evidence on this issue in preference to that of the patient As to the second issue—was the decision to perform the operation a negligent decision in that in making it the surgeon failed to exercise the proper care and attention which should be devoted by the surgeon to the consideration of a diagnostic problem during the course of an operation ?—he thought that the patient was quite wrong in thinking that Miss Baker had arrived at a firm decision to perform the hysterectomy before the curettage No surgeon with her experience would have done so as a result of a bimanual examination. The operation was unnecessary so far as carcinoma was concerned, and the case turned on whether he took the view that Miss Baker was telling the truth when she described her findings during the operation. He saw no reason to reject her evidence He was satisfied that she was justified in diagnosing fibrosis, and how could it be said that it was negligent to remove the uterus of a woman of 43 who was affected by fibrosis, even though it had not reached the advanced stage which would enable it to be detected by examination ? Miss Baker had had to reach her decision to perform a hysterectomy on clinical findings during the course of an operation, and he was satisfied that her decision was not only free from any taint of negligence but was a correct and proper decision to make The patient's complaint was without foundation.

On the question of costs his Lordship said that the litigation had to some extent been encouraged and complicated by the fact that wholly inaccurate documents compiled at the hospital, in particular the diagnosis and clinical abstract which were sent to the patient, showed the existence of a disease wholly different from that for which the operation was in fact performed. Miss Baker was in no way responsible for those notes, but she knew that they had been sent to the patient and her omission to point out to the patient that these were wholly inaccurate ought to be reflected in the order for costs, Miss Baker should, therefore, be awarded only four-fifths of the costs after the termination of the patient's legal-aid certificate Judgment was entered for the defendant with an order for costs accordingly

Breen *v* Baker *Queen's Bench Division* Barry *J*, Jan 26 1956, Gilbert Beyfus Q C, and Roger, Ormrod (Bower, Cotton & Bower) A. P Marshall, Q C, and Duncan Macrae (Hempsons)

J F LAMB
Barrister-at-Law

Every Man Expects England

A mother in her will, dated Oct 7, 1953, made no provision for her only son born in 1923, who was and always had been a mental defective In 1953 when the mother fell ill and was unable to continue looking after him, he was taken to a hospital in the National Health Service, where he was at the present time The mother, who died in December, 1953, left her estate of £2291 net to two friends The son's sole property was a sum of £750 The evidence of the doctor at the hospital where the son was a patient was that extra comforts such as games and gramophone records were beneficial to him, but that these now needed replacement By this application under the Inheritance (Family Provision) Act, 1938, the son (suing by his uncle as his next friend) asked that reasonable provision might be made for his maintenance out of the net estate of his mother.

Mr JUSTICE VAISEY, during the hearing, observed that some people expected the Welfare State to perform not only their financial obligations but also those of affection. Nelson's signal at Trafalgar should now be written "Every man expects England to do his duty."

Giving judgment, his Lordship said that in this case the mother had no doubt conceived the idea that the capital sum of £750 was adequate provision for the son, except in so far as he was maintained by the State The question was whether under the provisions of the Inheritance (Family Provision) Act, 1938, the son ought to receive some provision from the estate of the mother She had certainly not intended him to take anything from her estate, not from any lack of affection, but because he was being maintained by the State she thought that she was entitled to leave her property elsewhere

The son had some powers of enjoyment, such as the playing of games and of gramophone records, and there was no doubt that these extra comforts which the State did not provide were beneficial to him It was well-known that State hospitals were somewhat bare and lacking in the smaller pleasures of life such as could be provided with a little pocket money, and which a patient maintained by the State could have only from outside sources A testator was entitled to say that the State had assumed the burden of the parent, and a parent in making a will could, to that extent, assume that his parental duties would be carried out by the State There was nothing unparental or undutiful in that

The mother in her life-time had provided the son with the extra comforts, and his present application was that some grant should be made out of her estate so that he could continue to have those extra comforts indices, and standard deviations, to pause and think about Ethel Wise and her doctors They remind us of the reality among statistical shadows, of the humanity behind χ^2, and that Man is greater than his creations

Parliament

Purchasing Power of Incomes

Mr JOHN HALL asked the Chancellor of the Exchequer his estimate of the gross salary which, in 1938, would have given a married man with two children the same purchasing value, after tax, as he receives today from a gross salary of £2000 and £3000, respectively —Mr HENRY BROOKE replied About £633 and £859 respectively

Mr HALL Does the Minister think it right to impose additional taxation in the form of surtax on a purchasing value of £633 ?—Mr BROOKE My hon Friend is calling attention to the heavy burden of present-day taxation On that I could not agree with him more

Mr HALL asked the Chancellor what would be the gross earned incomes required today by a married man with two children to equal, after deduction of tax, the purchasing power of gross earned incomes in 1938 of £2000 and of £3000 per annum —Mr BROOKE replied About £12,200 and £34,600 respectively Mr HALL Is not this an apt illustration of the old saying that "The higher you go the fewer," and does not this act as a great discouragement to men and women who find that as they progress in their professions their standard of living falls ?—Mr BROOKE I think that what my hon Friend says is perfectly true

Mr HALL asked the Chancellor what salary he would need today to equal in purchasing power, after tax, the salary enjoyed by the holder of his office in 1938 Mr BROOKE replied About £75,000 Mr HALL Is my right hon Friend aware that I am almost overwhelmed by that figure ? May I ask him if he thinks that the holders of the august office of Chancellor of the Exchequer before 1938 were overpaid or alternatively, does he think that the duties and responsibilities of that office have lightened since 1938 ? If not, will he say when he proposes to take such measures as may be necessary to increase the salaries of the Chancellor and other Ministers and especially junior Ministers ? Is he aware that although it may be less difficult to become a junior minister than a bummaree, a bummaree is probably very much better off ?—Mr BROOKE I can scarcely answer all my hon Friend's questions, but I think that the original question has called attention to how hard it is, with present-day penal rates of taxation on large incomes, to remunerate adequately men in any walk of life who carry great responsibilities

In England Now

DURING the cold spell the only comfortable and contented creatures in the house have been the tropical fish in the surgery Thermostatically controlled at a steady 75°F, without a thought for the electricity bill, they watched us through their window on to the human world, passing and repassing with coils of electric cable, resuscitated oil lamps, and cans of paraffin, striving to keep ourselves and our environment unfrozen Indifferent to our difficulties two males out of the shoal of Rosy Barbs chose to don their mating dress, suffusing silver flanks with a blush of pink and edging their fins with borders of intense black They became quarrelsome, chasing one another through the water plants the other fish keeping judiciously out of their way The liveliest male lost none of his colour when he was netted and placed in a separate tank, and one of the plumper females was selected as his bride His display scored an instant success, for spawning began at once

It is regrettable that Barbs are bad parents, eating their own eggs or fry without compunction, so both fish were netted once again and returned to the shoal in the surgery The hatch was not a large one, but fry appeared from the thick of the plants in the next few days, thin threads of body behind two black eyes hanging under the surface film and darting an inch or so away if disturbed They are growing well now, fed on the fishy equivalent of 'National Dried,' a particulate suspension squeezed from a tube Apparently it is an acceptable substitute for the infusoria of the waters of India whence their forebears came

Letters to the Editor

REMUNERATION OF DOCTORS

SIR,—Following your publication last week of a letter from Dr Talbot Rogers and Sir Russell Brain on the subject of medical remuneration, I think it is desirable that your readers should be informed that at a very well attended meeting of the Royal College of Physicians of Edinburgh on Feb 7 the following motion was passed by an overwhelming majority

> "That the College, having received the report of a meeting between representatives of the General Medical Services Committee and the Joint Consultants' Committee, considers that no claim for a general increase in medical remuneration based upon 'the betterment factor' should be made at the present time, but believes that, if and when an appropriate time should arrive for such a claim to be made, the method of joint action proposed in the report is acceptable"

Royal College of Physicians
Edinburgh

STANLEY DAVIDSON
President

SIR,—I have been dismayed to read in the medical and lay press of the impending claim for increased remuneration for medical practitioners, and I hope you will allow me to state why I consider these claims to be ill timed and ill advised

It is stated that the object of the claim is to meet the decline in the value of money since 1950, or, in other words, to offset the effects of inflation I am fully conscious of the evils of inflation, but I believe the only effective counter measure is to do all one can to halt inflation At last the Government does appear to be making a serious attempt to grapple with this menace, but it seems highly probable that success will be achieved only if governmental action is supplemented by restraint and cooperation on the part of various sections of the community It is for this reason that I consider the present time to be particularly inappropriate for this claim Coming, as it does, from a big and reasonably prosperous professional group, which hitherto has been esteemed for its integrity, altruism, and intelligence, it will undoubtedly embarrass the present attempts to curb inflation, and if granted, will almost certainly contribute to further inflation and further taxation Obviously the granting of this claim would promptly be followed by similar claims from other groups in the Government services, the universities, nationalised industries, &c

This claim is to be deplored not only because it is contrary to the national interest, but also because it can result in no substantial benefit to the profession as a whole With the present structure of income tax it is obvious that against a background of continued inflation, as the gross income rises, increases in salary become of diminishing value in terms of both net income and purchasing power and thus can provide only a temporary relief, which would in the case of most doctors be small in degree and bear little relation to the increase in gross salary If the merry go round in inflation continues, the position of the higher salary groups must inexorably continue to deteriorate in relation to the rest of the community, despite repeated increases in salary

For these reasons I believe that, if the economic status of the medical profession is to be maintained or improved it is essential to do all that is possible to combat inflation and to resist, even if it entails apparent self sacrifice, any measure likely to encourage it If it is felt that more positive action is called for, I would suggest that, instead of pressing salary claims, consideration might be directed to the possibility of obtaining a modification of the present taxation system which would be more equitable to the professional classes It is some two years since the findings of the Millard Tucker Committee were published This report contained recommendations which would ease the financial position of many professional men, but I have heard no talk of its being implemented, nor of any interest in it being taken by those of our profession who claim to safeguard our economic welfare

University Department of Medicine,
Royal Infirmary Glasgow

L J DAVIS

CŒLIAC DISEASE

SIR,—Dr Véghelyi (Feb 4), commenting on Dr Sheldon's paper,[1] draws attention to his own work and that of others which showed that the pancreatic enzymes, particularly lipase may be inhibited by acute infectious fevers or gastro behind these memories of the past, the old road continues to its one contact with modern life, and it is the one thing of which modern life can justly boast—a country house that has been turned into the headquarters of the county library. So you must not think that the old road is a useless, stuffy, old fogey, for at its end it leads you into the world of books.

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[1] Sheldon W *Lancet*, 1955 ii, 1097

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It takes all sorts to make a laboratory as well as a world, as is shown by the delightful drawings in Professor Burch's book *Of Research People*.[1] The exhibitionist, the materialist measuring his bibliography with an inch-tape, the modest man, the cerebrator, the committeeman, and the research director are drawings fit to grace any laboratory bench. Unfortunately, perhaps, the text is more conventional. It is taken from a lecture on the problems confronting people in research today, and it gives, among other things, a serious account of the ideal research-worker, the ideal research director, and the ideal research assistant. It would be interesting to know if these ideal people exist in the flesh or if they are creatures of Professor Burch's imagination. Certainly it would be a thrilling experience to meet the ideal research-worker—a modest man, working peacefully in his garret, utterly absorbed in his own ideas, full of enthusiasm and zest, yet tempered with caution and deliberation. Professor Burch advises us to let him work alone, free from the responsibility of committees and teaching, free of all concerns about reports and research programmes. He might have added that our research-worker should be freed of all domestic chores. His clothes should be laid out for him in the mornings, his meals ready for him when he wants them, yet he should never be made to feel he must interrupt an important thought for food. He should do no gardening, no house-decorating or dish-washing, nor should he have to worry about the car, fuse-boxes, bills, holidays, income-tax, or shopping. On no account should his sleep be disturbed by crying children, and the advantages of a roughage-free diet seem worth exploring. If he does not produce lots of ideas under these conditions he should be wrapped in cotton-wool and sent to a conference abroad.

* * *

Fetching the coal from the basement the other evening, I was startled to find myself in the company of three attractive women in the altogether, two in the erect frontal position and the other reclining seductively on a discarded sofa. Far from being abashed they retained a distant haughty attitude, obviously socially indifferent to a mere menial. Lest my colleagues are tempted to volunteer for like duties, let me hasten to add that it was not a heavenly vision sent to reward the good deed.

Students, north of the Border, hold a Charities' Day each year. It started in the depressed 'twenties and has since become a highly organised procedure culminating in a fancy-dress procession second only to the Nice Carnival. The Eldest is having his first Charities Day and his crowd propose to convert a lorry into a pirate ship. A hunt round the female department stores produced the three young women temporarily housed in our basement before becoming the somewhat immodest captured maidens on the deck beneath the Jolly Roger.

As an anatomist I consider they have perhaps too much of the Grecian boy about the thighs and hips to promise fecundity, but that is a common feature of ladies of their profession—an unfortunate idealism perhaps, as the average mother of a family must find it difficult to squeeze herself into the clothes which fit so gracefully on the model. My wife's verdict was "It is like a basement in Paris." Again, let me hasten to add, an impression gained from lurid reading rather than factual knowledge.

* * *

One bad foot deserves another?—Brighton's "Happy Feet Week" is being held in the Corn Exchange.

Letters to the Editor

RESTRICTION OF ANTIBIOTICS ?

SIR,—I would like to compliment you on raising many important and topical matters in your leader (Jan. 28).

It is the duty of governments to safeguard the welfare of their subjects, and the New Zealand government has, I believe rightly, concluded that some control of antibiotics is necessary in order to protect the individual, even if it means restricting the doctor's freedom in prescribing the drug in question. There seems no danger of proper cases being denied the drug.

The unrestricted use of antibiotics, especially the wide-spectrum tetracyclines, has been shown to lead to two possible groups of harmful effects—toxic or sensitising reactions in the individual, and the development of resistant strains which will affect both the individual and the community as a whole. This state of affairs is believed to have arisen because of the excessive and unnecessary use of antibiotics in the past, and recent reports from hospitals quote figures suggesting that the majority of pathogenic staphylococci are now resistant to penicillin and to many of the other antibiotics. If this trend is allowed to go on then we shall soon reach the stage where these and other organisms are resistant to all of the known antibiotics, and then we shall have to rely on the ingenuity of the chemists to keep us supplied with an ever increasing number of new types to control these infections. The New Zealand government has therefore taken the bold step of restricting the use of one antibiotic, erythromycin, so that it is not abused and that it may be available for the treatment of infections which have proved resistant to other drugs.

After some ten years of the "antibiotic era" the time has surely come for us to reflect whether all these potent drugs are really necessary in the treatment of the many major and minor illnesses for which they are prescribed. The answer, in general practice at least, is undoubtedly that they are being used excessively. The vast majority of the common infections seen in practice will settle either on their own or with the aid of the relatively simple and safe penicillin and/or sulphonamides; the wide spectrum tetracyclines and chloramphenicol are only rarely necessary. This is appreciated by many practitioners. Thus in a recent study of acute chest infections in general practice in which eight practitioners took part it was found that in only 15% of cases were the tetracyclines used[1]; in a recent investigation, again on acute chest infections, organised by the College of General Practitioners and including some fifty-five practitioners from all over the country, it was found that in only 12% of cases were the tetracyclines or chloramphenicol used; and in my own practice over the past two years out of 722 cases of all forms of infection in which antibiotics were considered necessary these two types of antibiotic were administered in only 10%, all the others being satisfactorily controlled with penicillin or sulphonamides. These groups of general practitioners find, therefore, that tetracyclines and chloramphenicol are rarely needed in chest infections, which are probably the commonest group of infections in practice. It would be interesting to see similar figures from hospitals.

What of other infections in general practice? In my own practice I tried to assess the need for antibiotics in some common groups of infections. In series of 100 consecutive cases of each clinical group, penicillin or sulphonamides were found necessary in the following proportions: skin infections, 40%; acute bronchitis, 20%; pneumonia, 51%; acute tonsillitis, 32%; and acute otitis media, 32%. No complications were noted in those not given antibiotics. These are very small numbers, but they do suggest that we are tending to forget that in many cases the body's natural defences are quite adequate to deal with these common infections. It is also possible that, either because of or coincident with the introduction of the antibiotics, there has been a change in the nature of these diseases and that the causal organisms are not so virulent as in the past; this is probable in measles and scarlet fever, at least. Because of all these facts we should adopt more rigid criteria for the use of antibiotics both in general practice and in hospital. In the majority of cases where these drugs are considered necessary the safer penicillin, in adequate dosage, is usually

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[1] Of Research People. By GEORGE E. BURCH, professor of medicine, Tulane University School of Medicine, New Orleans. New York: Grune & Stratton. 1955. Pp. 56. $3.

[1] Batty Shaw, A., Fry, J. Brit. med. J. 1955, ii, 1584.

BILLROTH-I AND POLYA OPERATIONS

SIR,—In their paper (Feb. 4) comparing the results of these two operations Professor Goligher, Professor Moir, and Mr Wrigley report cases in which a recurrent ulcer appeared in the gastric stump after a Billroth I resection for an ulcer in the duodenum, and they speculate upon the cause of this unexpected complication.

Last year I showed,[1] from an analysis of 119 cases of associated gastric and duodenal ulcers, that such gastric ulcers usually develop after duodenal scarring has caused gastric retention. I reported that of 331 patients admitted to hospital with pyloric stenosis, 1 in 6 ultimately turned out to have a gastric ulcer as well, and I showed that gastric retention due to other causes might also lead to gastric ulceration. I quoted a prediction I had made in 1948 [2] that vagotomy alone, since it caused gastric retention, might well be followed by gastric ulcer. (Many instances have since been reported.) I also wrote of the Billroth-I gastrectomy: "I predict that its present widespread revival and popularity will lead to some recurrent *gastric* ulcers due to its use in cases where the creation of only small stomas has been possible."

May I join with Professor Goligher and his colleagues in urging restraint in the use of the Billroth I operation for patients with duodenal ulcer?

London, W.1. H. DAINTREE JOHNSON.

FACTORY IN A HOSPITAL

SIR,—Much as we may applaud Dr Baker's article last week as an attempt to improve the lot of the chronic psychotic, we accept his claims for its success only with considerable reserve and not a little scepticism. Those of us who have worked as institutional psychiatrists for, say, twenty years can remember other enthusiastic advocates of therapeutic procedures which have promised to empty, or half empty, our mental hospitals. With chagrin we recall, amongst others, the promise and relative failure of leptazol, deep insulin, leucotomy, and more recently acetylcholine and chlorpromazine.

The experiment at Banstead has lasted so far four months, during which time 3 patients have been discharged. On this evidence Dr Baker says: "It would not seem impossible in a hospital of this size, to discharge long stay patients at the rate of 100 a year, and this would mean that in twelve years the patient population of Banstead would be halved." By what arithmetical alchemy are these figures arrived at? Why not reduce to absurdity the estimated "emptying rate" and claim that in twenty-four years there would be no patients, no hospital, no factory!

We must point out, too, that rates of discharge and of cure are not identical. What follow-up studies has Dr Baker done on those patients discharged since the experiment began, and on those whose prior discharge, as he explains, made the room for the experiment available? What cognisance has he taken of the readmission-rate of patients discharged from Banstead into his own and other hospitals?

In all progressive mental hospitals—and it is obvious that Banstead must be included amongst them—there has been in recent years a change of policy and of heart in the handling of the chronic patient. "Total push"—that is, the attempt to keep all patients occupied on productive work or engaged in emotionally satisfying activities—has produced an enormous change in the atmosphere of the hospitals. Activity has usurped apathy; hope has replaced despair. As a practical consequence the superimposition of an "institutional psychosis" engendered by enforced idleness, which is the greatest insult to human dignity, on to the psychosis with which the patient was admitted is prevented. But, and this is the real heart of the matter, it is doubtful if this new policy has in any way altered the natural course and history of any of the so-called functional psychoses. Schizophrenia, for example, one of the greatest scourges of mankind, remains a chronic illness in which, despite all our efforts, remissions and relapses are to be expected.

In thus criticising Dr Baker's paper we have no wish to dampen his enthusiasm for his project. What we fervently hope is that he will not allow premature and extravagant claims to bring his good work into disrepute.

HENRY R. ROLLIN.
J. R. WATKIN.

Horton Hospital,
Epsom, Surrey.

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[1] *Lancet*, 1955, i, 266.
[2] *Postgrad. med. J.* 1948, 24, 193.

Notes and News

After the year 1949-50 no supplementary estimate for the National Health Service was submitted until last year when the revised estimate called for a further £6 million. For the current financial year a supplementary estimate totalling £12,671,... net for England, Wales, and Scotland has been submitted. This will bring the total net cost of the service to £479,337,405 in the present year. Most of the additional money is required for the hospital service, for which the original estimate (£304,680,...) is increased by £8,729,000 to £313,409,000. In England and Wales, but not in Scotland, additional money is required for the pharmaceutical and general dental services—£2,043,000 for the pharmaceutical service (revised estimate £41,179,000) and £1,324,000 for the general dental service (revised estimate £28,069,000). (1955-56 Supplementary Estimate. Civil Estimates and Estimates for Revenue Departments. H.M. Stationery Office. Pp. 147. ...)

At the annual general meeting of the National Fund for Poliomyelitis Research on Feb. 8, a letter was read from Sir Harold Himsworth, secretary of the Medical Research Council, to Admiral Sir Charles Daniel, chairman of the Fund. Sir Harold said that in the view of the M.R.C., while vaccination with the present formalin-inactivated poliomyelitis vaccine should prove a most important advance, it would be unjustifiable to assume that the final answer to the problem had been found. Judging from early experience in the United States and elsewhere it was unlikely that the present vaccine would abolish poliomyelitis completely, although we might expect it to give a substantial measure of protection. It would be premature, therefore, to stop investigating alternative preventive measures, of which the most hopeful seemed to be vaccine made from living attenuated virus which would be given by mouth. Development of such a vaccine was still at an early stage, Sir Harold said, and would require further extensive fundamental studies of the properties of the virus.

On Jan. 25 the degree of M.S. of the University of London was awarded to A. R. Anscombe and P. A. Ring.

At a meeting of the council of the Royal College of Surgeons of England on Feb. 9, with Sir Harry Platt, the president, in the chair, an honorary fellowship was presented to Sir Walter Mercer, president of the Royal College of Surgeons of Edinburgh. The Hallett prize was awarded to T. N. Shanmugalingam (Ceylon) and Handcock prizes were awarded to J. G. Cruickshank (U.C.H. Medical School) and to P. J. Stiles (Guy's Hospital Medical School). Fellowships were granted in the Faculty of Anæsthetists to the following: Isabel B. Schooling, Sheila M. Parker, C. R. Jolly, A. H. Phillips, A. J. Merrifield, T. M. Young, A. J. Sims, R. I. Kerr, Patricia M. Lumb, Freda E. Prince White, R. P. Wise, J. L. Anderson, B. E. G. D. Bras, Thomas Thomson, M. G. Rolfe, Norman Laurie Smith, J. C. S. Ainley Walker, Daphne Burkinshaw, E. J. Delaney, Leon Kaufman, Merlin Marshall, Yee Kit Poon, D. G. R. Wright, B. J. Brandstater, R. J. Genever, O. H. French, A. C. Webster.

At a meeting of the Royal College of Physicians of Edinburgh held on Feb. 7, with Sir Stanley Davidson, the president, in the chair, the following were elected to the membership: G. L. Montgomery, A. Kennedy, J. H. F. Brotherston, K. K. Nayak, J. G. Cowley, H. A. S. Joseph, S. Zacharias, J. B. Barr, H. Khoh, M. J. Raymond, J. F. Hare, A. H. Kitchin, R. Pirrie, N. A. Shaikh, P. C. Sikand, A. L. Minhas, J. O'Neill, F. G. Roux, M. G. Williams, R. A. Main, M. L. Suri, D. Glaichen, I. B. Hales, M. Hallowell, P. F. Soysa, B. T. Dave, V. G. Wills, F. Chigier, J. F. Adams, J. T. Hughes, S. Sivasithamparam, S. L. Bhargava, S. Janardhana, R. A. W. Ratcliff, F. M. Narielvala.

At a meeting of the Royal College of Physicians of Ireland held on Feb. 3, with Dr F. J. O'Donnell, the president, in the chair, the following were admitted as licentiates and members: C. F. Brennan, John M. MacCarthy, N. J. O'Doherty.

A public conference on The Atomic Age—Perspectives and Problems is to be held on Saturday, March 10, at 2 P.M. at the Holborn Assembly Hall, John's Mews, London, W.C.1. Prof. J. B. S. Haldane, F.R.S., will speak on genetic effects of radioactive substances.

Dr Richard May has been appointed surgeon-apothecary to the household of Queen Elizabeth, the Queen Mother, at the Royal Lodge, Windsor.

Dr R. M. Hardisty, at present senior lecturer in clinical pathology, St. Thomas's Hospital Medical School, London, has been appointed senior lecturer (clinical pathologist) at the Welsh National School of Medicine.

The annual general meeting of the Mental Health Research Fund will be held at 1, Wimpole Street, London, W.1, on Tuesday, March 6, at 5.15 P.M. Sir Russell Brain, P.R.C.P., will give an address and Dr Arthur Hughes will show his film on the growth of nerve cells.

The National Institute for the Deaf has issued a new edition of its booklet containing an approved list of dealers in hearing aids. Copies may be had from the institute, 105, Gower Street, London, W.C.1.

Eighty nurses at a Manchester epileptic colony have decided to ban overtime work from March 1 (*Manchester Guardian*, Feb. 7). The nurses in four Lancashire mental hospitals have already imposed a similar ban as a protest against their pay and conditions of service.

At an extraordinary general meeting on Feb. 2 the National Association for the Prevention of Tuberculosis passed a special resolution to alter its constitution to enable its work to include all cases of the chest and heart. Proposing the resolution, Sir Robert Young, vice-chairman of council, said that the change was in line with current tendencies. Chest clinics nowadays dealt with many non-tuberculous conditions of the thorax and under the resolution voluntary help could in future be extended to such patients. The N.A.P.T.'s concern with tuberculosis would not diminish so long as there was need for it.

at they should take responsibility for this work for which lly qualified doctors are considered unsuitable Of the maining three technicians, one is a biochemical technician ho has little experience of blood grouping, and I am therefore ft with my hæmatological technician who does the day to day ouping and cross matching, and the senior technician As ese two live in the country and have neither transport nor lephones, and as the hospital has no transport of its own vailable at night, the only way these people could be obtained ould be by sending a taxi from the nearest town A delay f at least one hour would be inevitable before the grouping f the patient could even be begun, and several hours before he technician got home again, perhaps only to be wanted gain for an emergency in another department With only wo available technicians it is quite unreasonable to ask them o sacrifice their domestic arrangements to live in every econd or third week throughout the year

If the regional boards have taken note of the comments in our columns we may confidently expect either a considerable xpansion of existing pathological establishments, or instruc ions to send our emergencies elsewhere Meanwhile, we must eal with the situation by the best attainable, if not the most esirable means, with the limited staff allotted to us—and *this must, of necessity*, include residents performing emergency cross matching This difficult task is not made easier by the uncompromising statements attributed to Dr French and Dr Loutit, which can serve only as ammunition for use against the next victim of litigation

Department of Pathology
Pembury Hospital Kent

W M R HENDERSON
Pathologist

THE ÆTIOLOGY OF CLEFT VERTEBRAL ARCH IN SPONDYLOLISTHESIS

SIR,—Dr Mutch and Professor Walmsley are to be congratulated on their lucid description of the mode of ossification of the vertebral arch (Jan 14) This is highly relevant to the ætiology of separation from the rest of the vertebra of the inferior articular process, lamina, and spinous process This condition has a plethora of names—e g , pars interarticularis lesion, cleft arch (surely a misleading name ?), spondylo-schisis, and separation of the lamina—and is (as the authors say) only associated with spondylolisthesis (forward slipping of a vertebra) in about half the cases, whilst spondylolisthesis certainly occurs very frequently without any bony vertebral lesion There is therefore, only a loose association between the two conditions

But the authors should be criticised for their sweeping statement that "all critical observations have substantiated the view that a cleft in the pars interarticularis is the result of fracture of an ossified arch " This is by no means so, and the evidence for a purely traumatic cause is far from convincing For despite a century's research we are today unable honestly to answer the ætiological questions first asked by Killian [1]

Examination of fœtal and neonatal material by such careful workers as Mall,[2] Willis,[3] Batts,[4] and Rowe and Roche [5] has failed to bring to light examples of the anomaly in fœtal or neonatal material How then is it acquired later in life ? To say simply that it is a fracture begs the question

If the fracture (= the separation of the arch) is caused by trauma, what is the explanation of the widely differing ethnic and sex incidence ? How can this fracture be due to indirect trauma *and* be unilateral (as it sometimes is) ? Why is the thoracic region commonly affected in East Africans, the cervical region in Japanese and Eskimos, and the lumbar region in North American whites ? [6]

It is extremely difficult to answer these somewhat awkward questions The facts alone should make one wonder whether perhaps a genetic factor is not directly involved

It is a common fallacy to assume that a genetically determined defect is always congenital In fact the overt effect of genetic abnormality may only be revealed in late life Perhaps this may be the explanation of the present problem For Grüneberg (personal communication) has found a genetically controlled lesion in laboratory mice comparable to human spondyloschisis Willis [3] considered that structural failure at this point was facilitated by its penetration by large nutrient vessels In East African skeletal material the pars interarticularis of thoracic and lumbar vertebræ was pierced in about 10% of cases only with a nutrient foramen of variable size Possibly these nutrient blood-vessels are genetically determined phenotypes They are often absent, but if present, and large, may themselves cause the separation in childhood and adolescence or may so weaken the thin shell at the pars interarticularis that fracture follows trauma later on in life This would account for the rise of incidence with increasing age shown by Stewart [7]

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DAVID ALLBROOK

TUBERCULOSIS STATISTICS

SIR,—Dr Baldry (Jan 28) raises an important point about the tuberculosis mortality rate If the number of deaths is obtained from the return to the Ministry of Health (T145) it should bear some relation to the figure given on the form T137 that is sent in by the medical officer of health, but these figures can never be the same In the case of T137 the public health authorities, certainly in this borough, enter persons as having died from pulmonary tuberculosis if those words are mentioned anywhere on the death certificate This is true whether or not the patient died from suicide, diabetes, or a cerebral catastrophe , but the official mortality-rate for pulmonary tuberculosis is calculated at the General Register office from the first part of the death certificates

If this absurd anomaly is to be corrected the whole problem of annual returns to the Ministry, regional hospital boards, and public health authorities must be considered afresh if only to prevent overlapping and unnecessary work This applies not only to pulmonary tuberculosis but to all medical, and especially clinical, statistics To what use do the Ministry put this information ? Is there any suggestion that their long term planning is in any way influenced by this information ? Is all the information ever published, not only in an accessible but also in an intelligible form ? (Some appears in the annual report of the chief medical officer of the Ministry of Health) Some regional hospital boards and some public-health authorities ask, either quarterly or annually for information that is almost identical to that supplied to the Ministry Do these bodies decide their future policy as the result of this information ? How do the returns from the mass miniature radiography units ,throughout the country relate to the information that is supplied to the Ministry from chest clinics, and especially to the notification rate ?

Reverting to the particular form T145, this is meant to reflect the work of the chest clinic but is badly designed Not only does the covering circular make extremely difficult reading but the questions asked on the form are obscure and local interpretation must vary considerably For example, in "Number of separate individuals (excluding transfers) examined during the year " the word " examined " means any patient examined by a medical officer *or who could have been deemed to have been so examined by virtue of the scrutiny of the radiographs* Consequently the total figures will of necessity be considerably higher in those clinics which run a chest service for general practitioners than in those where clinical examinations only are carried out

It is not possible to bring out in the returns that many contacts are examined by tuberculin testing only, others by radiography only, and a third group by clinical and radiographic examination and tuberculin testing There are other lacunæ in this form which make it almost worthless As a result the true over all state of tuberculosis in this country cannot be determined

I suspect that the Ministry working party on statistics has either been disbanded or has not met for some considerable time In any case a chest physician has never been a member The time has come to reconsider the whole problem of medical statistics as supplied to the Ministry of Health, and in particular the returns that are made from chest clinics These returns should include not only figures about tuberculosis but also information about chronic bronchitis, carcinoma of the lung and the many other important conditions that are now seen at chest clinics

Regarding the latter part of Dr Baldry's letter about notifications, one wonders how much uniformity is shown throughout the country—do all chest physicians notify primary hilar disease and cases of tuberculin conversion, or do they limit their interpretation of the term to overt clinical disease ?

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[1] Killian H F De spondylolisthesi gravissimae Bonn, 1854
[2] Mall F B *Amer J Anat* 1905 5 433
[3] Willis T A *J Bone Jt Surg* 1931 13 709
[4] Batts M *Ibid* 1939 21 879
[5] Rowe G G Roche M B *Ibid* 1953 35A 102
[6] Allbrook, D B *Amer J phys Anthrop* September, 1955
[7] Stewart T D *Ibid* 1951 9, 251

Derby Derbyshire Royal Infy Pre reg H O
Epping St Margaret's H O's
Huddersfield Royal Infy H O
Kingston Surrey Pre reg H O
Kirkcaldy Victoria H O
Lincoln County Locum H O
Manchester West Manchester H M C Pre reg H O
Newcastle United Hosps Reg
Nottingham City Sr H O
Reading Area Dept of Med H O's
Romford Victoria H O
Slough Upton Locum Reg
Southampton Gen H O
Westcliff, Essex Sr H O
Winchester Royal Hants County Pre reg H O
Woking Victoria Sr H O
York County Locum Sr H O
New Zealand Otago Hosp Board Sr Asst

NEUROLOGY
Sheffield United Hosps Sr H O

NEUROSURGERY
Newcastle Gen Sr H O's

OBSTETRICS AND GYNÆCOLOGY
Hammersmith, West London & St Mark's Hosps H O
Plaistow Maternity, E 13 H O
Queen Mary's Hosp for the East End, E 15 Sr H O & H O
Whittington N 19 H O's
Beverley Westwood H O
Birmingham R H B Regs
Cardiff H M C Sr H O
Derby Derbyshire Hosp for Women Pre reg H O or Sr H O
Derby Derbyshire Hosp for Women Reg
Edinburgh Central Hosps B O M H O
Epsom Dist Reg
Hitchin North Herts Reg
Isleworth West Middlesex Reg & Pre reg H O's
Leeds R H B Reg
Liverpool United Hosps H O
Llanelly Sr H O
Manchester R H B Regs
Manchester United Hosps Sr H O & H O
Manchester West Manchester H M C Pre reg H O
Manchester Withington Sr H O
Plymouth South Devon & East Cornwall Sr H O
Rochdale & Dist H M C Sr H O
Salisbury Gen H O
Salisbury Group H M C Reg
Sheffield United Hosps Sr H O
Stockport Stepping Hill Sr H O & H O
Stoke on Trent City Gen Pre reg H O's
Stoke on Trent North Staffs Royal Infy Sr H O
Sunderland Royal Infy H O
Ibadan Nigeria Univ College Hosp Sr Reg

OPHTHALMOLOGY
Coventry & Warwickshire Sr H O
Doncaster Royal Infy Sr H O
Exeter West of England Eye Infy Sr H O
Isleworth South Middlesex Sr H O
Maidstone Kent County Ophthalmic & Aural Sr H O
Manchester United Hosps Sr H M O
Nottingham & Midland Eye Infy Sr H O
Scotland Eastern R H B Sr Reg
Welsh R H B Reg

ORTHOPÆDICS
Alton Lord Mayor Treloar Orthopædic Reg
Birmingham R H B Reg
Birmingham Royal Orthopædic Sr H O
Colchester H M C H O & Locum H O
Leeds R H B Reg
Newcastle United Hosps Temp H O
Nottingham Gen Sr H O
Paisley & Dist Hosps B O M Jr H M O
Portsmouth Group H M C Pre reg H O
Romford Oldchurch H O
Southampton Royal South Hants Sr H O
Southend on Sea Gen Temp Sr H O
Welsh R H B Regs
Winchester Group H M C Reg
Wolverhampton Royal Sr H O or H O
Tasmania Royal Hobart Asst

PÆDIATRICS
Queen Mary's Hosp for the East End, E 15 H O
Whittington N 19 H O
Bournemouth East Dorset H M C Sr H O
Carshalton Queen Mary's Hosp for Child Sr H O
Manchester Duchess of York Hosp for Babies & Wythenshawe Sr H O
Manchester Duchess of York Hosp for Babies H O
Manchester West Manchester H M C H O
Nottingham Child's Sr H O
Swindon & Dist H M C Sr H O
Canada Child's Hosp, Vancouver Residents

PATHOLOGY
Royal Masonic W 6 Sr Reg
St Andrew's E 3 Sr H O
West London, W 6 Reg
Birmingham Dudley Road Sr H O or Jr H M O
Birmingham R H B Regs
Rotherham Clinical Lab Reg
Scotland Eastern R H B Sr Reg
Scotland Western R H B Reg
Sheffield United Hosps Sr H O

PSYCHIATRY
North Middlesex, N 18 Sr H O
Bristol Clinical Area Sr H M O
Bromsgrove Barnsley Hall Jr H M O & Locum H O's
Derby Kingsway Jr H M O
East Anglian R H B Regs
Hove Lady Chichester Jr H M O
Isle of Man Ballamona Sr H O
Knaphill Woking Brookwood Jr H M O
Leeds R H B Reg
Macclesfield Parkside Mental Jr H M O
Nottingham Saxondale Reg
Prestwich Jr H M O or Sr H O
Retford, Notts Rampton Jr H M O
Retford Rampton Sr H M O
Scotland Western R H B Reg
Scotland Western R H B Cons
Sheffield R H B Sr Reg
Welsh R H B Reg

RADIOLOGY
Manchester R H B Sr H M O
Manchester R H B Sr Regs
Watford & Dist Peace Mem [illegible]
Wigan & Leigh H M C Reg, [illegible]

RADIOTHERAPY
Edinburgh Northern Group of Hosps Sr H O

RESEARCH
Sheffield United Hosps & R H B Reg

RHEUMATOLOGY
Taplow Canadian Red Cross Mem H O

SURGERY
Battersea Gen, S W 11 H O
Charing Cross, W C 2 Reg
Highlands Gen, N 21 H O
Hosp of St John & St Elizabeth N W 8 H O
Nelson S W 20 H O
North Middlesex, N 18, Pre reg H O
Prince of Wales's Gen, N 15, Sr H O
Queen Mary's Hosp for the East End, E 15 H O
St George's, S W 1 Regs
St George in the East [illegible] H O
St James', S W 12 Sr Reg
Whittington N 19 H O's
Ashington, Northumberland H O
Barrow in Furness North Lonsdale H O
Bath Royal United H O
Bexhill Sussex Pre reg H O
Birmingham R H B Regs
Bishop Auckland Gen H O
Blackpool Victoria Pre reg H O
Boston Gen Reg
Broxburn Bangour Gen Pre reg H O's
Caernarvon & Anglesey H M C H O's
Cambridge Addenbrooke's H O
Canterbury Kent & Canterbury H O
Carlisle Cumberland Infy H O's
Carshalton St Helier H O
Chelmsford & Essex Pre reg H O
Chesterfield Royal H O
Chichester Royal West Sussex H O
Darlington Mem Sr H O
Dewsbury Staincliffe Gen H O
Dunfermline & West Fife H O
Edinburgh Central Hosps B O M H O's
Enfield Chase Farm H O
Glantawe H M C Pre reg H O's
Glasgow Royal Hosp for Sick Child Pre reg H O
Halifax Gen H O
Haslemere & Dist H O or Locum
Hastings Royal East Sussex Pre reg H O
Hastings St Helen's Pre reg H O
Hereford County H O
Huddersfield Royal Infy H O
Ilkley Middleton Sr H O
Kingston Surrey Sr H O
Liverpool Booth H O
Manchester West Manchester H M C Pre reg H O's
Manchester Wythenshawe Sr H O
Middlesbrough North Ormesby H O's
Newport, I W St Mary's H O
Nottingham Child's Sr H O
Nottingham Child's Reg
Nottingham Gen Pre reg H O
Peterborough Mem H O
Perth & Dist Jr H M O
Portsmouth Group H M C Pre reg H O
Reading Royal Berks H O
Rochdale & Dist H M C H O
Romford Oldchurch H O
Salisbury Gen H O
Scotland South Eastern R H B Reg
Sheffield United Hosps Reg
Slough Upton Locum Sr Reg
Stirling & Clackmannan Hosp B O M Pre reg H O
Stockport Infy H O's
Stockport Infy Sr H O
Taunton & Somerset H O
West Bromwich & Dist Gen Pre reg H O
Weymouth & Dist H O
Winchester Royal Hants County H O
Wolverhampton Royal Pre reg H O's & Locums
Worcester Royal Infy Sr H O

THORACIC SURGERY
Bristol United Hosps & South Western R H B Sr Reg

VENEREOLOGY
St Mary's, W 2 Sr Reg

GENERAL
U S A Bethesda, Cincinnati Rotating Interns

PUBLIC APPOINTMENTS
Barbados Govt Bact & Path
British Guiana Govt Med Supt (Mental Hosp Berbice)
Derbyshire C C Asst Maty & Child Welfare M O's & Sch M O's
Doncaster County Borough Asst M O H
Dublin—Local Appointments Comm Anæsthetist (P t)
Durham C C Senior Maty & Child Welfare M O (Temp)
Factory Doctors Epping, Essex, Shilton Warwick
Gateshead County Borough Asst M O H & Sch M O
Gold Coast Local Civil Service M O's & M O H's
Govt of Federation of Rhodesia & Nyasaland Asst Med Supt, Govt M O's & Path
Royal Naval Medical Service M O vacancies
Singapore Govt Anæsthetist
Smethwick County Borough Asst M O H & Sch M O
South Australia Public Service (Queen Elizabeth Hosp) Deputy Med Supt (Maty)
South Western Gas Board A M O (P t) based Truro
Trinidad Govt M O (Duty primarily in Mental Hosp)
Warwickshire C C Asst County M O H
Yorkshire C C (West Riding) Senior Asst County M O & Sch M O

NON-MEDICAL VACANCY
Scotland Northern R H B Non-med Asst Bact

(Further particulars of above vacancies available on request to Advertisement Manager)

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Goldberger I have merely demonstrated a second way of illing the cat and in doing so have in no way repudiated the irst, and I think that most people who have surveyed all the acts that bear on the ætiology of lung cancer would be reluctant to admit that cigarette smoking alone subsumes them all

I strongly agree that smoking habits in New Zealand merit investigation, and I am well aware it is a defect in my thesis that this has not been done, but I have been unsuccessful in rousing interest in this though I have been trying hard for several years Perhaps the British Empire Cancer Campaign might support such an investigation, or the tobacco companies?

Petone New Zealand D F EASTCOTT

MEDIASTINAL SURGICAL EMPHYSEMA

SIR,—The curious complication of perforated duodenal ulcer described by Mr O'Donoghue (Jan 28) calls to mind a very similar case

The patient, a man aged 73, was admitted as an "acute abdomen" in March, 1954 He had been ill for two days with griping abdominal pain, abdominal distension, and occasional vomiting He was sent in with a diagnosis of large bowel obstruction There was nothing relevant in his previous history

The patient was obviously ill, with a grossly distended abdomen which was tender in all areas Extensive subcutaneous emphysema was present over the anterior and lateral aspects of both sides of the chest, this was more pronounced on the right side, where it extended up into the neck Radiography confirmed the presence of a pneumoperitoneum and of mediastinal and subcutaneous emphysema

The diagnosis presented certain difficulties Because of the patient's account of the onset of his trouble, and his subsequent progress, spontaneous rupture of the œsophagus seemed unlikely, in any event, this diagnosis would not explain the pneumoperitoneum No reasonable alternative explanation of the picture being forthcoming, laparotomy was undertaken A considerable amount of gas and gastric contents were present in the peritoneum A gastric ulcer was found on the posterior wall of the lesser curve at about its mid point This was adherent to the pancreas and had perforated at its inferior margin into the lesser sac The ulcer was freed from the pancreas and the perforation closed Examination of the abdominal œsophagus and cardia disclosed no obvious abnormality The peritoneal cavity was sucked out and the wound closed without drainage Convalescence was complicated by a burst wound which required re suture The patient has since remained in good health

As Mr O'Donoghue rightly points out, mediastinal emphysema is listed as a recognised complication of artificial pneumoperitoneum, but information on the subject appears to end there and I could find no published report on the mechanism by which this complication occurs Eventually I came to the conclusion that air must have entered the retroperitoneal plane at the site of the ulcer I believe that when leakage into the mediastinum occurs in artificial pneumoperitoneum, the air emerges from the peritoneum via the site of puncture and that spread occurs in the loose extraperitoneal layer to the under surface of the diaphragm The mediastinal tissues are then involved probably by way of the œsophageal opening

I find Mr O'Donoghue's suggestion that leakage took place as a result of rupture of the peritoneum of a hiatus hernia a little difficult to believe It would not have been applicable in my case, as no hiatus hernia was present In any event, we know from hernia at other sites how well the peritoneum stands up to stretching forces in the absence of injury Hiatal deficiency and herniation is very common, so also is peptic perforation

The inference is fairly clear The extreme rarity of mediastinal emphysema associated with peptic perforation must surely signify that its occurrence depends on the presence of some very rare circumstance or combination of circumstances Obviously a rare congenital peritoneal deficiency is a possible explanation, but I suggest that it is more likely to depend on some freak location of the site of the ulcer or some abnormality in the pathological progression of the lesion which allows access of air from the ulcer wall into the loose retroperitoneal plane In the vast majority of cases this is rendered impossible by obliteration of tissue planes in the vicinity of the ulcer as a result of inflammatory reaction

County Hospital
Lincoln DENIS EBRILL

HOMOSEXUALITY

SIR,—May I explain to Dr Learoyd and Dr Howard, whose letters appeared last week, the purpose of sex codes ? They exist, firstly, to maintain the family as a social unit hence the prohibition of incest and adultery, and secondly, to balance the reproductive and non reproductive types of sexual activity with the population needs of the community Thus the ancient Greeks, who had to restrict the numbers of their ruling class to maintain their slave economy, encouraged a very moral type of pederasty, whilst the Hebrews, from whom our sex codes are derived, prohibited all non reproductive forms of activity, for they needed as large a population as possible to survive in competition with their warlike neighbours

Morality is and always will be the supremely important quality in any civilised community, but it is independent of any particular code Codes can and must change with changing conditions if a community is to survive in competitive circumstances

This principle is nicely illustrated by the history of the Lenten fast When this fast was established there was virtually no fresh meat in the country in the early months of the year, and it was important that such livestock as there was should be kept alive to fatten on the summer grass It was therefore advantageous that those who were not compelled by economic necessity should be encouraged to abstain from meat during Lent But *if the fast had* been continued by industrial workers once refrigeration had made supplies available all the year round, nutrition and output would have suffered relatively to non fasting groups Fortunately an excess of refined carbohydrates became available at the same time, so the principle of fasting was preserved by changing the code from meats to sweets without physiological harm

Our reproductive needs have changed so greatly in the last fifty years owing to reduced mortality at all ages that it is difficult to see how our society could have remained stable if Marie Stopes had not succeeded in her campaign for contraception Our code in respect of contraception is so far changed that a man who does not now control his reproductive capacity incurs no less censure than the man who did so only thirty years ago

Logically, those who are opposed to homosexual activity in the community should encourage homosexuals to persist in their activity For, as Professor Penrose pointed out to the B M A Committee, homosexuals represent one end of the scale of continuous variation of sexual polarity like height, and, if we wanted to reduce the number of tall men, surely we should welcome any activity that makes it less likely for them to reproduce themselves ?

Those who appreciate the contributions made by homosexuals in many walks of life might protest at the loss which this policy, if successful, would cause the community, but I feel it is just as immoral to enjoy the books, plays, or music of a homosexual, whom we should imprison if our policemen could trap him, as it would be to share in the profits of a fraudulent financier

Because the public hears very little of homosexual relationships other than those that pass through the police court, they think that all such relations are immoral But those who see cases, or anyone who cares to re read Havelock Ellis, will discover that most homosexuals have very high moral standards

London, N W 1 J F TUTHILL

ATHEROMA

SIR,—Dr Balme (Dec 24) asks whether hæmophiliacs ever got atheroma, should they live long enough, and also wonders if their aortas develop normally This was in reference to Dr Levene's interesting work with the electron microscope (Dec 10) The following case may partly answer the first question, but the evidence is highly suggestive only, since luckily this patient is alive and well and there is thus no microscopic confirmation

The patient, aged 67, has a family history of hæmophilia and himself has a classical and hæmatological picture of the disorder This man has lived a long and precarious existence, with multiple bleeding episodes—from circumcision, after tooth extractions, following many minor operations, into knee-joints, and finally from the urinary tract He is normotensive These severe bleeding episodes have become less frequent with advancing age I looked at the radiographs of his chest with a radiologist, and there was definite calcification may be first recognised The importance of a quick decision when the sex of a newborn child is in doubt needs no emphasis We recently reviewed[4] the value of the various techniques available From the point of view of treatment, the diagnosis of female pseudohermaphroditism (congenital adrenal hyperplasia) is urgent, for these girls may be salt losers and often have an addisonian crisis They are born with a phallus of varying size, but with fallopian tubes, uterus, and vagina The vagina commonly communicates with the urethra to form a urogenital sinus with an orifice at the base of the clitoris[5] Some types of intersex have identical external genitalia, and here cytological sexing—a positive chromatin test in patients with congenital adrenal hyperplasia—establishes the diagnosis, and this can be confirmed by an output of urinary 17 ketosteroids which is high for the patient's age Cortisone therapy must begin at once, and electrolyte abnormalities must be corrected Rare cases have been described in which the external genitalia have an identical conformation but in which, although the nuclear sex is also female, the output of 17 ketosteroids is normal and not raised as in adrenocortical hyperplasia These children should be brought up as girls, and may require plastic surgery later[6]

In girls with a webbed neck or coarctation of the aorta, cytological sexing and the finding of chromatin negative cells establishes the diagnosis of gonadal dysgenesis, allows a prognosis to be given about height and sexual development, and permits the important œstrogen therapy to be given at the age of puberty Gonadal dysgenesis is the extreme form of male pseudohermaphroditism, the patients are genetic males in whom complete feminisation has occurred (without mullerian-duct development—i e, fallopian tubes and uterus) Hypospadias may be regarded as the least extreme form of male pseudohermaphroditism, for here the urogenital sinus has not been quite converted to the normal male urethra Varieties of male pseudohermaphroditism between these two extremes may still pose problems in management and raise considerable difficulties for the plastic surgeon The general principle is that, both in male pseudohermaphroditism and in "true" hermaphroditism, the character of the external genitalia must still be a determining factor in the management of the patient If the plastic surgeon thinks it possible to construct a penis out of the phallus and if the cytological sexing is male, no problem arises If the external genitalia are so feminine that the plastic surgeon will be unable to construct a male organ and a penile urethra, then the child should be brought up as a female whatever the cytological sexing, and, if necessary, testes must later be removed and œstrogens given at adolescence These problems in male pseudohermaphrodites usually appear at puberty in "girls" who do not menstruate or who are developing external male characters Opinions differ, however, about their management, and sometimes no treatment can hope to achieve full success

We shall never remedy all the errors of sexual development we cannot bestow fertility where Nature has ordained barrenness, but we can ensure a normal gender rôle, a satisfactory sexual orientation, and the possibility of a happy married life for these patients These are great advances which until recently, have been won for us entirely by the chemists, the endocrinologists, and the plastic surgeons It is pleasant to record our indebtedness to a biologist, JOST,[8 9] who, by his brilliant experiments on rabbits, demonstrated that the rem of the foetal testis produced males with a feminine p development (the experimental equivalent of hu gonadal dysgenesis), while the castration of the fe foetus did not prevent differentiation in the female ge system, and to the cytologists, BARR and his associate who were the first to observe a sex difference in t nuclear chromatin of somatic cells

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Annotations

FRESH MILK OR TABLETS?

THE idea of giving schoolchildren a third of a pint of m a day for a halfpenny originated with the Milk Marke- Board, and, in 1934, the Board of Education recomme local education authorities to take advantage of the sch The Education Act of 1944 required local authorities to g milk to all children in maintained schools, and since 19 there has been no charge Until October, 1954, the sup was arranged and paid for by the Ministry of Food At th time regulations made by the Minister of Education placed local education authorities the responsibility of ordering a paying for the milk Local authorities were asked to introd normal tendering arrangements not later than April 1, 19 Fresh milk must be supplied other forms of milk cannot substituted without the approval of the Ministry of Educatio

Lately some remotely placed schools have been unable get fresh milk, and in a reply to a question in Parliament la October it was stated that seventeen education authori had, for this reason, been given approval to supply ch dried milk or milk tablets instead But the difficulty getting fresh milk to schools is not the only point at issue, a the question of cost has been causing concern to some counc The national bill for school milk is about £10 million a ye London pays about £750,000 and Surrey £270,000 per annu Both these county councils have discussed recently t reluctance of milk suppliers to allow discount, or to agre competitive tenders The Ministry of Education, in a let to local authorities on Dec 12, reaffirmed the policy that m for schools should be bought at competitive prices, and t Ministry gave assurance of Government support in pursua it Support is evidently necessary, for the recent report the Committee on Public Accounts shows that there is wid spread opposition from the milk trade to competitive tende ing "efforts to secure genuinely competitive prices h generally met with opposition by the trade even to the exte in some cases of denial of supplies to tenderers who offered discount" It seems that in the past year at least six lo authorities have been permitted by the Minister to use m tablets because the price asked for fresh milk was unreas able[11] Pending further decisions on policy, the Ministry advised local education authorities not to enter into long te contracts when they are unable to obtain reasonable suppl of milk at reasonable prices

The Minister of Education said in Parliament on Oct that although there was no suggestion that milk tablets w as good as liquid milk, they were an adequate substitu Fruit flavoured tablets have been produced (ten daily equivalent to a third of a pint of milk) and children are s to like them, especially children who have not previously fresh milk at school But in one area the children's react to the tablets was described rather cryptically as "by means unfavourable"

Many people will feel that there is little justification this country for substituting tablets for fresh milk except few country districts where there is no adequate supply pasteurised milk And certainly it seems very wrong to h to make the change because prices are kept up by suppl We are glad to note that in some places the introductio tablets has induced the milk suppliers to change their attitu and after further negotiations a lower price has been ag to But in many parts of the country the milk supp persist in their refusal to let local authorities have mil competitive price, and the Committee of Public Acco does well to speak severely of this unwillingness to coöpe in a service of such undoubted value to the children of country ere adhered to by all expectant mothers, the result would rtainly be drastic reductions in the numbers of maternal eaths, stillbirths, and neonatal deaths, in the number of xæmic patients occupying hospital beds, and in the number f babies filling the cots of premature baby units It ould save many lives, much expense, and much domestic pheaval, and obstetricians would be spared many grey airs

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[4] See *Lancet*, 1955, ii, 645

[5] Wilkins L The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence Oxford, 1950 p 262

[6] Broster L R *Brit med J* Jan 21, 1956, p 119

[7] Armstrong, C N *Ibid*, 1955 i 1175

[8] Jost, A *Arch Anat micr Morphol exp* 1947, 36, 271

[9] Jost A *Gynéc et Obstét* 1950 49, 11

[10] Moore, K L, Graham, M A, Barr M L *Surg Gynec O* 1953, 96 641

[11] *Times* Jan 5 1956

Reading K Douglas Salzmann

LEPTOSPIROSIS AMONG BRITISH TROOPS IN MALAYA

Sir,—Dr Fairburn and Dr Semple (Jan 7) suggest that enicillin and chloramphenicol play no useful part in the reatment of leptospirosis Having just returned from Malaya, where I was in charge of the medical wards in the third military hospital there at Kluang, Johore may I state briefly my opinions on treatment of this disease ?

In one year, during which time approximately two cases of leptospirosis a month were admitted, penicillin therapy in no case failed to give dramatic amelioration of symptoms and prompt (within forty-eight hours) reduction in pyrexia and other signs The dosage employed was 600,000 units four hourly for five days

I hope this letter may dissuade others from following the non antibiotic régime suggested by Dr Fairburn and Dr Semple

Dublin Lewis Clein

THE HOSPITAL STAPHYLOCOCCUS

Sir,—In your issue of Jan 7 Dr Brodie and his colleagues report finding that the carrier rate of staphylococci was doubled as a result of admission to hospital, and suggest that pseudomembranous enterocolitis in the first eight days after partial gastrectomy may be explained by the frequency of antibiotic resistant (serotype ac/–) staphylococci

That the hospital reservoir of staphylococci, rather than the strains carried by patients on admission, is in fact the main source of infection in staphylococcal enterocolitis is strongly suggested by evidence recently obtained at the Surgical University Clinic in Berne

In 10 out of 17 cases seen between June and December, 1955, a complete investigation was done, consisting of nose and throat swabs with tests for antibiotic sensitivity on admission, examination of the fæces at the onset of the disease, and (thanks to the kind assistance of Dr R E O Williams, of Colindale) bacteriophage typing The results showed that 2 cases were due to endogenous superinfection of the gastro intestinal tract from the nose with strains resistant to penicillin, streptomycin, and tetracyclines The remaining 8 cases were, however, caused by cross infection—in 7 cases with the same "house type" (phage combination 7/47/54/77, with minor deviations in some cases) This "house type" was encountered altogether 9 times over a period of four and a half months on three different wards 1 case was traced directly to a member of the nursing staff harbouring this strain in the nose We were fortunate enough not to lose any patients in this series 5 cases were treated with erythromycin, and 12 with the new antibiotic 'Rovamycin' ('Spiramycin')[1]

Berne, Switzerland A Senn
P Lundsgaard Hansen

THE MUNDESLEY SANATORIUM A DISCLAIMER

Sir,—As Mark Twain said on a similar occasion, "Report of demise greatly exaggerated" Like all private sanatoria and most National Health Service sanatoria we have had to close whole blocks from lack of patients, and the prospects of survival as an establishment for the treatment of pulmonary tuberculosis are by *no means rosy*, but we have every intention of carrying on a bit longer

Mundesley was one of the first British private sanatoria to open 57 years ago, and we rather hoped to be among the last to close

The Sanatorium
Mundesley,
Norfolk
E C Wynne-Edwards
George Day

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[1] Senn, A Lundsgaard Hansen P *Helv med acta* (in the press)

Obituary

JOHN GEORGE FOSTER

O B E, B A, M B Dubl

Colonel Foster, who died on Jan 13 at the age of 83 in Queen Alexandra's Military Hospital, London, had served in the Royal Army Medical Corps for nearly forty years His retirement in 1937 he regarded only as an opportunity for service of a different kind, and as secretary of the Corps's charitable funds and as its historian he continued to work for it with devotion, kindliness, and scholarship

He was born in Athlone and graduated M B from Trinity College, Dublin, in 1896 Four years later he joined the R A M C During the South African war he saw active service in Cape Colony, Orange River Colony, and the Transvaal In the first world war he served in Mesopotamia till 1920 He was three times mentioned in despatches and received the brevet rank of lieut-colonel He was appointed O B E in 1919

In 1929 he took over the secretaryship of the R A M C Benevolent Society and the R A M C Fund, and he continued this work throughout the second world war, visiting his office daily whatever the state of the blitz might be An operation for the removal of an eye in 1944 he allowed to be only a temporary handicap "It causes errors in typing," he wrote, "but I hope I shall surmount this very quickly"

As a historian he was responsible for part of the roll of the Army Medical Services which goes back to 1666 Foster's Roll, which covers the years from 1898 to 1933, will be a fitting memorial to its compiler From the records which he had gathered for this work and from his own wide knowledge of the Corps, he had for many years helped us in preparing obituaries of serving officers He was also an authority on military medals and decorations, and he had lately given his own fine collection to the R A M C historical museum

A colleague writes "By the death of Colonel Foster all ranks of the R A M C have lost a real friend For the 20 years he was secretary of the R A M C Benevolent Society and the R A M C Fund, I was closely associated with him on their committees and I would like to record what a devoted secretary he was and how deeply interested in his work He would spare no trouble in seeking information which might enable officers, other ranks, or their families who were found to be in distress or in need to receive such help as could be granted to them Each case became his personal interest He possessed in a remarkable degree the faculty of detecting an applicant for help whose case was not genuine How great a friend he was to the R A M C may not, I fear, be fully realised, because he was a quiet and unassuming man very kindly and considerate, who shunned the limelight and worked unobtrusively He showed his interest in the Army generally by his knowledge of its history, which he implemented by a magnificent collection of British war medals"

A Scandinavian correspondent informs us of the death last month in Sweden of Dr Ivan Bratt, well known for his system of alcohol control known as Bratt's system Soon after qualifying in medicine at the age of 25 he threw himself into the discussions raging over the abuse of alcohol in Sweden His system of alcohol control hinged on the right of every individual to a certain amount of alcohol, but only so much and no more for each Sweden has only recently abandoned this system in favour of greater freedom of alcohol consumption Bratt also made his mark as director of Svenska Kullager Fabriken and in this post he showed great administrative ability He retired during the war, and he spent his last years on his estate in Södermanland, Sweden His life was saddened in 1940 by the death of his wife in a German air attack outside Paris, during which he himself was also wounded by a bomb splinter He was 77 years of age

Births, Marriages, and Deaths

BIRTHS

Dickinson—On Feb 6, at University College Hospital, London to Elizabeth, wife of Dr C J Dickinson, son—Mark John widely held and best substantiated view, however, is that the cavernous transformation is entirely secondary to a slowly developing occlusion due in most cases to thrombosis The remarkable extent of the compensatory changes is, according to Gibson and Richards,[8] due to local conditions around the portal vein, especially the relatively high venous pressure and the close anatomical relationship between the accessory portal veins and the main stem It is these factors that favour the formation of cavernous tissue around the portal stem, since all the compensatory collateral vessels are bunched together with the main vein in the hepatoduodenal ligament Usually there is little evidence of the underlying cause of the thrombosis Predisposing conditions such as syphilis or blood disorders (e g , polycythæmia) have proved to be unimportant The most probable cause is some low-grade intra abdominal infection leading to a chronic pylephlebitis

Treatment must obviously be directed towards the relief of the hypertension in the portal system The involvement of the portal vein and usually the splenic vein may make a short circuit operation difficult or even impossible In such cases direct treatment of the œsophageal varices may become a necessary life saving measure

A HYPOGLYCÆMIC PUZZLE

SEVERE spontaneous hypoglycæmia is uncommon, and of several possible causes,[1] islet cell tumour of the pancreas and liver disease are probably the best recognised A more unusual cause is a large upper abdominal tumour not arising from the pancreas and not associated with extensive destruction of the liver, and such a case has recently been described by Silvis and Simon [2] The presenting features were personality changes and weakness and faintness in the morning Later the patient had two episodes of hypoglycæmic coma in which his blood-sugar levels fell to 35 and 32 mg per 100 ml Consciousness was promptly restored by intravenous glucose A large hard mass was felt in the right flank, and he was accordingly prepared for operation by the administration of 400 g of glucose daily for four days A huge ovoid retroperitoneal tumour was found, occupying the entire right posterior part of the abdomen and involving the iliopsoas muscle The tumour extended posteriorly between the transverse processes of the upper lumbar vertebræ, and this part had to be removed at a later operation The specimen weighed 1200 g and proved to be a retroperitoneal fibroma Immediately after operation the glucose requirements and the glucose-tolerance test became normal Eighteen months later there was no evidence of a recurrence and there had been no hypoglycæmic attacks or other symptoms

Silvis and Simon draw attention to 5 previously reported cases in which hypoglycæmia was associated with large tumours not arising from the pancreas In Seckel's case,[3] hypoglycæmic coma was associated with a massive fibroma above the right lobe of the liver, bulging against the medial aspect of the right leaf of the diaphragm The pancreas was normal and no metastases were found An assay of the fibroma for insulin was negative The patients of Hines [4] and of Arkless [5] had sarcomas in the upper part of the abdomen and suffered from hypoglycæmic attacks, in both the pancreas was normal Rosenfeld's 2 patients[6] had peritoneal pseudomyxomatous cysts

No one has produced a convincing reason why these patients had hypoglycæmia The pathology of the tumours varied In the one assay reported no insulin was detected, and from the histology of the other tumours it seems improbable that they produced any internal secretion with a hypoglycæmic action Hepatic failure could not be blamed Excessive utilisation of glucose by the tumour is unlikely since extensive carcinomatosis and large benign growths generally lead to a rise rather than a fall in blood sugar [7] The common features of the reported cases are large tumours pressing on structures in the upper and posterior part of the abdomen and displacing viscera The riddle remains to be solved

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[1] Conn, J W *J Amer med Ass* 1940 115 1669
[2] Silvis R S Simon, D S *New Engl J Med* 1956, 254 14
[3] Cited by Brunschwig A Surgery of Pancreatic Tumours St Louis 1942, p 337
[4] Hines R E *Med Bull Veterans' Adm*, *Wash* 1943 20, 102
[5] Arkless H A *Ibid*, 1942 19, 225
[6] *Rosenfeld* E D *Arch Path* 1949 48 255
[7] Woodward, G E, Fry E G *Biochem J* 1932 26 889

Letters to the Editor

Anticonvulsant Action of Acetazolamide—After reading your annotation (Feb 11) we feel that it is a matter of duty to describe some results of a research on the biochemistry of epilepsy in progress at the Burden Neurological Institute In view of the trend of your annotation, it appears to be a matter of some urgency to point out the great therapeutic efficiency of acetazolamide in inhibiting petit mal attacks

In assessing any drug in the treatment of epilepsy the usual rule is to add the drug to the treatment that the patient has been receiving for some considerable period Without, therefore, varying the treatment that had obtained for a minimum of three months, 70 such cases of petit mal were given in addition a daily dose of 250 mg of acetazolamide (Diamox kindly supplied in ample quantity by Messrs Lederle) 51 of these cases were attending the Burden Neurological Institute clinic, and to these were subsequently added 19 similar drug resistant cases attending the Musgrove Park Hospital, Taunton It must be emphasised that only patients with daily minor attacks were selected The patients were mostly children and adults aged 6–35, and the fit incidence varied from about a hundred attacks to one attack a day, and all cases had resisted attempts to abolish the daily incidence of attacks with every form of drug treatment No case with a daily incidence of less than one attack was considered Of all 70 cases, only 2 were recorded as having shown no improvement at all 25 patients had no further attacks during the first month of treatment with acetazolamide In the remaining 43 cases the attack incidence dropped to one or two during the month During the second month of treatment the improvement was maintained and the number of those still having occasional petit mal attacks diminished to about 20 In the third month some of the cases which had responded by total absence of attacks had one or two further attacks, and in 1 case, where before treatment the daily incidence had been almost uncountable (probably more than 200), the incidence after being inhibited completely for the first two months reverted to two or three a day In such cases increasing the dose to 500 mg per diem led to some further improvement Most convincing were the effects of suspending the treatment Even twenty four hour abstention generally resulted in reversion to the pre condition

At this stage we prefer to make no assessment of the effect on major attacks, and it is only the feeling that we are not justified in withholding information any further as to the phenomenal effect of acetazolamide on cases of resistant petit mal attacks that has led us to ask you to publish this letter No side effects, beyond somnolence and occasional formication of the extremities in a couple of cases, were noted—
Prof F GOLLA, F R C P, R SESSIONS HODGE, M R C S
(Burden Neurological Institute, Bristol)

Billroth-1 and Polya Operations—The high incidence of re ulceration after a Billroth I partial gastrectomy in the treatment of duodenal ulcers, demonstrated by the Leeds professorial unit (Feb 4, p 220), is of great importance at this time when the popularity of the operation is increasing In the majority of cases the recurrent ulcer was in the stomach This gastric ulceration is possibly comparable to that after simple vagotomy for duodenal ulcers (L R Dragstedt, H A Oberhelman jun, O S Evans, S P Rigler, *Ann Surg* 1954, 140, 396) which is apparently produced by gastric stasis due to the reduced gastric tone and incoordinated peristalsis since it does not occur if the stomach is adequately drained by a gastroenterostomy If the gastric recurrences after gastrectomy are also due to stasis, vagotomy would be expected to increase stasis and worsen the condition—as appears to have happened in a third of the cases so treated

The cause of gastric ulceration after operations for duodenal ulcers, in which gastric stasis has been produced, is unknown but Dragstedt has demonstrated experimentally a possible explanation In dogs with a denervated Pavlov pouch artificially produced pyloric stenosis increases the rate of gastric secretion and may produce a gastric ulcer, if the stasis is relieved by a gastro enterostomy, there is no increase in secretion and ulceration does not occur Similarly vagotomy by decreasing the tone and peristalsis, causes gastric stasis and produces an increased flow of gastric secretion from the denervated gastric pouch

While conclusions drawn from experimental findings are sometimes invalid for man, the similarity of the results here roved treatment by clearing secondary infection but no g is known to be specific against the trachoma virus, which never been satisfactorily isolated, and which does not vive the journey to laboratories in other countries The r laboratory will be the first built in a trachomatous area l its position is medically ideal because most of the 400,000 ugees in Jordan have trachoma

The Order of St John has maintained a hospital in Jeru- em since the 7th century, the present hospital was ended by no less than 183 000 outpatients last year, but it too small, and land has been bought and building plans are advanced for a new 75 bed hospital, which will take part the trachoma investigation The research will be sponsored d guided by the Medical Research Council, and the research am will work in association with the virus laboratories of the ster Institute and the Institute of Ophthalmology in London nancial support has been received from the British and iddle East governments, the World Health Organisation, cal oil companies, and the Wellcome Trustees, and with its wn contribution of £290,000, the Order has sufficient funds o launch the research scheme and maintain it for seven years

APPROVED NAMES FOR DRUGS

The British Pharmacopœia Commission has issued the ollowing new supplementary list of approved names

pproved name	*Other names*
usulphan	1 4-Dimethanesulphonyloxybutane Myleran
uthalitone Sodium	A mixture of 100 parts by weight of the mono sodium derivative of 5-allyl 5-*iso*butyl-2 thiobarbituric acid and 6 parts by weight of exsiccated sodium carbonate Transithal
Diacetylnalorphine	Diacetyl N allylnormorphine
Halopyramine	N *p*-Chlorobenzyl-N N dimethyl-N-2 pyridylethylenediamine Synopen is the hydrochloride
Nicoumalone	3 (2 Acetyl 1 *p* nitrophenylethyl)-4 hydroxy coumarin Sinthrome
Probenecid	*p* (Di *n* propylsulphamoyl) benzoic acid Benemid
Promethoestrol	3 4-Di (4 hydroxy 3 methylphenyl) hexane
Propylhexedrine	1-*cyclo*Hexyl 2-methylaminopropane Benzedrex
Trimetaphan	4 6-Dibenzyl 5-oxo 1 thia 4 6 diazatricyclo [6 3 0 $0^{3\,7}$] undecanium Arfonad is the (—)-camphorsulphonate
Verazide	1-*iso*Nicotinoyl 2 veratrylidenehydrazine

University of Cambridge

On Jan 26 the following degrees were conferred

M.B, *B Chir*—D J Bartlett (in person), P G A Bloomer F L Cole J F H Keighley, S M Madeloff D J Roberts D W T Roberts, M P Sherwood (by proxy)

M.B—A H Bottomley A E Boyo Donald King Price B W G Orr Samuel Priestman (in person) Joyce F Baron N L Burrell Frank Heyes J P E Hubbard J H L Lloyd-Thomas W J E McKee D J Moorhouse N H Moynihan (by proxy)

Royal College of Physicians of London

On Tuesday and Thursday, March 13 and 15, at 5 P.M, Prof A C Frazer will deliver the Oliver-Sharpey lectures, when his subject will be intestinal absorption in man The lectures will be given at the college, Pall Mall East S W 1

Biochemical Society

On Saturday, Feb 18, at 11 A M at the London School of Hygiene and Tropical Medicine, Keppel Street W C 1 this society will hold a symposium on the structure of nucleic acids and their rôle in protein synthesis

Royal Statistical Society

On Tuesday Feb 28 at 5 30 P M the medical section of this society will hold a meeting at the Westminster Medical School, Horseferry Road, London S W 1 when Mr F Le Gros Clark will speak on Ageing in Industry

Course on Chronic Rheumatic Diseases

A course on this subject will be held at the rheumatism unit of St Stephen s Hospital Fulham Road, London, S W 10, on Saturday and Sunday, March 17 and 18 1956 The opening speaker will be Prof D V Davies whose subject will be the Capsule and Synovial Membrane of Joints The following will also speak Dr Francis Bach, Dr Grace Batten Dr Raymond Daley, Dr Philip Ellman Mr H. E Harding, Dr F Dudley Hart, Dr J A Purser, Dr P D Samman, Dr Gordon Signy Further particulars can be had from the secretary, Fellowship of Postgraduate Medicine, 60 Portland Place, W 1

British Tuberculosis Association

This association is to hold a joint meeting with the Irish Tuberculosis Society in Dublin on May 4 and 5 The programme will include papers on primary tuberculosis in adults the relation between cardiovascular and chronic lung diseases, and the M R C chemotherapeutic trials Further particulars may be had from the administrative secretary of the association, 59, Portland Place, London, W 1

British Diabetic Association

The annual Banting meeting of this association will be held on July 6 and 7 at King s College Hospital, Denmark Hill, London, S E 5 This year it will consist of a postgraduate course for doctors in charge of diabetic clinics, registrars and others Early application should be made to the Association at 152, Harley Street, London, W 1

Arthur Hall Memorial Lecture

In memory of the late Sir Arthur Hall the Sheffield Medico Chirurgical Society and other bodies in Sheffield have endowed a triennial memorial lecture The first lecture is to be delivered by Sir Francis Walshe, F R.S, on Thursday March 22, at 8 P M at the University of Sheffield His subject will be Medicine in the Framework of the University Applications for tickets should be made to the registrar of the university Sheffield 10, before March 10

National Association for Maternal and Child Welfare

The annual conference of this association will be held at Cardiff from June 20 to 21 The theme of the meeting will be Safeguarding the Family, and the speakers will include Prof Dugald Baird, Prof Wilfrid Gaisford, Prof A G Watkins, Dr Elenora Simpson, Dr Harold Cohen, and Dr J Stevenson Logan Further particulars may be had from the secretary of the association, Tavistock House North, Tavistock Square London W C 1

Nutrition Society

On Saturday, March 10, at the London Medical College Turner Street, E 1, this society will hold a symposium on Diet and Anæmia The chair will be taken by Sir Stanley Davidson and the speakers will include Dr P B B Gatenby Dr G R Wadsworth, Prof B S Platt, and Prof A W Woodruff Further particulars may be had from the hon programmes secretary of the society, Dr R J L Allen c o Beecham Foods Limited, Brentford, Middlesex

Laboratory Animals Bureau

The ninth congress of this bureau will be held at the Royal Veterinary College, London, on Wednesday and Thursday, April 11 and 12 On Friday, April 13, there will be a symposium, under the chairmanship of Prof J W Howie, on infections in laboratory animals Further particulars may be had from the bureau, Medical Research Council Laboratories, Holly Hill, London, N W 3

Diencephalic Control of Endocrine Activity

The Milan section of the Italian Society of Experimental Biology is to hold an international symposium on this subject from May 3 to 5 under the presidency of Prof W R Hess and Prof Emilio Trabucchi Further particulars may be had from Dr S B Curri and Dr L Martini, c/o, Instituto Farmacologia, Universita di Milano Via Andrea del Sarto, 21, Milan.

Compulsory Nursing ?

The difficulties of many hospitals in recruiting nurses were discussed last month at a meeting of the Wakefield A Group Hospital Management Committee (*Yorkshire Post*, Jan 26, 1956) Mr Lawrence Richmond the chairman, said that the position was so grave that it should be dealt with at a national level He was tempted to ask whether the time might not come when compulsory service might have to be contemplated, under which young women could be directed to nursing in a category equivalent to a State-enrolled assistant nurse Dr Moray Melvin, the vice-chairman said that one small measure after another had been tried but they had never got down to anything really effective ' At the back of my mind I have felt that we may be driven to compulsion " After discussion the committee decided to ask the Ministry of Health to take immediate steps to examine salary grades and conditions of service, to ascertain whether they are such as to attract young women to nursing way to hospital on the day he was first sent there, and the cause of the death was described as extensive pulmonary tuberculosis *which would have been discovered if he had been X rayed* Surely, physical signs and symptoms have not disappeared to the extent that only at death is it possible to see that the patient was not healthy ?

Mass radiography must not claim the discoveries made by practitioners An increasing discovery of active pulmonary tuberculosis *by mass radiography* would indicate a progressive degeneration of clinical medicine In fact I regard the propaganda associated with such "medicine" as mass radiography as *the* iridescence of decay —JAMES F BRAILSFORD, F R C P (Birmingham)

Homosexuality —Dr Tuthill's reasoning (Feb 11) is throughout based on expediency and not morality People are inclined to call "right" that which is common or necessitous behaviour Right behaviour is based on personal judgment in given circumstances, and depends solely on the dictates of conscience Common practice has never really been the yardstick of moral behaviour, *much as some moralists would have us accept this* Numbers do not sanctify Dr Tuthill's "logical" inference—that encouraging homosexuality ensures a limiting of their numbers—depends *on an analogical argument*, which is dangerous, and on the implication that homosexuals beget homosexuals, which is a non sequitur Homosexuals may well have "high moral standards", but this part, Sir, by no means presupposes the whole —D O HANCOCK, M B (Manchester Royal Infirmary)

Tuberculosis and Liver Biopsy—You have drawn attention (Dec 31) to work on liver biopsy in tuberculous patients You regard the finding of tuberculous lesions in the liver in a *fair number of these cases as of considerable importance from* various points of view Most of the patients had no clinical signs of generalised tuberculosis

Tuberculous lesions and tubercle bacilli have previously been demonstrated in bone marrow obtained by aspiration from patients with miliary tuberculosis (E M Schleicher *Amer Rev Tuberc* 1946, 53, 115) In acute hæmatogenous tuberculosis other workers (S Katz, S Lifschutz *Med Clin N Amer* 1950, 34, 1817) have cultivated tubercle bacilli from the bone-marrow in 67 out of 75 patients They believed that the method was of diagnostic value

However, the simpler and safer procedure of bone marrow aspiration seems to be worth considering also in less fulminating cases of tuberculosis It might be as informative as liver biopsy —LARS ENGSTEDT, M D (Department of Medicine, Karolinska sjukhuset, Stockholm, Sweden)

Electro-encephalography in Children with Recurrent Abdominal Pain —The painstaking investigation reported by Dr Apley and his colleagues (Feb 11) demands careful analysis The groups of children described are not quite comparable Of the 133 who had abdominal pain 96 came for investigation as outpatients, while 37 were picked up at routine school medical inspections For the 133 with no such pain the corresponding figures were 55 and 78 Though it is not stated in the paper, the outpatient children were drawn from far and wide, and include children of all social classes and all grades of mentality In the countryside of the West of England children drink much raw milk Tuberculous mesenteric adenitis and brucellosis, which may cause recurrent abdominal pain, are still extant here The outpatient group may be unduly loaded with such cases The school group, however, came from schools in Bristol (where only safe milk is drunk) It is not stated how many they were or of what type I suspect that special schools for the educationally subnormal and physically handicapped were not included Certainly the children of richer parents and those who go to boarding or private grammar schools have not been included Attending school medical inspections armed with a questionnaire is of doubtful value Dr Apley and I have done this together in the past I have pointed out before that the parents of "normal" children at such inspections are very loth to admit any abnormality in their children (*Dent Rec* 1953, 73, 519) When they come to hospital a different story may be obtained I understand that different persons interviewed the parents in the outpatient department and at the schools

What is more important is that patients who had fits have been excluded from both groups I have tried to show that an important factor in the diagnosis of masked epilepsy is a history of fits, or fits occurring later in the disease (*Brit med J* Jan 28, 1956, p 233)

Finally these workers ignore abnormalities shown by the response of the electro encephalogram to hyperpnœa and photic stimulation If these are included 18 of the 133 children with pain had abnormal electro encephalograms while of the 133 without pain only 13 had abnormalities —HUGH WALL M R C P (Bath)

In England Now

"ALL change here for the North Pole" our genial bus conductor called as the bus stopped at Euston, his only outward concession to the weather a woollen scarf His muffled apathetic passengers, clumsy in their clumping boots, smiled wanly but politely "Cold enough here" one of us murmured in a gallant attempt at the response which is the London bus conductor's due "That's where you're wrong" he said, 'it's colder here One degree warmer here than it was in the Arctic Circle yesterday " Congenital hibernators to a man, we gazed at him with admiration Master of his bus and his fate, by our standards lightly clad, abreast with the latest—most stimulating, if not most accurate—weather reports, he refused to lower his professional standards On his bus passengers should still be offered tickets, encouragement, and the news of the day

Obituary

Dr W L H DUCKWORTH

Dr Duckworth, the Cambridge anatomist and anthropologist, has died at the age of 85

Looking back over the years (writes Sir Lionel Whitby) it is simple to give a general appreciation of the influence of "Ducker" on the Cambridge Medical School, but it is more difficult to describe this subtle influence in appropriate words His brilliance as a teacher was outstanding, for he could clothe *the dry bones of anatomy* with living and vivid fact beautifully illustrated with a few deft strokes on the blackboard in coloured chalk But perhaps his greatest impress *was on the student as an individual, and thousands* of them in his time must have passed through his sensitive hands—which had the long and restless fingers of the accomplished artist

During the more than sixty years that he served the Medical School as demonstrator, lecturer, and reader, it was Duckworth who captured the admiration, the devotion, and the sincere *affection of all medical students* who *came to* Cambridge And this, irrespective of class, college, creed, colour, or whether they were just nice men (or women), or ordinary men, or *lazy* men, or energetic men, or *great athletes*, or clever men who took a first in part I of the natural sciences and another first in part II devoted to the vagaries of embryology, morphology, and comparative anatomy in which Duckworth had an international reputation The laggard loved him (he was kind in a viva though he would not tolerate ignorance), the women adored him (not only was he tall and lithe and handsome but also he was always the natural courtly and courteous gentleman who never bullied, and they respected him because he never allowed feminine charm to take the place of factual knowledge when his signature was required), the average student was happy, indeed flattered, that *Ducker* always knew his name, and he could *straighten* a chaotic dissection in a few seconds with his familiar "and here, or hereabouts, we hope to find, in fact we do find "

Duckworth was happy in his work, his play, *his* college, and his innumerable friendships He never murmured nor wavered for a moment in his loyalties, when he was not elected to the chair of anatomy, to which the *whole student* population over many years would have hailed him with unanimous acclamation At a difficult period of the last war he was chosen to be Master of his college, Jesus College , *and in* his declining years, well into the 80s, the wheel turned full circle, for he became a demonstrator again as well as an occasional lecturer *to the delight* and profit *of many young enough* to be his great grandchildren , they were fortunate to be taught by a master and to share the privilege and rich experience which so many Cambridge men *have* treasured all *their* lives

He suffered a great *sorrow* with the death of his wife on *St* Valentine's day in 1955 He himself joined her exactly one *year afterwards*

Dr C J WILSON, C M G , has died in East Africa at the age of 76

February 18, 1956

Pages 293 to 300

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Date 14·3·56...
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THE LANCET

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LONDON, SATURDAY, FEBRUARY 18, 1956
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Printing of The Lancet

The difficulties that we mentioned a fortnight ago have now come to a head, and issues of The Lancet are likely to be in token form until normal work is resumed in the London printing-houses We can only express our regret that for the time being, we are prevented from fulfilling properly our obligations to subscribers, contributors, and advertisers

Violence

Violence, whether elemental or human is always news But reports, and even investigations, of its effects seldom reveal its cause In the past month two such reports have come from mental-deficiency institutions in Scotland in one[1] some nurses were tried and acquitted on charges of ill treating patients, and in the other[2] there was an apparently spontaneous outbreak of violence by a group of patients Happenings of this kind are, of course, more likely in institutions—ranging from prisons to mental hospitals—where groups of people are detained against their will, and the basic causes are no doubt always much the same Just as the force of an explosive charge depends on its chemical instability and the degree of compression to which it is subjected, so also do instability and constraint determine the violence of human reactions It is largely because they are unstable that mentally sick persons come for treatment and mental defectives have to be placed under care unsoundness of mind and a deficiency in mother wit are not in themselves grounds for medical or legal action Hence, all mental hospitals contain potentially explosive material and one certainly cannot expect minor individual outbursts to be less common in them than in the community outside But they will not act as detonators for a major explosion unless the main charge has been unduly constrained

There are two historical reasons for the constraint of the mentally sick (who of all people, are least able to tolerate it) first, the public demand for protection from something fearful and unintelligible, and secondly the belief that self discipline could be instilled by force Modern "open door" methods of treatment have done a great deal to reduce tension and the chances of violence, but where they have been most successful they have consisted in much more than the unlocking of doors Freedom to do nothing is not worth having, but so many patients have been inactive for most of their lives that to fit them for a measure of liberty is really hard work, of which the nurses bear the brunt The custodial attitude of the mental attendant is deeply rooted and to alter it requires both imagination and courage In its early stages so radical a change imposes considerable strain on the nurses, and these, feeling insecure, may be tempted to deal with the inevitable setbacks by resuming restrictive and even punitive measures But there is ample evidence that, once this stage is passed, the new liberty to be occupied, backed by the means to live a more active life, relieves the very ills for which restraint was imposed

In the prevention of violence much attention is still paid to the classification of mental patients, because it is manifestly unwise to store the detonators with the charge, but this reasoning loses much of its force if the charge is dispersed In fact there is evidence that an unstable patient is less likely to cause trouble if he is admitted to a well-behaved group than if he is forced to associate with his own kind Modern treatment aims to build up self-respect and self discipline from within The diminution in outbursts of violence among patients, and in allegations of ill treatment against nurses, are true measures of its success

Barbiturate Poisoning

In one of our recent issues[1] Miss Eileen Brooke gave some figures about deaths from barbiturate poisoning in England and Wales in the years 1939–54 In 1954 391 people committed suicide by taking an overdose of barbiturates—eight times as many as in 1945 As there was no corresponding rise in the total number of suicides during these years, it is clear that barbiturates are increasingly preferred as a means of self-destruction One obvious reason for this is the ease with which the mentally ill can obtain them in lethal amounts About 1 in 12 of all National Health Service prescriptions are for drugs containing barbiturates and as we have said before[2] there are considerable risks in repeatedly handing out barbiturates to neurotic patients particularly when a prescription allows the patient to acquire at once a quantity large enough to kill him

The development in the past few years of ultraviolet spectrophotometric methods for the estimation of barbiturates in body fluids has added much to our knowledge of poisoning by these drugs In our issue of Jan 28 Mr Broughton and his colleagues described their work at Oxford in the investigation of 36 patients during 1952–55 and similar studies have been described by Wright[3] of the London Hospital Broughton et al used a modification of Goldbaum's ultraviolet spectrophotometric method,[4] and this enabled the laboratory to identify and to estimate the concentration of barbiturates in tissue fluids within one hour thus making the information of practical value to the clinician Wright found that barbiturates were distributed fairly evenly throughout the body-water, and quite an accurate estimate of the ingested dose could be made from the blood concentration and the patient's weight The concentration of drug in cerebrospinal fluid was rather lower than that in blood which is further evidence that the old advice to drain the cerebrospinal fluid in barbiturate poisoning has nothing to commend it Estimations of the concentration of barbiturate in the urine are of no clinical value because large doses of barbiturate depress urine secretion The short acting and medium-acting barbiturates being largely destroyed in the body appear unchanged in only low concentration in the urine and the presence in urine of other chromogens interferes with the accuracy of the estimation Phenobarbitone is more easily detected but Broughton et al were unable to correlate its concentra-

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[1] *Scotsman* Jan. 27 28 1956

[2] *Glasgow Herald* Jan. 25 1956 Statement by General Board of Control for Scotland, Jan. 26 1956

[1] Brooke E. M. *Lancet* Jan. 21 1956 p 150

[2] *Ibid* 1954 ii 75

[3] Wright, J T *Quart J Med.* 1955, 24 95

[4] Goldbaum L P *Anal Chem.* 1952 24 604

Bristol Ham Green Sr H O
Chelmsford Broomfield Locum Sr H M O
Driffield Northfield San Sr H O
Leeds R H B Sr Reg
Manchester R H B P t Cons & Sr H M O
Paisley & Dist Hosps B O M Jr H M O
Warwick King VII Mem Chest Jr H M O

DENTAL SURGERY

Leeds United Hosps P t Cons
Leicester Royal Infy H O

DERMATOLOGY

Sheffield United Hosps Sr Reg

EAR, NOSE, AND THROAT

North East Met R.H B Reg
Royal National T N &E, W Reg or Sr H O
Whipps Cross E 11 Sr H O
Birmingham & Midland Ear & Throat Sr H O or H O
Glasgow Victoria Hosps B O M Sr H O
Hull A Group H M C Sr H O
Kingston, Surrey Sr H O
Portsmouth Group H M C Sr H O
Reading Royal Berks H O
Welsh R H B Locum Cons
Welsh R H B Reg

GERIATRICS

Cardiff St David's Sr H O
East Anglian R H B Reg

MEDICINE

Bolingbroke, S W 11 H O
Dulwich S E 22 H O
Elizabeth Garrett Anderson, N W 1 H O
German, E 8 H O
Lambeth, S E 11 H O
New End, N W 3 Sr H O & H O
North East Met R H B Regs
Royal Northern, N 7 H O
South East Met R H B Reg
Aylesbury Stoke Mandeville H O
Birmingham R H B Reg
Bristol Southmead Gen Hosp Group M C Sr H O
Cardiff United Hosps Reg
Croydon, Mayday Reg
Derby Derbyshire Royal Infy Pre reg H O
East Anglian R H B Reg
Enfield Chase Farm Sr H O
Enfield War Mem Sr H O
Hillingdon, Middx Reg
Hull Kingston Gen Pre reg H O
Huntingdon County H O
King's Lynn Area H M C Sr H O
Manchester West Manchester H M C Pre reg H O
Luton & Dunstable Reg
Newcastle R H B Reg
N. Ireland Roe Valley Hosp Limavady Sr H O
Nottingham City Sr H O
Reading Area Dept of Med H O's
Romford Victoria H O
Southend Gen Locum Reg
Westcliff Essex Sr H O
Worcester Royal Infy H O

OBSTETRICS AND GYNÆCOLOGY

Elizabeth Garrett Anderson, N W 1 H O
North Middlesex, N 18 H O
St Mary Abbots W 8 H O
Birmingham R H B P t Cons
Canterbury Kent & Canterbury H O
Chichester Group H M C Reg
Derby City Pre Reg H O or Sr H O
Derby Derbyshire Hosp for Women Pre reg H O or Sr H O
Dorking Gen Sr H O
Glasgow Southern Gen Sr H O
Hastings Buchanan H O
Hitchin North Herts Reg
Llanelly Sr H O
Manchester Northern Sr H O
Manchester West Manchester H M C Pre reg H O
Nottingham City H O
Portsmouth Group H.M C Pre Reg H O
Rochford Essex Gen Sr H O
Salisbury Gen H O
Shrewsbury Royal Salop Infy & Copthorne H O
Stockport Stepping Hill Sr H O & H O
Stoke on Trent City Gen Pre reg H O's
Sunderland Royal Infy H O

OPHTHALMOLOGY

Moorfields Westminster & Central Eye Reg
Coventry & Warwickshire Sr H O
East Anglian R H B Reg
Epping Group H M C P t Sr H M O
Isleworth South Middlesex Sr H O
Leeds R H B Sr Reg
Maidstone Kent County Ophthalmic & Aural Sr H O
Manchester United Hosps Sr H M O
Nottingham & Midland Eye Infy Sr H O
Oxford R H B P t Cons

ORTHOPÆDICS

St James, S W 12 Sr H O
Bebington Clatterbridge Jr H M O
Braintree Black Notley H O & Locum H O
Bridge of Earn, Perthshire Sr H O & H O
Doncaster Royal Infy Reg
Ipswich & East Suffolk Sr H O
Louth County Infy Reg
Newcastle Gen Sr H O
Newcastle R H B Reg
Northern Ireland Hosps Auth Reg
Nottingham Gen Sr H O
Paisley & Dist Hosps B O M Jr H M O
Romford Oldchurch H O
Scotland South Eastern R H B Reg
Southampton Royal South Hants Sr H O
Tasmania Royal Hobart Asst

PÆDIATRICS

Edgware Gen Reg
Hereford County H O
Manchester West Manchester H M C Sr H O
Manchester West Manchester H M O
Newcastle R H B Reg H O
Nottingham Child's Sr H O
Reading Royal Berks H O
St Alban's City H O
Swindon & Dist H M C Sr H O
Canada Child's Hosp, Vancouver Residents
Ibadan, Nigeria Univ College Hosp Reg

PATHOLOGY

Bath St Martin's Sr H O
Group Pathological Lab, W 8 Sr H O
Royal Masonic W 6 Sr Reg
Liverpool United Hosps Sr H O & Sr Reg
Birmingham Dudley Road Sr H O or Jr H M O

PSYCHIATRY

South Western R H B Sr H M O
South West Met R H B Sr H M O
St Thomas's S E 1 H O
Bury & Rossendale H M C Jr H M O
Newcastle R H B Cons
Newport I W Whitecroft Jr H M O
Northern Ireland Hosps Auth Reg
Norwich Hellesdon Sr H O
Retford Rampton Sr H M O
Scotland Eastern R H B Cons
Sheffield Middlewood Jr H M O or Sr H O
Sheffield R H B Sr Reg
Shrewsbury Group Locum Reg
Willerby, E Yorks De la Pole Jr H M O

RADIOLOGY

Birmingham R H B
Cardiff United Hosps Cons
Cardiff United Hosps Sr Reg
Leeds R H B Sr Reg
Manchester R H B Sr H M O
Manchester R H B Sr Regs

RADIOTHERAPY

Hammersmith Hosp & Postgrad Med School W 12 Sr H M O

RESEARCH

Sheffield United Hosps & R H B Reg

SURGERY

Central Middlesex, N W 10 Reg
Elizabeth Garrett Anderson N W 1 H O
Highlands Gen N 21 H O
Hornsey Central N 8 Sr H O
New End N W 3 H O's
North East Met R H B Regs
North West Met R H B Cons
South Lodge, N 21 H O
Bexhill Sussex Pre Reg H O
Birmingham Accident H O's
Bishop Auckland Gen H O
Blackpool Victoria Pre reg H O
Bolton & Dist H M C H O's
Canterbury Kent & Canterbury H O
Carlisle Cumberland Infy H O
Chelmsford & Essex Pre reg H O
Chesterfield Royal H O
Chichester Royal West Sussex H O
Chichester Royal West Sussex Reg
Darlington Mem Sr H O
Dorchester Dorset County H O
Dudley, Stourbridge & Dist Sr H O
Enfield Chase Farm H O
Glantawe H M C Pre reg H O
Haslemere & Dist H O or Locum
Hastings Royal East Sussex Pre Reg H O
Haverfordwest, Pembroke County War Mem Sr H O
Hitchin Lister H O
Huddersfield Royal Infy H O
Hull Kingston Gen H O
Kidderminster & Dist Gen Pre reg H O
King's Lynn Area H M C H O
Louth County Infy Sr H O
Macclesfield & Dist H M C Pre reg H O
Manchester R H B Reg
Manchester United Hosps Sr H O
Manchester West Manchester H M C Pre reg H O's
Middlesbrough North Ormesby H O's
Northern Ireland Hosps Auth Cons
Nottingham Child's Sr H O
Nottingham Gen Pre reg H O
Nottingham Highbury Sr H O
Portsmouth Group H M C Sr H O & Pre reg H O
Redhill County Pre reg H O
Rochdale & Dist H M C H O
Romford Oldchurch H O
Sheffield City Gen H O
Stockport Infy H O's
Stockport Infy Sr H O
Wakefield Pinderfields Gen Sr H O
Wolverhampton Royal Pre reg H O's & Locum Pre reg H O's
Worcester Royal Infy Sr H O
Worksop Victoria Reg

THORACIC SURGERY

Brompton, S W 3 Sr H O or Reg
North Middlesex N 18 Sr H O
Ilkley Middleton Sr H O
Southampton Chest Reg

GENERAL

U S A Bethesda Cincinnati Rotating Interns

NON-MEDICAL VACANCIES

St Alban's Hill End Biochemist (Sr grade)

PUBLIC APPOINTMENTS

Aldermaston Atomic Weapons Res Est Med Lab Tech
Bedfordshire C C & Bedford Borough Div M O, M O H & School M O
Birmingham City Temp M O's
Bristol City & County Deputy M O H, Deputy Princ Sch M O & Deputy Port M O
Derbyshire C C Asst Maty & Child Welfare M O's & Sch M O's
Doncaster County Borough Asst M O H
Durham C C Senior Maty & Child Welfare M O (Female)
Govt of U K of Libya Path & Bact
H M Overseas Service Western Nigeria M O's
National Coal Board (East Midlands Div) Asst Area M O
Nigerian Federal Gov't Service Path
Nottinghamshire C C Sr Clin M O & Asst County M O
Peterborough Joint Education Board School M O & Asst M O H
Smethwick County Borough Asst M O H & Sch M O
Warwickshire C C Asst County M O H

GENERAL PRACTICE

(Executive Councils Form E C 16A)
Lechlade Glos—Rural List approx 1800

(Further particulars of above vacancies available on request to Advertisement Manager)

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d with malignant hypertension and congestive failure nd on one occasion he required treatment with an rtificial kidney for uræmia and convulsions After the operation, the transplanted kidney began to hyper-rophy, the patient improved rapidly, and his blood-ressure was reduced to a range of 130–160 mm Hg ystolic and 80–90 diastolic Because of the persistent nd mild hypertension, his two damaged kidneys were emoved 3 and 5$^1/_2$ months after the renal transplant, and is blood-pressure then fell to normal levels The patient s now in good health, his activity is unlimited, and he has no apparent physical disability Examination of the urine from the new kidney showed a proteinuria of 4 5 g per 24 hours but no other abnormality

Before the operation a geneticist determined beyond reasonable doubt that the twins were identical This was done on the identity of their anthropological, immunological, and physiological (ability to taste phenylthiocarbamide) characteristics when compared with their sibs Later, immunological and genetic similarity was proven by the crossed transplantation of small skin grafts between the twins The skin transplants took and when biopsies were taken a month later, they appeared to have survived as normal skin

At the operation the vessels of the transplanted kidney were grafted on to the recipient's hypogastric artery and common iliac vein The ureter was implanted into the bladder This site was selected because experience with 13 previous renal transplants in man had pointed out the disadvantages of the renal fossa and the right thigh as recipient sites The ureter was implanted into the bladder because experience in Boston with autotransplants of kidneys in dogs had shown that the organs survived permanently when the ureter was transplanted into the bladder rather than into other organs, when the autografted dog kidney deteriorated rapidly[26] Simultaneous operations were performed on recipient and donor in adjacent operating-rooms, and although the donor kidney was ischæmic for 82 minutes the entire organ became turgid and pink immediately the clamps on anastomosed vessels were released A ureteral catheter was left in the donor ureter until the 9th postoperative day when normal function of the donated kidney was proven beyond doubt by prompt excretion of injected indigo carmine

Identical twins are born approximately once in 350 births and there cannot therefore be many patients with renal failure who will be able to benefit immediately from this work But the fact that the operation is technically feasible should encourage those who are investigating the causes of failure in renal and dermal transplants in man and in animals These and other related problems were discussed at length at a Ciba symposium held in London two years ago[27] At the meeting of the Central Society for Clinical Research in 1954 Good and Varco of Minneapolis, reported successful transplantation of a homograft of skin in a child with agammaglobulinæmia[28] Since skin and kidney possess a common antigen,[29] it is reasonable to speculate that renal homografts might take in patients ill with this rare disease If agammaglobulinæmia can be produced artificially in patients with renal failure, it may provide the answer to renal transplantation in man On the other hand it may exchange one fatal disease for another

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26 Dempster, W J Joekes, A M *Quart J exp Physiol* 1953 38 11

27 Preservation and Transplantation of Normal Tissues Ciba Foundation Symposium London 1954 p 100

28 Good R A Varco R L *J Amer med Ass* 1955 157 713

29 Billingham R E Brent L Medawar P B *Ann N Y Acad Sci*, 1955 59 409

Annotations

ARTERIOGRAPHY IN BONE TUMOURS

EVEN after careful assessment of the history, the clinical signs, and the straight radiographs, it is often hard to say whether a particular bone lesion is malignant or not Many of these doubtful lesions are in children or young adults for whom a major amputation undertaken because of a wrong diagnosis of malignancy would be especially tragic Moreover, the pathologist is often unable to clinch matters because the biopsy specimen may not be typical of the whole In view of these difficulties, it is surprising that other ancillary methods of diagnosis, such as percutaneous arteriography, have not been used more widely The technique was introduced by Dos Santos et al[1] as long ago as 1932 Since that time there have been relatively few reports of its use in this way The introduction of less toxic contrast media, and recent work by Lasser and Von Schowingen[2] in America and Sutton[3] in London, may stimulate research and encourage the further application of arteriography in the diagnosis of bone tumours

Percutaneous puncture of the femoral or subclavian vessels is a safe operation in experienced hands, and a skilful operator can get successful results in over 90% of cases Puncture of the brachial artery is less satisfactory owing to its variable anatomy and the risk of inducing spasm In over 250 cases of percutaneous arteriography, Sutton encountered no severe or important complications He recommends 42% diodone, except for the brachial artery, where he uses a 35% solution Percutaneous arteriography is uncomfortable for the patient, who usually experiences a feeling of intense heat in the limbs, and the examination should be performed either under general anæsthesia or after adequate sedation

With rapidly growing malignant tumours an abnormal vessel pattern is often displayed The arrangement of these vessels differs strikingly from the normal orderly arborisation. There are more vessels than normal, venous channels can be seen more readily, and a 'tumour stain" is often distinguished Osteoplastic metastases do not usually show tumour vascularity but the osteolytic secondaries show varying degrees of abnormal vessel formation, similar to that produced by primary malignant tumours Osteochondromas usually leave the normal vascular pattern unchanged, but giant-cell tumours become diffusely opaque within three or four seconds of the injection, and the opacity persists for at least six seconds In some tumours of low malignancy, such as fibrosarcoma, Sutton saw no abnormal vessels In fibrous dysplasia the vessels are dilated but normal in distribution Lasser and Von Schowingen report that in Paget's disease there is no vascular abnormality, but in one such case they noted abnormal vessels, and the patient later died from neoplastic bone changes

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1 Dos Santos R, Lamas C, Caldas P *Bull Soc nat Chir* 1932 48 635

2 Lasser E C Von Schowingen, R S *N Y St J Med* 1955 55 3425

3 Sutton D *Brit J Radiol* 1955 28 13

"A GREAT PATIENT"

Ethel Wise was born in 1886 at Stratford, Essex During her 69 years of life she was admitted to the London Hospital 53 times, and she died there in April, 1955 She was "in service" until an accident in 1926 started her long odyssey of illness Rheumatoid arthritis, rheumatic heart-disease streptococcal septicæmia pernicious anæmia, carcinoma of the breast, X ray dermatitis and pulmonary fibrosis, these, with their complications and sequelæ, were the life of Ethel Wise 7 consultants and 32 house physicians cared for her in hospital She complained little, and endured all things After her death her last clinical clerk wrote her history,[1] and in a foreword Dr A E Clark-Kennedy, her physician, says

> "We read the obituaries of great doctors and surgeons but never I think of great patients Yet those of us who have been in practice for any length of time have all come across some great patients Some had been born great Others were great and some had had greatness thrust upon them By no stretch of imagination could Ethel Wise be said to have been born great but all who knew her remain convinced that she was by nature great and that ill health forced greater greatness on her In her body she taught us much about disease in her mind very much more about courage in the face of adversity'

It is good, in the midst of such things as occupied bed percentages problems of medical man power, morbidity

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1 Sorapure J B *Lond Hosp Gaz* 1955, 58 271

on Conditions in Iron Foundries, which had the late Mr H E **Chasteney**, H M Chief Inspector of Factories, as its chairman, led to the creation of the Joint Standing Committee The latter [6] has made many investigations into practical methods of dust and fume control, which are described and illustrated in its report Until 1943 the known cases of pneumoconiosis in iron foundry workers were few, and indeed, until the results of the survey by **McLaughlin** and his co workers became known, they were excluded from the compensation schemes for silicosis under the Workmen's Compensation Acts The difficulty about bringing them under such a scheme was partly due to the fact that hitherto the classical silicotic nodule had dominated the study of the pathology of the industrial diseases of the lungs Any case in which classical silicotic lesions were not found could not be diagnosed as silicosis and hence was not eligible for compensation The new pathological studies, however, showed that the main lesion in the lungs of iron foundry workers (particularly iron fettlers or dressers) was another type of nodule with a linear and radial pattern as opposed to the whorled arrangement of fibres in the classical silicotic nodule To this type of lesion **Harding**, **Gloyne**, and **McLaughlin** applied the term "mixed dust pneumoconiosis" or "mixed dust fibrosis" When it was established that iron foundry workers did contract pneumoconiosis they could be brought under the compensation schemes, and this emphasised the need for more intensive efforts to control dust and fume

The engineering section of the report deals, among other things, with the control of dust and fume in pedestal, surface, and swing frame grinding, in fettling with the pneumatic chisel, and in "*knocking out*" *the castings from the sand* moulds in mechanised, light, and heavy and jobbing foundries The methods of dust control by water are described and in particular a new type of wet decoring bar As regards cupola furnaces, various types of spark arresters are discussed, and also the evolution of, and control of, carbon monoxide and sulphur dioxide Original work in this connection has been done on heating and core stoves, and also on mould drying by various appliances The electric mould dryer is regarded as the best type, because less fumes and gas are evolved when it is used

The Joint Standing Committee has also given attention to the irritable and objectionable fumes which may be given off when certain kinds of binders are used in core making, such as synthetic resins and oils New foundry processes such as shell moulding and the carbon dioxide process of mould and core-making are mentioned. These two processes are spreading rapidly in foundries and are likely to revolutionise the industry Because there is less burning on of sand on the moulds, the risks associated with the fettling of castings are reduced, but the new methods might bring with them other health risks

We welcome the report as an indication that much time and energy has been directed to minimising the risks to life and limb of the workers of one of Britain's most important basic industries And it is pleasing to note that the effort is a concerted one by employers, trade unions, and Government departments, and by doctors and engineers

Mental Health and the Schools

In recent years we have come to understand something of the relation between the training of children and their health in later life Psychological investigation has displayed the primary importance of the parent-child relationship especially in the early years, and we are now beginning to extend this scrutiny to the child's relationships with *subsequent parent substitutes* of whom the teacher is commonly the *most* influential For a very long time schools were adult centred pupils were expected to behave as though they were merely undersized adults and obliged to conform completely to grown-up standards of behaviour But the insights which psychologists and brilliantly intuitive educational practitioners like Madame Montessori have turned upon the learning situation and the teacher child relationship have already wrought a great change Schools are now progressively child-centred, and norms of achievement development, and discipline are related to pupils' real needs and abilities But this advance is of course by no means universal, and there is room for further experiment Such conferences as the one organised by Unesco in Paris in 1952, of which a report is now published[1] show how much has still to be learnt and done

A smaller follow-up study,[2] dealing exclusively with the periods of possible stress in British primary school outlines the steps needed to safeguard younger children and again draws attention to the conception of education *as a partnership between home and school, parents and* teachers Its authors have no doubt that parent teacher associations help to promote such a partnership, enabling teachers to pass on to parents "something of what they have learned   for in regard to their own children parents are incomparably the most influential teachers" While this latter statement may be questioned—not least by parents—there can be no denying that parent teacher associations are often valuable Some feel, indeed, that it is one of the weaknesses in the present British system that in many parts of the country the decision whether or not an association shall be formed is *left* entirely *to the* discretion of the head teacher, whose own faulty emotional attitudes *may prejudice him against too* close a partnership with the parents of his pupils But as the advantages of such a partnership are demonstrated, and it becomes more familiar, the opposition is likely to fade

The *British report directs special attention* to the stress and strain that the selective nature of the 11+ transition period has on primary school life The coming secondary school entrance examination looms ahead, like a huge *question-mark overshadowing a child's present* and future Where he comes from an ambitious and over-anxious home the strain of this period may become excessive and lead to mental breakdown and acute anxiety Parents, children, and teachers alike become involved in the general anxiety, *each stimulating* the other until the child is so worried that he is unable to do himself justice in the examination itself There will be no way to avoid this time of stress and strain in primary school education until the system itself is modified Fortunately there are signs that some local education authorities are taking steps to reduce the feelings of inequality between pupils with differing gifts and between schools with different curricula Bilateral, multilateral, and comprehensive schools are possible means of reducing this tension and of killing the purely snob value of a grammar school education An improved system of selection and more accurate psychological assessments would also go a long way to produce a fairer outcome and to allay widespread anxiety But, as the report concludes, "a reduction in the number of children for whom any one teacher is responsible is perhaps the most urgent single reform in education in England today Its urgency is evident when one pauses *to* realise that the future of the nation depends increasingly on the quality of the day-to day teaching and the personal relationships of the teachers and the children in our schools intestinal disease, sometimes producing symptoms similar to those of cœliac disease

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[6] The members are Mr T W McCullough (chairman) Mr Colin Gresty Mr A E Pearce Mr E C Happold, Mr P Leonard Gould and Mr H V Shelton (employers' representatives), Mr J Gardner Mr A Hardy Mr J Higham Mr J H Wigglesworth (trade union representatives), Mr J Dobson and Mr J Owen (Iron and Steel Board representatives) Mr W B Lawrie Dr A I G McLaughlin and Mr W A Attwood (secretary) (Factory Department representatives)

[1] Education and Mental Health Unesco London Harrap 1955 Pp 334 17*s* 6*d*

[2] Periods of Stress in the Primary School London National Association for Mental Health 1956 Pp 38 3*s*

Over the last three years I also have observed in my cases of acute infectious disease in young children that some have developed, during convalescence, symptoms like the early manifestations of cœliac disease These symptoms respond dramatically (usually within two or three days) to a gluten free diet and reappear when a premature return to normal diet is made Typically, a child between 1 and 5 years of age becomes naughty and difficult a few days after the onset of an acute infectious illness such as measles or gastro enteritis He is irritable, negativistic, and spiteful, sleep is disturbed and he wakes up many times in the night and often screams, his appetite is poor, he fails to gain weight, his abdomen is often distended, and the stools resemble those of cœliac disease This condition, if left untreated, usually rights itself after a month or two, but may last for much longer, in which case slight petit mal like attacks may develop, in addition to worsening of the other symptoms Even at this stage, a gluten free diet can still cause complete remission of symptoms

The adult equivalent of this syndrome seems to be the headache, insomnia, and depression that commonly follows infectious illnesses such as influenza These three symptoms are often associated with irritability, abdominal distension, and pruritus ani The response of all symptoms to a gluten free diet is prompt in most cases, and they reappear if the diet is discontinued too early The animal counterpart of these syndromes may be canine hysteria

Circumstantial evidence suggests that these conditions are caused by an allergic reaction to an amino acid digestion product of wheat flour affecting nerve, intestinal, or other cells temporarily damaged by the infective process Unfortunately skin tests are no help in establishing the allergic basis of these syndromes, any more than of cœliac disease itself If the conditions are in fact allergic the allergens involved must be blood borne, because of the diversity of the manifestations, therefore the allergens must be digestion products of wheat-flour rather than the wheat proteins (glutenin and gliadin) themselves The exact nature of the allergen remains obscure, but my observations lead me to believe that it is closely connected with the "staling" process of flour and flour products

Some of this work has been published in detail,[2] and I propose to publish the rest shortly I hope that others will be able to observe similar cases and undertake a controlled study

Hove Sussex **GUY DAYNES**

LEPTOSPIROSIS AMONG BRITISH TROOPS IN MALAYA

SIR,—The views expressed last week by Captain Clein are to be respected in that they represent his own personal opinion I feel I should point out, however, that at present the weight of specialist opinion in the Army Medical Services is that penicillin is of little value in the treatment of leptospirosis as encountered in Malaya and Singapore

W A D DRUMMOND
Deputy Director General
Army Medical Services

War Office
London S W 1

HYPERTROPHIC PULMONARY EMPHYSEMA

SIR,—Although Dr Oswald terms your leader (Jan 7) as "conventional," his own letter (Feb 4) might surely be more justly described by this adjective For the whole difficulty of the interrelationship between chronic bronchitis and emphysema lies in the most *unsatisfactory nature of the* conventional explanations

The clinical and pathological problems were well described by Dr Samual Gee sixty years ago To suggest that the observation of "repeated infection" in chronic bronchitis thereby resolves its aetiology begs the difficult questions Does this infection suddenly start, de novo, in a previously healthy lung? Have the changes in lung function, recently demonstrated in normal people with increasing age, any importance in this development? Why do some patients produce a considerable amount of sputum for years without emphysema developing, while others first seek advice when they have a considerable degree of lung destruction, and tell us that they very rarely cough?

So far as I am aware there is no authority for Dr Oswald's statement that the most useful pulmonary function test in practice is the measurement of the oxygen saturation of the blood before and after exercise In my experience this is one of the least useful tests in the assessment of emphysema To remark that the accurate diagnosis of emphysema is largely academic, is premature, since we will be aware of the problems only when accurate diagnosis is possible, there is little doubt that the measurement of lung damage by tests of function has a major part to play in this task

St Bartholomew s Hospital,
London E C 1 **D V BATES**

BENZATHINE PENICILLIN

SIR,—May I draw your attention to a possible objection to the use of long acting benzathine penicillin preparations, particularly injections said to give therapeutic blood-levels for up to one month I am concerned about the chance of an allergic reaction developing soon after injection, yet there will remain in the body penicillin potent for days or even weeks Hitherto no serious reaction to these injections has been reported, but it would seem that a special hazard may exist

Mayer de Rothschild Hadassah
University Hospital, Jerusalem **ELI DAVIS**

FAMILIAL HEMIPLEGIC MIGRAINE

SIR,—Dr Blau and Dr Whitty have written a most interesting paper on this subject[1] However, their statement that "The condition appears to be inherited through a recessive gene " is correct only if they change the word "recessive" to "dominant"

Department of Medical Genetics
Montreal Children s Hospital,
Quebec, Canada **JULIUS METRAKOS**

*** This letter has been shown to Dr Blau and Dr Whitty, who write "We are grateful to Dr Metrakos for drawing attention to our error Inheritance appears to be by an irregularly dominant gene"

HOMOSEXUALITY

SIR,—Dr Learoyd's criticisms (Feb 4) of Dr Comfort, and his oblique championship of the B M A report, would have carried more weight if he had been more objective Had he, for instance been able to adduce statistical evidence to support the claim that punitive measures such as martyrdom, witch-hunting, inquisitions, pogroms, and the odium attaching to illegitimacy had significantly reduced the numbers of Christians, witches, heretics, Jews, and bastards, then, by parallel argument, he might have developed a less gratuitous case against Dr Comfort Alas for sophistry! History, rather perversely, tends to show that whereas persecution supported by legislation has ever achieved but little, the repeal of some *of the relevant civil laws has, in most cases, at least mitigated* the associated evils

London N W 3 **PHILIPPE BAUWENS**

"MUNCHAUSEN'S SYNDROME"

SIR,—On the evening of Feb 2 a young Irishman, with a crew cut, claiming to be a ship's radio officer and ex-mental nurse, appeared in this hospital He said that two hours previously right postauricular pain and unsteadiness of gait had developed

He was afebrile, with a right facial palsy, a healthy right mastoid cavity, and papillœdema of the right optic disc, although this was not easily seen because of continual to-and-fro movements of the eye He bore the scars of many operations on the right side of his skull, with a recent endaural scar which he claimed was due to a mastoidectomy in Dublin nine months before This identified him as the man described by Dr Robson last week and by earlier correspondents

Despite heavy sedation, he was troublesome throughout the night and the following morning During the afternoon he became violent and aggressive Dr J T Hutchinson, the visiting psychiatrist, considered him to be a hysteric rather than a malingerer, he was remarkably suggestible He had apparently lost 4 stone in weight, and it was difficult to see the cause of his behaviour He was admitted to a mental hospital that day

St Giles Hospital
London S E 5

W MACKENZIE
T L BOWEN

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[2] *Coll gen Practit Res Newslett* 1955 no 9, p 128

[1] Blau J N Whitty, C W M *Lancet* 1955 ii, 1115

Dr Mouchot continues, "how and where to resettle the wine producers, publicans, still owners and others who would become redundant, it is childish to expect politicians to do anything" Meanwhile, the consumption of alcohol per head in France is the highest of any nation (Italy is second) both absolutely and in relation to national income The total consumption in France is three times that in Great Britain

Lest this comparison lead to unjustified feelings of complacency, it is as well to remember that (according to the latest available returns) no fewer than 50,000 persons were convicted of simple or aggravated drunkenness in 1953 before magistrates' courts in England and Wales

STREPTONIVICIN

A NEWLY discovered antibiotic, streptonivicin (albomycin, 'Albamycin'), is produced by an actinomycete, *Streptomyces niveus* (*Actinomyces subtropicus*) By comparing ultraviolet absorption curves, Welch and Wright[1] have shown that streptonivicin is identical with two other new antibiotics, cathomycin ('Cathocin') (obtained from *Streptomyces spheroides*) and 'Cardelmycin' (crystallinic acid) Streptonivicin has been known to Soviet workers for about five years but has only lately become available in the West It was first isolated in 1951 by Gause and Brazhnikova,[2] of the Institute for Antibiotic Research in Moscow They obtained it from cultures of *Actinomyces subtropicus*, and named it albomycin The antibiotic has been investigated in the United States under the name streptonivicin It inhibits the growth of gram-positive cocci, chiefly pneumococci, staphylococci, and *Streptococcus pyogenes*, and what is equally important it inhibits the growth of sensitive organisms resistant to other antibiotics, including penicillin, streptomycin, the tetracyclines, and erythromycin[3] Resistance to streptonivicin can, however, develop It is also effective against a number of gram negative bacteria, such as Friedländer's bacillus and the coli dysentery group, klebsiella, *Aerobacter aerogenes*, and *Micrococcus pyogenes* (which is highly sensitive) Rather less sensitive are meningococci and *Hæmophilus pertussis* *Mycobacterium tuberculosis* is insensitive The pure substance inhibits the growth of staphylococci at a dilution of 1 in 700 million, the figure for penicillin is 1 in 80 million Brazhnikova et al[4] found that streptonivicin is a basic compound forming an amorphous red sulphate, readily soluble in water, slightly soluble in methanol, but insoluble in other organic solvents The pure substance contains 4 16% iron, which can be removed by treating with acetone containing hydrochloric acid, but this treatment reduces its antibiotic activity It is thought that the iron is chelated to the hydroxy group in serine, which is part of the molecule On hydrolysis a number of amino acids are formed Streptonivicin appears to be a complex metal containing polypeptide with a molecular weight of about 1300 Chromatography shows that the constituent amino acids are ornithine, serine, glutamic acid, alanine, glycine, and another unidentified one A solution of the antibiotic is stable for only two days[5]

Since streptonivicin inhibits the growth of sensitive bacteria only in the presence of oxygen, it may interfere with the oxygen-transporting iron containing enzyme in susceptible bacterial cells[6] Its chemical structure is possibly related to this enzyme, with which it may compete in a respiratory-enzyme system Pharmacologically streptonivicin seems to be inert, it produces no local reactions, and, like penicillin, is of extremely low toxicity A mouse, for example, tolerates a dose of 50 million units per kg body weight No effect on the liver, kidneys, or hæmopoietic system has been observed in patients given the antibiotic A remarkable property of streptonivicin is its ability to form a reversible complex with serum proteins, which facilitates its circulation in the body[2] This complex has chemotherapeutic properties, but unfortunately it interferes with the assay of the antibiotic in the blood The serum-proteins, which bind about 90% of a single dose of streptonivicin, must be precipitated by trichloracetic acid before the assay is made The protein streptonivicin complex apparently dissociates in vivo, because it is active when injected intraperitoneally into mice infected with pneumococci or dysentery bacilli, whereas in vitro it has no effect on these organisms Since this complex is not readily excreted by the kidneys, an initial dose of streptonivicin is slowly excreted After repeated injection the amount excreted rises sharply because the serum proteins have become saturated and free antibiotic circulates in the blood The free streptonivicin is excreted for six to eight hours after injection[8] The antibiotic is absorbed in man if given by mouth, and doses of 0·1–0·5 g six hourly produce effective blood levels There is, however, great variation in the concentration in the serum, a fact for which there is no ready explanation The drug appears in the bile and in ascitic and pleural fluids, but not in the cereb spinal fluid[5]

Mice infected with 500,000 lethal doses of pneumococci show 100% survival-rates after a single subcutaneous injection of 750,000 units of streptonivicin per kg Mice infected with various strains of staphylococci and hæmolytic streptococci have also been successfully treated There seems to be a synergistic action with penicillin and streptonivicin Turning to the clinical use of streptonivicin, in Russia[2,4] it has been used mainly in the treatment of infections by pathogenic cocci, particularly when they are penicillin resistant Intrathecal injections of 100,000–200,000 units gave good results in the treatment of meningitis due to susceptible organisms Other uses include the treatment of peritonitis and surgical infections, and penicillin resistant prostatitis and gonococcal urethritis We do not know of any other clinical reports and await further news with interest

DIRECT ACTION

On Monday it was stated that about 10,000 nursing staff in 33 mental hospitals have now declared that they will no longer work overtime They have done this to express their dissatisfaction with their pay and with the conditions of their service, under which longer and longer hours are demanded of a dwindling staff who (unlike people in most other occupations) do not get a higher rate when they come early or stay late

Working conditions cannot be substantially improved until there are more nurses, but it is hard to find new recruits for an aggrieved profession, and even harder to hold them In some hospitals, indeed, the turnover of nurses must almost rival the turnover of patients It is reported,[9] for instance, that in the Manchester region six hospital management committees, with an establishment of 2929, in one year accepted 1842 recruits, but were worse off at the end of it because they had had 1891 resignations Nor will incidents such as the unfortunate demonstration by nurses at the Ministry of Health's exhibition at Manchester speed the recruiting drive With the best will in the world on all sides, it will need patience and a different climate of public opinion to provide the extra staff that alone will enable these conditions to be greatly changed

On the other hand it is obvious that the nurses' other and closely related reason for dissatisfaction—the insufficiency of their pay—could, at a cost, be adjusted immediately, and they complain of the slowness of negotiations in the Whitley Council That they are not alone in this complaint was shown again in an adjournment debate[10] in the House of Commons when the Whitley Council machinery of the National Health Service was criticised Negotiations, Mr Arthur Blenkinsop declared, were delayed because the Treasury insisted that no suggestion should be put forward by the management side without its prior approval He warmly supported the recommendation of the Guillebaud Committee that the representation on these councils of regional hospital boards and hospital management committees should be increased At present, as Mr. Herbert Butler put it, the Ministry of Health had interposed Ministry and Treasury officials between the hospital authorities and the council, and in consequence the machinery did not move fast enough to deal with day to day problems Meanwhile, not only in mental hospitals, management committees grow more and more uneasy at their inability to offer rates of pay bearing a reasonable relation to those to be had at the nearby factory or airport

We note with deepening anxiety the tendency of people in the health service to adopt the mental attitudes and techniques of organised labour, which are often irreconcilable with those of a profession But in this case, as so often in industry, part of the responsibility for direct action lies with those who tend to delay necessary concessions until these are made urgent by a threat

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[1] Welch, H, Wright, W W *Antibiot Chemother* 1955 5 670

[2] Gause G F, Brazhnikova, M G *Nov Med*, *Mosk* 1951, 23, 3

[3] Gause, G F *Brit med J* 1955 ii, 1177

[4] Brazhnikova, M G Lomakina N N Muravieva, L I *C R Acad Sci U R S S* 1954 99, 827

[5] Martin W J Heilman F R Nichols, D R, Wellman, W E, Geraci, J E *Proc Mayo Clin* 1955, 30, 540

[6] Shapiro S L *Nov Med Mosk* 1951, 23, 53

[7] Shorin, V A *Ibid* p 7

[8] Judinzev S D *C R Acad Sci*, *U R S S* 1954, 99 115

[9] *Tribune* Feb 17, 1956

[10] *Hansard* Feb 8, 1956, col 1751

Diary of the Week

FEB 19 TO 25

Monday, 20th

HUNTERIAN SOCIETY
8 30 P.M (Mansion House) Sir Henry Cohen Reflections on the Hunterian Method (Hunterian oration)

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road W 12
4 P.M Dr Denis Williams Disturbances in Sleep

Tuesday, 21st

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine Keppel Street W C 1) Mr K C Richardson Problem of Mammary Growth and Structure

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
5 P M *Pathology and Epidemiology and Preventive Medicine* Dr D D Reid, Dr Lynne Reid Prof J Mulder (Leiden) Prof C H Stuart-Harris Chronic Bronchitis

ST MARY S HOSPITAL MEDICAL SCHOOL Paddington W 2
5 P M Dr Kenneth Cross Resuscitation of the Newborn

INSTITUTE OF DERMATOLOGY, Lisle Street, W C 2
5 30 P M Dr R T Brain Skin Diseases of Children

SOUTH WEST LONDON MEDICAL SOCIETY
8 30 P.M (Bolingbroke Hospital) Sir Theobald Mathew The Queen's Peace

SOCIETY FOR THE STUDY OF ADDICTION
8 P.M (11 Chandos Street, W 1) Mr Lawrence Abel Dr A H Douthwaite Sir Harry Greenfield Dr R Hale White Dr J A Hobson Sir Hugh Linstead Prof P O. Wolff The Recent Legislation on Heroin

Wednesday, 22nd

ROYAL SOCIETY OF MEDICINE
10 A.M. *Endocrinology (Joint meeting with the Society for Endocrinology)* Symposium on Hormone Administration in Animals and Man

INSTITUTE OF ORTHOPÆDICS, 234, Great Portland Street, W 1
8 P M Mr J N Wilson Cancellous Bone Grafts

INSTITUTE OF DISEASES OF THE CHEST Brompton, S W 3
5 P M Mr N R Barrett Diseases of the Chest Wall

INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Differential Diagnosis of Fungous Infection of the Skin

ST MARYLEBONE HOSPITAL FOR PSYCHIATRY AND CHILD GUIDANCE, 48 Cosway Street, N W 1
5 P M Dr J N Milnes Blackouts

BIRMINGHAM MEDICAL INSTITUTE, 154 Great Charles Street, Birmingham 3
8 P M *Psychiatry* Dr R E Hemphill Writer's Cramp and Other Disorders in Writing

NOTTINGHAM MEDICO CHIRURGICAL SOCIETY 64, St James's Street, Nottingham
8 30 P M Sir Clement Price Thomas Carcinoma of the Lung

MANCHESTER MEDICAL SOCIETY
4 30 P M *Medicine and Pathology* Dr Sheila Sherlock Acute Hepatic Failure

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St Vincent Street, Glasgow
5 P M Dr W F M. Fulton Coronary Circulation in Health and Disease

Thursday, 23rd

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields W C 2
3 45 P M Dr B E Heard Endometriosis (Erasmus Wilson demonstration)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine) Dr M W Goldblatt Industrial Toxicology

WEST LONDON MEDICO CHIRURGICAL SOCIETY
9 P M (Fellows' Restaurant Zoological Gardens) Mr H B Cott SC D Wild Life in Uganda

UNIVERSITY OF ST ANDREWS
5 P M (Queen's College Dundee) Prof Dugald Baird Problems in Obstetrics Today

Friday, 24th

ROYAL SOCIETY OF MEDICINE
8 15 P M *Obstetrics and Gynæcology* Prof Gordon King (Hong Kong) *Hydatidiform Mole and Chorion-Epithelioma—the Problem of the Borderline Case*

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Prof R B Hunter Noradrenaline in Medicine

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3 30 P M Mr Anthony Radcliffe Dysphagia

Saturday, 25th

INSTITUTE OF ORTHOPÆDICS
10 A M Mr J I P James Scoliosis

Births, Marriages, and Deaths

DEATHS

IRVING —On Jan 22 at Port of Spain Trinidad B W I, Joseph Kenneth Irving M B D A D OBST consultant anæsthetist Colonial Medical Service formerly anæsthetist, London Clinic Surgeon Lieut Commander R N V R aged 42

Vacancies

ACADEMIC AND EDUCATIONAL
Manchester University Asst Lecturer or Demonstrator in Path
Sheffield University Lecturer in P H
Medical Research Council (Labs Gambia W Africa) M O
Royal College of Surgeons of England Surgery Lectures & Clinical Conferences Mar /Apl
Institute of Basic Medical Sciences Lectures & Demonstrations in Anatomy, Physiology & Path Sept /Dec
Cambridge Gonville & Caius College Berkeley Bye F ship
Tancred s Studentships (Divinity Medicine Law)
Glasgow University & Royal Fac of Physicians & Surgeons Refresher course for G P s 14th/26th May
Saskatchewan University Canada Lecturer in Bact
Royal Inst of P H & Hygiene Course of Instruction (C P H), 16th March
Aberdeen University Refresher Course for Med Practs 14th/26th May
King s College University of Durham &c 1st Asst in Neurology
University College Cork Ainsworth Med Scholarship
Faculty of Anæsthetists of the Royal College of Surgeons of England 5th A G M , 21st March
Royal Society Govt Grant for Scientific Invest
London University Grants for Research
Edinburgh University Lectureship Psych Med
Christian Medical Fellowship Meeting & Lecture

ANÆSTHETICS
Charing Cross W C 2 P t Cons
Hackney Group H M C Sr H O
Queen Charlotte s & Chelsea Hosps Sr H O
St Bart s E C 1 London E 1 & North East Met R H B Sr Reg
St Charles W 10 Sr H O
Enfield Chase Farm Sr H O
Leeds R H B Regs
Manchester R H B Sr H M O
Medway & Gravesend H M C Locum
Norwich United Hosps Sr H O
Plymouth South Devon & East Cornwall Sr H O
Scotland Eastern R H B Sr Reg
Scotland South Eastern R H B Cons
Sheffield R H B Sr H M O
Southend Gen. Sr H O s
Welsh R H B & Cardiff United Hosps Sr Reg
Wolverhampton Royal Sr H O
Ibadan Nigeria Univ College Hosp Reg & H O
Tasmania Royal Hobart Specialist
U S A Cambridge Mass Residencies

CARDIOLOGY
National Heart (Country Bch) Sr H O

CASUALTY
Hackney E 9 H O
Poplar E 14 Sr H O
South West Met R H B Sr Casualty Officer
Wanstead E 11 Sr H O
Whittington, N 19 Sr H O
Chesterfield Royal H O
Hemel Hempstead West Herts Jr H M O
Hertford County Sr H O
Kingston Surrey Sr H O 's
Manchester Ancoats Sr H O
Nottingham Gen Sr H O
Plymouth South Devon & East Cornwall Sr H O
Reading Battle H O
Sheffield R H B Sr Casualty Officer
Sheffield United Hosps H O
Slough Upton Locum H O
Watford Peace Mem Sr H O
Weston-super Mare Gen Sr H O
York City Locum Jr H M.O

CHEST AND TUBERCULOSIS
London Chest E 2 H O s
Bristol Ham Green Jr H M O
Bristol Ham Green Sr H O
Chelmsford Broomfield Locum Sr H M O
Driffield Northfield San Sr H O
Manchester R H B P t Cons & Sr H.M.O
Paisley & Dist Hosps B O M. Jr H M O
Skipton The Hosp Sr H O or Jr H M O
South Brent Devon Didworthy Chest Jr H M O
South East Met R H B Regs
South West Met R H B Locum Sr H M O
Welsh R H B Sr H M.O

DENTAL SURGERY
Leicester Royal Infy H O

DERMATOLOGY
Guy s S E 1 P t Reg
Cambridge United Hosps P -t Clin. Assts
Glasgow Stobhill Gen Pre reg H O
Nottingham City Hosp & Skin Clinic Reg

EAR NOSE, AND THROAT
North West Met R.H B P t Cons
Royal National T N &E , W P t Clin Assts & O P Assts (G P s)
Royal National T N &E W Reg or Sr H O
Edinburgh Central Hosps B O M H O
Hull A Group H M C Sr H O
Portsmouth Group H M.C Reg
Reading Royal Berks H O

GERIATRICS
Whittington N 19 H O
Cardiff St David s Sr H O

INFECTIOUS DISEASES
Sheffield Lodge Moor Reg

MEDICINE
Hammersmith West London & St Mark s Hosps H O 's
Lambeth S E 11 H O
North Middlesex N 18 H O
St Bart s E C 1 & North East Met R H B Sr Reg
St George in the East E 1 H O
St Stephen s S W 10 H O
Whittington N 19 H O s
Ashford Middx. H O
Aylesbury Stoke Mandeville H O
Birmingham United Hosps Reg
Bristol Southmead Gen Hosp Group M.C Sr H O
Buxton Devonshire Royal Sr H O
Cambridge Addenbrooke's H O
Carshalton St Helier Reg

higher cerebral centres but from the midbrain" I wrote (*Lancet*, 1950, i, 881) "My observations (in my work with mentally handicapped children) have strengthened my belief that many mental defects are the result of unrecognised birth hæmorrhages affecting tributaries of the vein of Galen and injuring ganglia of the mesencephalon and telencephalon" And where did Dr Bourne read that "the vital lesion lay constantly in the corpora quadrigemina and the lateral geniculate bodies"? I wrote "Pathological changes in the above mentioned ganglia (i e, the corpora quadrigemina and the corpora geniculata) and in their afferent and efferent tracts may play one of the most important roles in the causation of mental defect" (*Brit med J* 1953, i, 936) And in a later letter (*Brit med J* 1953, ii, 392) I stated explicitly "My topographical reference embraces the whole length of the visual and auditory pathways from receptor organ to cerebral cortex This shows that my hypothesis is not primarily concerned with the actual anatomical level affected by the impairment, but with the circumstance that mainly or even exclusively disturbances affecting to some degree the integrations of the visual or auditory system will lead to a mental defect" One can hardly be more precise in regard to the widespread possibilities of localisation —LISE GELLNER, M D (St Lawrence's Hospital, Caterham, Surrey)

Deaths During Anæsthesia —In your annotation (Jan 21) you say that "about 8 million" anæsthetics were given in the hospitals of England during 1954 The figure is presumably taken from the Ministry of Health's report, and owing to your omission of the words "alone or in combination" a total considerably in excess of the true one has been achieved The correct total is obtained by multiplying the total number of operations for the sample week—56,062—by 52 (or more accurately 51 owing to bank holidays) This gives a grand total of some 2,860,000 operations for the year, each operation involving the use of about 2 3 anæsthetic agents (oxygen having been excluded as an anæsthetic) This total of 2,860,000 anæsthetics does not of course include operations in nursing-homes, maternity cases, and dental anæsthetics, *and I do not suppose that the number of these can ever be computed* But it is very gratifying to learn that the total number of deaths under anæsthesia continues to diminish —MASSEY DAWKINS, F F A R C S (London, W 1)

Intragastric Milk Drip —I must apologise to Dr Watkinson and Dr Chandler (Jan 28) for not quoting their paper more fully, but this seemed unnecessary as I was merely investigating the use of a Ryle's tube in predicting massive gastrointestinal hæmorrhage They wrote (*Lancet*, 1953, ii, 1170) "The bedside observation of bloodstaining in the aspirated specimens was useful because further hæmorrhage could be detected before other clinical criteria had indicated its presence" Unfortunately, this is not supported by my experience (Jan 14)

I was surprised to see the resurrection of that hoary old red herring, the overall death rate I thought that this had been decently buried in 1947 (F Avery Jones, *Brit med J* 1947, ii, 441, 477) Suffice it to say that in Chandler and Watkinson's published series 8 5% of the patients were older than 70, in my series 19% of the patients were older than 70, and of the 8 deaths 6 were in this group —A M DAWSON M R C P (Central Middlesex Hospital, London, N W 10)

"Infectious Roseola" —Dr Fletcher reports (Jan 7) that in Sarafand in August and September, 1941, 'some fifty cases of what I termed (for want of a better name) 'infectious roseola occurred Similar small outbreaks were noted in the surrounding district" During the same period in Tel Aviv, notably in the suburbs, I saw *some hundred patients* with apparently the same disease (We knew of the outbreak in Sarafand) We described the outbreak as "an unknown epidemic infectious disease" (M Leffkowitz, *Harefuah* 1942, 22, 3) The picture was identical with that reported by Dr Fletcher The incubation period was 3½–5 days We, too, suggested that the cause was a virus In the years 1950–53, particularly in the same districts there were further outbreaks (P Radt *Harefuah*, 1955 49, 41) The evidence indicates that the disease was caused by West Nile virus (E Olejnik, *Bull Res Coun Israel*, 1952 2, 210 H Bernkopf, *Harefuah*, 1953, 45, 101 N Goldblum et al *Amer J Hyg* 1954, 59, 89 M Benjeh N Goldblum, *Harefuah*, 1955, 48, 58) Accordingly the disease has been called West Nile fever —M LEFFKOWITZ M D (Belinson Hospital, Petah Tiqva, Israel)

Unfair to Surgery —In your issue of Jan 14 (p 107) tw doctors said that after having several feet of gut removed many years ago for regional ileitis they were "as fit as fiddl May I add that one of them, not so many months after h titanic operation, climbed the Schreckhorn by way of th N W arete I submit that he was then as fit as ten 'cellos —A E STEVENS M D (Jersey, Channel Isles)

Anticoagulants in a Hot Climate —In reply to Dr Merker and Miss Scholtz (Feb 4), I would point out that the Egyptia summer is much warmer than that at Cape Town (12–22 C At Suez the temperature may be as high as 41°C In patien on maintenance doses of phenylindanedione bleeding ma occur only on very hot days The maintenance dose of th drug I use is larger, as I aim at a prothrombin index of 10–30 and not 40–60% I agree that moderate heat (12–30°C) do not affect the maintenance dose of phenylindanedione —Ima TAWFIC, M D (Suez, Egypt)

Homosexuality —Dr Tuthill (Feb 11) uses the wor 'purpose" in relation to sex codes, and implies it in oth illustrations Whose purpose? Are we not often guilty of unwarranted abduction of this word from another system? Do we not usually mean "function"? Sex codes have maintained "the family as a social unit" that, from anthropological study, has evidently been one of their functions But whose purpose, whose intention, is it that they should? That surely, is another question altogether, consideration of which may throw a larger light on all cod by which they may be seen to fail or succeed in fulfilling a good or bad function —J N COZENS HARDY, B M (Holt Norfolk)

Inguinal Herniorrhaphy —Mr Doran has asked (Feb 4) how the conjoined tendon contributes to the integrity of the inguinal canal without literally acting as a shutter May I suggest that the conjoined tendon muscles do this by resistin anterior (or posterior) displacement of the "primary fixed point This prevents upward displacement of the "arch" It is perhaps better to regard the conjoined tendon as a 'partly closed shutter" in a state of dynamic equilibrium, tending to maintain its vertical position in the face of varying disruptive forces In this sense, the shutter like action may be said to occur, though paradoxically it moves little if at all Unchecked, the arch would rise as much as an inch in a person of average build This does not happen of course, and the function of the conjoined tendon must be deduced from what does not happen If this is so suture of conjoined tendon to inguinal ligament may so far displace the arch below its position of equilibrium that the muscles of the conjoined tendon would themselves tend to pull the arch upwards This effect should be only partly compensated for by relaxing incisions in the rectus sheath —J F ROBINSON M B (London, W 11)

Obituary

Mr G E NELIGAN

George Neligan was one of those men who give life to institutions and the corporate spirit of old students of the London Hospital owes much to his example in treating any Londoner as a personal friend He went to the hospital from Oxford in 1907, qualified in 1910, and was surgical registrar in 1914 Returning to the same post in 1919, with a Military Cross, he became assistant surgeon ("Howard and Neligan") in 1922, *specialising* in urology He did much to organise and build the students' hostel, and in the late war he lived in the hospital with the title of medical superintendent—a cheerful and reassuring figure After his retirement to Walmer in 1951, he was brought back to preside at the London Hospital dinner in 1953 when he was given an ovation The hospital and its students, it was said, had never had a better or more generous friend in all his years his attitude had been 'with malice toward none and charity toward all" He died at Folkestone on Feb 24, aged 71

We regret to record also the death of Mr HAROLD KING D SC, F.R.S, formerly of the National Institute for Medical Research

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The Death Penalty

THE practice of taking the life of one who had taken the e of another originated in primitive societies as an act family vengeance, and this reprisal has persisted in me communities as vendetta In Britain the death enalty is a solitary instance of punishment matched ith crime Last week the House of Commons resolved, n a free vote and against the Government's advice, that uch punishment should be abolished or suspended

The issue between the defenders of this penalty and 's opponents has now been narrowed to a single question—whether its application has a unique deterrent ffect In the debate MAJOR GWILYM LLOYD GEORGE, the Home Secretary, declared ' Let me say emphatically hat I believe capital punishment to be justified only if it s likely to reduce the amount of murder " The Royal Commission on Capital Punishment found "no clear evidence in any of the figures we have examined that the abolition of capital punishment has led to an increase in the homicide rate, or that its reintroduction has led to a fall " But it added "The negative conclusion we draw from the figures does not of course imply a conclusion that the deterrent effect of the death penalty cannot be greater than that of any other punishment It means only that the figures afford no reliable evidence one way or the other "

There being no good evidence that hanging murderers checks the number of murders, the case for discontinuing this rough justice seems to us unanswerable Firstly, by ending the life of a murderer we impose gross suffering on his relations, before and after the execution Secondly, in a trial for murder, juries, aware of the grim decision before them—and perhaps of the conceivable risk of exterminating an innocent victim—are reluctant to bring in a verdict of guilty (A law which may thus be imperfectly applied is a bad law Nor is the final decision by one man regarding reprieve fair to the prisoner, whose life depends on the decision, or to the Home Secretary, who must make the decision) Finally, our society damages itself by giving its warrant to the killing of any of its members, and this damage is made the worse by newspaper accounts of the final days and hours of the murderer's life, which, like the public executions of bygone days, satisfy and promote a morbid appetite

At the start of the 19th century over two hundred crimes were punishable by death The curtailment of the death penalty was accompanied by widespread forecasts of increases in crime These forecasts were not fulfilled We welcome the Prime Minister's assurance that he will seek to give effect to the Commons decision, and we hope that when the time comes the House of Lords will bear in mind the country's growing uneasiness about this grotesque legacy from our forefathers

The Patient and his Cell Nuclei

THE development of a new and important diagnostic technique creates fresh difficulties, even though it contributes to the solution of existing ones There is, for example, the practical problem of ensuring that the new method when it has left the hands of its pioneers and is put to routine use in laboratory or ward, is performed and interpreted by those who are aware of its difficulties and its limitations For these reasons Professor BARR's views[1] on the conclusions to be drawn from the cytological tests of sex are particularly welcome He reminds us that it is too early to assume that the "female" sex chromatin is in fact derived from two X chromosomes, and therefore we should not yet use the expressions "chromosomal sex" or "genetic female" or "genetic male" He proposes the sensible alternative, for use in the clinic or outpatient department, of "chromatin positive" (female) or "chromatin negative" (male), in order that no suggestion can, by mischance, be conveyed to any patient that the "maleness" or "femaleness" of the body-cells is at variance with sexual anatomy—and, he might have added, with the patient's body-image and inner concept of sexual status Nor should this information be deliberately given to the patient or to relatives GRUMBACH et al[2] believe "it is most important that the patients and their families should not be informed concerning their chromosomal sex when a male chromatin pattern is found, in view of present day misconceptions of the importance of chromosomes in determining psychosexual outlook " This opinion has the authority of the senior author, LAWSON WILKINS, whose experience of the sexual deviations of children, chromosomal and hormonal, is unrivalled

Few will dispute this advice, but the reason for it should perhaps be further emphasised The sexual orientation of an individual is not determined either by the sex chromosomes or by the hormones, and still less by the chromatin in the cells of the skin It would be very unwise to attempt to change the psychosexual habit which has been established through the years of growth or even to convey information which will challenge the integrity of this personal image HAMPSON et al,[3] working in Wilkins's clinic, studied 11 girls and women with gonadal agenesis who were chromosomally male, and all of them "were found unequivocally to fulfill the cultural and psychological expectations of femininity The salient finding to emerge from the study was that a person's conviction of himself as a man or herself as a woman—the gender rôle and erotic orientation—is a variable quite independent of genes and chromosomes " Cytological sexing is therefore another of the findings which the doctor should not pass on to patients and their relatives, for its exact significance will not be understood and its real importance may be misconstrued The doctor's duty is to shoulder, on behalf of his patient, the diagnostic and therapeutic responsibilities involved

In the management of hermaphrodites, female pseudohermaphrodites, male pseudohermaphrodites, and patients with gonadal dysgenesis, the new methods have done much to increase diagnostic precision, and they enable a rational plan of treatment to be made in the first few weeks of life, when these anatomical deviations

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[1] Barr, M L *Lancet* Jan 7, 1956, p 47

[2] Grumbach M M, Van Wyk, J J, Wilkins, L *J clin Endocrin* 1955 15 1161

[3] Hampson, J L Hampson, J G, Money, J *Bull Johns Hopk. Hosp* 1955 97, 207

EAR, NOSE, AND THROAT

Ashford, Middx H O
Birmingham & Midland Ear & Throat Sr H O or H O
Blackpool Victoria Sr H O
Doncaster Royal Infy Sr H O
Hosp for Sick Child W C 1 Reg
Hull A Group H M C Sr H O
Hull Victoria Hosp for Sick Child Locum Sr H O
Mid Glamorgan H M C Sr H O
Newcastle R H B Reg
Northampton Gen Sr H O
North West Met R H B P t Cons
Portsmouth Group H M C Sr H O
Reading Royal Berks H O

GERIATRICS

East Anglian R H B Reg
East Anglian R H B Sr H M O

HÆMATOLOGY

South West Met R H B Jr H M O

INFECTIOUS DISEASES

Sunderland Havelock Hosp & Grindon Hall San Jr H M O

MEDICINE

Bolingbroke, S W 11 H O
Charing Cross, W C 2 Reg
Elizabeth Garrett Anderson N W 1 H O
Paddington Gen W 9 Reg
St Leonard's N 1 Sr H O
Whipps Cross E 11 H O
Ashford, Middx H O
Birmingham Dudley Road H O
Bournemouth Royal Victoria H O
Bristol Southmead Gen Hosp Group *M C Sr H O*
Buxton Devonshire Royal Sr H O
East Anglian R H B Reg
Enfield War Mem Sr H O
Guildford Royal Surrey County Reg
Hull Kingston Gen Pre reg H O
Huntingdon County H O
Ilford King George Pre reg H O
Leeds R H B Regs
Luton & Dunstable Reg
Maidenhead H O
Manchester R H B Reg
Portsmouth Group H M C Sr H O
Scotland Western R H B P t Cons
Swansea Mount Pleasant Jr H M O
Tredegar, Mon St James H O
Worcester Royal Infy H O

OBSTETRICS AND GYNÆCOLOGY

Elizabeth Garrett Anderson, N W 1 H O
Lambeth S E 11 H O
Birmingham United Hosps H O 's
Canterbury Kent & Canterbury H O
Cheltenham Maternity H O
Chichester Group H M C Reg
Derby City Pre Reg H O or Sr H O
Derby City Reg
Glasgow Southern Gen Sr H O
Halifax Area Hosps M C Sr H O
Hastings Buchanan H O
Manchester Crumpsall H O
Nottingham City H O
Nottingham Firs Maternity Sr H O
Portsmouth Group H M C Pre Reg H O
Reading *Combined Hosps* H O 's
Rochford Essex Gen Locum Sr Reg or Reg
Rochford Essex Gen Sr H O & H O
Scotland Western R H B Reg
Sheffield R H B Sr Reg
Shrewsbury Royal Salop Infy & Copthorne H O
Stoke on Trent City Gen Pre reg H O 's
Sunderland Royal Infy H O

OPHTHALMOLOGY

St Thomas, S E 1 *P* t *Refractionist*
St James S W 12 P t Reg & Locum Reg
Broxburn West Lothian Bangour Gen Sr H O
East Anglian R H B Reg
Exeter Clinical Area P t Cons
Leeds R H B Reg
Leeds R H B Sr Reg
Manchester United Hosps Sr H M O
Newcastle R H B Locum Cons or Sr H M O
Oxford R H B P t Cons
Oxford United Hosps H O

ORTHOPÆDICS

Queen Mary's (Roehampton) S W 15 Reg
Royal National Orthopædic, W 1 Sr H O
South East Met R H B P t Cons
South-East Met R H B Regs
Westminister S W 1 Sr Reg or Reg
Ashford, Middx H O
Bath St Martin's H O
Birmingham R H B P t Cons
Bournemouth Royal Victoria Reg
Braintree Black Notley H O & Locum H O
Brighton Gen H O
Durham County H O
Ipswich & East Suffolk Sr H O
Northampton Gen H O
Portsmouth Group H M C Pre reg H O
Romford Oldchurch H O
Southampton Royal South Hants Sr H O

PÆDIATRICS

Hosp for Sick Child, W C 1 Sr H O
Birmingham United Hosps Sr Reg
Chelmsford St John's H O
Edgware Gen Reg
Manchester Duchess of York Hosp for Babies H O
Manchester Duchess of York Hosp for Babies & Wythenshawe Sr H O
Northampton Gen H O
Reading Royal Berks H O
Scotland Western R H B Reg
Canada Child's Hosp, Vancouver Residents

PATHOLOGY

Leeds R H B Sr H M O
Manchester *R H B* Reg
Manchester West Manchester H M C Sr H O
North East Met R H B Reg
Rochford Essex Gen Locum Reg & Sr H O
Sheffield United Hosps Reg or Sr H O

PHYSICAL MEDICINE

North East Met R H B P t Cons

PSYCHIATRY

Middlesex, W 1 (M O Sr Grade)
North West Met R H B P-t Sr H M O
North East Met R H B Reg
South East Met R H B Sr Reg & Regs
South East Met R H B Cons
South West Met R H B Reg
St George's, S W 1 Sr Reg
Aylesbury St John's Jr H M O
Bury & Rossendale H M C Jr H M O
Bournemouth, St Ann's Jr H M O
Epsom Horton H M C Reg
Exeter Digby/Wonford Jr H M O
Leeds Menston (Mental) Sr H O & Jr H M O
Leeds R H B Regs
Manchester R H B Sr Reg
Oxford R H B Sr H M O
Scotland Eastern R H B Cons
St Alban's Hill End Reg
Wallingford, Berks Fair Mile Jr H M O

RADIOLOGY

Middlesex W 1 Cons
Colchester Essex County Locum Sr Reg
Leeds R H B Sr Reg
Southend on Sea Gen Temp P t Cons or Temp Sr H M O
St *Bartholomew's*, E C 1 Sr H O or Reg

RADIOTHERAPY

Scotland Western R H B Reg

SURGERY

Bethnal *Green* E 2 *H O*
Elizabeth Garrett Anderson, N W 1 H O
Hosp for Sick Child, W C 1 P t Sr Reg
Nelson S W 20 H O
Norh East Met R H B Reg
North West Met *R H B Cons*
Queen Mary's *Hosp* for the East End, E 15 Pre reg *H O*
South Lodge N 21 H O
South Western S W 9 Sr H O
Bath Royal United H O
Blackburn & Dist H M C H O's
Birmingham Accident H O 's
Birmingham Accident Hosp & Rehab Centre Sr H O
Bristol United Hosps & South Western R H B Reg
Canterbury Kent & Canterbury H O
Carshalton Queen Mary's Hosp for Child Reg
Chelmsford & Essex Pre reg H O s
Edinburgh Central Hosps B O M H O
Edinburgh Northern Group of Hosp H O
Enfield Chase Farm H O
Halifax Gen H O
Haslemere & Dist H O or Locum
Hastings Royal East Sussex Pre-
Haverfordwest, Pembroke County War Mem Sr H O
Hitchin Lister H O
Hosp for Sick Child, W C 1 P t Sr Reg
Huddersfield Royal Infy H O
Hull Kingston Gen H O
Ipswich & East Suffolk Pre reg H O
Leeds R H B Reg
Leeds United Hosps R H B Sr Reg
Louth County Infy Sr H O
Maidenhead Reg
Manchester R H B Reg
Mid Glamorgan H M C H O
Mitcham Surrey Wilson Sr H O
Newcastle Gen Sr H O
Northampton Gen H O
Nottingham Gen Pre reg H O
Nottingham Highbury Sr H O
Portsmouth Group H M C Sr H O & Pre reg H O
Richmond, Surrey Royal Sr H O
Scotland Western R H B P t Cons
Scotland Western R H B Regs
Sheffield City Gen H O
St Helen's & Dist H M C H O s
Wakefield Clayton Pre reg H O
Wakefield Pinderfields Gen Sr H O

THORACIC SURGERY

Brompton, S W 3 Sr H O or Reg
Cottingham (nr Hull) Castle Hill Jr H M O
Ilkley Middleton Sr H O

UROLOGY

Edinburgh Northern Group of Hosp. H O

VENEREOLOGY

London, E 1 P t Cons

GENERAL

U S A Bethesda / Cincinnati Rotating Interns
Oxford United Hosps Sr H O
Canada Grace Hosp, Winnipeg Residencies & Sr Internships

GENERAL PRACTICE

Walsden, Todmorden (Urban & Rural) List Approx 1940

NON-MEDICAL

Dundee Royal Infy Biochemist

PUBLIC APPOINTMENTS

Barbados Gen Hosp Specialist Anæsthetist
Bedfordshire C C & Bedford Borough Div M O M O H & School M O
Birmingham *City Temp M O 's*
Factory Doctors (Kincardine)
Govt of U K of Libya Path & Bact
H M Oversea Service, S Pacific Health Service M O 's
H M Oversea Civil Service Somaliland M O
H M Oversea Civil Service, Trinidad Radiologist
Ministry of Supply (Microbiological Research Dept, Porton) Safety Officer
Nottinghamshire C C Sr Clin M O & Asst County M O
Treasury Medical Service P t Local Treasury M O 's
West Riding of Yorks C C Asst County M O & School H O

(Further particulars of above vacancies available on request to Advertisement Manager)

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GLUTEN TO BLAME ?

In a letter in our last issue, and in more detail at a meeting f the section of general practice of the Royal Society of ledicine on Feb 15, Dr Guy Daynes described what he called he "pre coeliac syndrome", a disturbance of convalescence in oung children and possibly also in adults He has noted over 0 examples in children in his own practice and clinics in 2½ years Most of those affected were between 1 and 5 years old They were just getting over an acute infection when they began to be irritable and spiteful, to wake screaming in the night, and to lose appetite and weight At the same time the stools became bulky The child usually recovered slowly but spontaneously in a few weeks But, Dr Daynes found, recovery was complete in two days when the child took a diet containing no wheat flour, and relapse was equally dramatic if this diet was stopped too soon Dr Daynes thinks that adults with insomnia, headache, and depression also respond well to such a diet, and suspects that the gluten of the flour is toxic, because it is the gluten which is altered by the chemical improver, agene, with the production of methionine sulphoximine, which causes hysteria in dogs And it is well known that true coeliac disease improves promptly when gluten is excluded from the diet

Some speakers at the meeting felt that Dr Daynes had carried his views rather further than the evidence warranted It was pointed out that there was little apparent similarity between canine hysteria and coeliac disease Prof A C Frazer remarked that true cœliac disease varied considerably in its manifestations from patient to patient, if the condition Dr Daynes described has a similar origin one would expect the same sort of wide variation

The exclusion of wheat flour means the exclusion of all bread and pastry, sausages, chocolate, tinned meat-loaf, and much else, and this obviously alters the starch and roughage content of the diet Before gluten alone can be convicted, the evidence must show clearly that the addition of pure gluten causes a relapse The question of vitamins and calcium must also be considered Individuals may differ considerably in their vitamin requirements Hersov[1] recently described an English schoolboy who had pellagra with mental symptoms while eating fairly normally—apparently because his need for nicotinamide was far higher than normal What happens to the intestinal flora during acute infection and convalescence, how glands like the pancreas respond to virus infections, and how the individual's biochemical requirements vary, are little studied but important matters General practitioners are often in the best position to observe the phenomena of convalescence, and to delineate the syndromes which may appear But the clinical pathologist is needed when it comes to disentangling the underlying causes A syndrome may be the final manifestation of several distinct pathological processes, and only the laboratory can differentiate them

THE EMBOLIC CANCER CELL

THE lymphatic spread of cancer is so common and so apparent that its detailed study may not get the attention it deserves In his book on the spread of tumours, Willis[2] described with great accuracy the morbid anatomy of 500 necropsies he had himself performed and he made an extensive, though admittedly incomplete, survey of the literature of the spread of cancer Some further work is now in hand in Philadelphia where a group of workers is studying experimentally the spread of cancer in the lymphatic system Their first task was to find a reliable experimental technique[3] By injecting suspensions of cancer cells into the afferent lymphatic vessels in the calf of the rabbit, they were able to show that tumour-cell emboli, on entering the regional lymph gland, were immediately held up in the subcapsular sinus and did not reach the hilar sinus, or escape from the gland Moreover, they found that at least three weeks (and sometimes longer) elapsed before tumour cells escaped from the lymph gland. This did not occur until the gland was almost completely replaced by tumour, at which stage cancer cells might spread from it to the blood stream. Zeidman et al[4] then tried to find out whether it was possible to attack secondary deposits in the lymph glands by injecting chemotherapeutic agents into the afferent vessel, but they were unable to demonstrate any lymphatic channels in such carcinomatous deposits The next extension of the work[5] was to ascertain what happened to tumour cells injected into the thoracic duct In all the rabbits so treated many pulmonary tumours developed, owing to the direct passage of tumour cell emboli from the duct to the veins, and in all but one secondary deposits appeared in mediastinal and intercostal lymph-nodes, despite the fact that there was no obstruction to the thoracic duct at its entrance to the venous system By injecting dyes into the thoracic duct, it was shown that channels pass from it to the lymph-glands When tumour cells leave the thoracic duct and lodge in the glands, they are found in the subcapsular sinuses, and it seems therefore that they are taken there by true afferent vessels This was also the case when *tumour cells reached* the left supraclavicular glands Zeidman et al conclude that tumour cells reach thoracic lymph glands more commonly by direct spread via afferent lymph vessels than by retrograde embolism Thus Troisier's sign of enlarged supraclavicular glands may be explained by the direct passage of tumour cells from the thoracic duct to the glands, without the intervention of retrograde embolism aided by obstruction or of direct extension through the wall of a cancerous thoracic duct

These experiments remind us that the lymph glands are the first barriers to the embolic spread of tumour cells It would be well to consider what means might be used to increase the effectiveness of this lymphatic barrier by chemicals or hormones One grave objection to the use of radiation for the treatment of cancer already established in lymph glands is the fact that adjacent unaffected lymphoid tissue is thereby depressed Should we not do less chasing of the hare from behind and make more effort to trap it from in front

CAVERNOUS PORTAL VEIN

PROGRESS in the surgical treatment of portal hypertension has reawakened interest in the various causes of portal obstruction Among the less common is the so called cavernous transformation of the portal vein Although the first example was reported in 1868[6] and only 22 further case reports appeared in the next sixty years,[7] two recent accounts,[8,9] based on 6 and 4 cases respectively, probably give a truer impression of its frequency

In this condition, the naked eye appearance of the structures in the portal fissure is characteristic The portal vein itself is usually unidentifiable amongst the sponge like mass of vessels This apparent replacement of the portal vein by a cavernous angioma usually extends in both directions, upwards into the liver along the portal tracts and downwards into the hepatoduodenal ligament But histological examination, especially with elastic tissue stains, shows that the portal vein is still present but obscured by thrombotic obstruction and recanalisation of its lumen and by the mass of collateral vessels around it

The clinical picture is remarkably uniform and is, in the main, what one would expect from a slowly developing portal obstruction Hæmatemesis from œsophageal varices is usually the presenting symptom, although it is often preceded by upper abdominal pain of varying severity Ascites is almost always absent—a finding in harmony with the present view that ascitic fluid is produced almost exclusively within the liver as a result of obstruction to its venous outflow[10] Jaundice is rare and there is seldom any evidence of impaired liver function The spleen is enlarged, often considerably so, and hæmatological indications of hypersplenism are common, although the anæmia is more probably due to the recurrent hæmatemeses Almost inevitably the illness ends fatally within a few months or years of the clinical onset—often when extension of thrombosis into the superior mesenteric veins leads to infarction of the small bowel

Three views have been advanced to account for this anomaly The first regards the lesion as a tumour-like overgrowth of vascular tissue corresponding to cavernous angiomata in other parts of the body The second regards it as a developmental abnormality comparable to the cavernous type of portal vein found in amphioxus and some of the cyclostomes The most should be given intravenously as soon as possible, the initial dose should be 4 g, and this may be enough or may need to be repeated later If fibrinogen is not available, blood can be given, taking 1 litre of blood to correspond to 1 5 g of fibrinogen The American workers agree that in all these patients the uterus should be emptied as soon as possible if labour does not ensue within twelve hours of induction, since the fibrinogen level always rises within forty-eight hours of delivery If treatment is to be effective, it must be given promptly, so some method for the quick assessment of the fibrinogen level in the plasma is needed **Barry** et al [8] give details of a method for a rapid but rough assay based on an original method of **Schneider**, and also of a rapid biuret method, devised by **Shea**, which gives a rough quantitative answer in ten minutes and a 90% accurate estimation in thirty minutes **Pritchard** and **Ratnoff** [7] describe a very simple "clot observation test", blood carefully withdrawn from a vein is run into a small tube containing a little bovine thrombin (now commercially available) Normally a firm clot should form in a few seconds, in hypofibrinogenæmia a clot may form, but it soon retracts, spontaneously or on tapping the tube, into a small ball from which most of the red cells are extruded Once the diagnosis of hypofibrinogenæmia is established, emptying of the uterus should be carefully considered, though the case-records suggest that dangerous hæmorrhage is not inevitable If bleeding has to be dealt with, the best treatment is certainly the intravenous injection of fibrinogen as soon as possible As most of the National Blood Transfusion Centres in this country hold stocks of dried human fibrinogen available for immediate use, treatment need not be long delayed The prognosis is usually good, but sometimes, especially with amniotic-fluid embolism, the patient dies despite the administration of fibrinogen Awareness of the possible diagnosis and prompt treatment can, it is clear, eliminate almost completely this cause of maternal mortality

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[1] Hersov L A. *J ment Sci* 1955 101, 878

[2] Willis R A. The Spread of Tumours in the Human Body London 1952

[3] Zeidman I, Buss, J M *Cancer Res* 1954 14 403

[4] Zeidman I., Copeland B E Warren S *Cancer* 1955 8 123

[5] Zeidman I *Cancer Res* 1955, 15, 719

[6] Balfour G W, Stewart, T G *Edinb med J* 1868–69 14 589

[7] Klemperer, P *Arch Path* 1928 6 353

[8] Gibson, J B Richards R L *J Path Bact* 1955, 70, 81

[9] Parker R A, Seal R M E *Ibid* p 97

[10] Madden, J L Lore J M Gerold F P Ravid J M *Surg Gynec Obstet* 1954 99 385

Impetigo

In the past, impetigo has been attributed to infection with either *Staphylococcus aureus*, *Streptococcus pyogenes*, neither, or both **Hope Simpson**,[1] in 1941, argued that impetigo was a specific infection which "bred true" it was not contracted from patients with boils, nor did it give rise in contacts to pyogenic lesions of other kinds Such a specific superficial reaction of the skin must therefore be due to an organism with peculiar properties and for this he proposed the name "impetigococcus" The specificity of the responsible organism was also suggested by **Spittlehouse**,[2] who reported a small series in which he had carried out phage typing of staphylococci derived from impetigo and sycosis barbæ In the former he found 81% of phage-type 71, but only 14% were of this type in the sycosis group Moreover, the majority of impetigo organisms were penicillin-resistant

These findings have been abundantly confirmed in two larger studies **Barrow** [3] found type-71 staphylococci in 80% of strains recovered from impetigo, contrasting with about 6% of this type in strains derived from a large control group Penicillin resistance in vitro was demonstrated in 71% of staphylococci from impetigo, and of the resistant organisms 84% were type 71 The results of **Parker** et al [4] are closely similar Of *Staph aureus* strains derived from impetigo, three quarters were of type 71 and most of them were penicillin-resistant

It seems unlikely that the high incidence of type-71 staphylococci in all three reports is due to a purely local distribution of the organism, for the areas concerned are reasonably far apart—Sheffield, Bradford, and Manchester **Parker** et al also examined cultures from impetigo lesions supplied by various Public Health Laboratories in widely separated areas and found that type-71 staphylococci were common *in all* The suspicion naturally arose that since many of the organisms were penicillin-resistant, they might have been hospital bred under the penicillin parasol This seems to be disproved, however, by the fact that most penicillin-resistant staphylococci are of phage types other than type 71 (In fact type 71 organisms were rarely recovered by **Parker** and his colleagues from superficial skin infections other than impetigo and they were absent in deep infections such as boils) Moreover, **Parker** et al also report an investigation carried out in Cambridge in 1941 before phage typing was adopted In this study, it was found that staphylococci derived from impetigo in young Servicemen had the property of inhibiting the growth of corynebacteria in 47% of cases (This property was present in only 19% of staphylococci derived from other skin lesions and in 10% of those from nose and throat swabs) Repeating these studies in the recent investigation they found that 90% of type 71 staphylococci and *very few others* had this property of inhibition This led to the tantalising supposition that the organisms studied in 1941 before penicillin came into use were probably also penicillin-resistant

Barrow doubts whether the presence of staphylococci in the nose is of the same significance in impetigo as it appears to be in deeper pyogenic infections (**Valentine** and **Hall-Smith**,[5] for example, reported up to 80% nasal carriage in furunculosis and as high as 91% in sycosis barbæ) In **Barrow**'s series, 46% of cases of impetigo carried the same staphylococcal type in the nose and in the skin lesions, but in his control groups a similar rate *of nasal carriage of staphylococci* was discovered He feels that if nasal carriage were important in the origin of impetigo, the rate would be much higher, Moreover, his cases of impetigo did not recur or relapse although no nasal treatment was given

These recent papers also consider the role of streptococci in impetigo **Barrow** cultured *Staph aureus* alone in 81% of lesions, *Strep pyogenes* alone in 5 6%, and a mixed growth in 13 2% He considers that in a third of the patients yielding the streptococcus it was probably the primary cause and that it was a secondary invader in the remainder **Parker** et al report that of the streptococci recovered from their patients, three quarters were of one of two closely related serological types, *one of* which was rarely found in other situations

These findings therefore support the conclusion *that* impetigo is a fairly distinct infection and that it is not an opportunist invasion by arbitrary organisms which happen to reside normally on the skin **Barrow** says that "there seems to be good clinical, epidemiological and bacteriological evidence in favour of the existence of two forms of impetigo, caused by staphylococci and streptococci respectively" It is interesting to note however, that "no clinical distinction was observed between those lesions yielding pure staphylococci and *those yielding pure streptococci*," and it is clear that, as **Parker** and his colleagues say, there is further need for correlation of clinical and bacteriological findings in this disease

Patent Ductus Arteriosus

The diagnosis of patent ductus arteriosus is seldom difficult in a typical case with a continuous machinery murmur in the pulmonary *area* With shunts of any size from aorta to pulmonary artery, there will be in addition *a* collapsing pulse, distension and pulsation of the pulmonary artery and its branches, and perhaps left ventricu points to stasis as the cause of gastric ulceration in both Why recurrent gastric ulceration after a Billroth I operation for a gastric ulcer is rare, is uncertain It could be that the less radical resection and easier anastomosis carry less risk of stenosis , more probably, there is some essential difference in gastric physiology in gastric and duodenal ulcers

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[1] Hope Simpson R E *Lancet* 1941 i 683
[2] Spittlehouse, K. E. *Ibid* 1955 ii 378
[3] Barrow, G I *J Hyg Camb* 1955, 53 495
[4] Parker, M T, Tomlinson A J H Williams, R F O *Ibid* p 458
[5] Valentine F C O Hall Smith S P *Lancet*, 1952, ii 351

Whether the high incidence of gastric ulceration is going to prove universal or is due, in this series, to some variation in technique producing stasis, only further follow up series will show Meanwhile, these results demonstrate that recurrent gastric ulcers should be treated, not by vagotomy, but by alteration of the anastomosis to a Polya type and that the combination of a vagotomy with Billroth I gastrectomy is unlikely to be satisfactory —B V McEVEDY, F R C S (University College Hospital, London, W C 1)

Vaccinia versus Poliomyelitis —I read with great interest Dr MacIver's article (Feb 4) In the United States vaccination against smallpox is required before a child may enter a school supported by State funds This usually occurs by the age of 6 7 and has not, as far as can be discovered, had any moderating effect on the reported cases In fact the Polio Foundation has regarded this as the most susceptible group The first trial of Salk vaccine was on children in the first and second grades —Colonel CHARLES H MORHOUSE, M D (Third Air Force, Ruislip, Middlesex)

The Future of the Chest Service—Your annotation of Feb 11, entitled Tuberculosis Then and Now, makes some far reaching suggestions with regard to the chest service in this country without producing evidence to give them weight and substance The degree of misapprehension of the present position it exhibits is considerable and could lead to much undesirable friction between chest physicians and clinicians in general hospitals , as future considerations will demand their closer collaboration, the whole situation requires to be examined most carefully

Prior to 1948, the tuberculosis services in this country were the responsibility of the local authorities , some were good, others indifferent in many districts radiological facilities were limited, diagnosis was thereby delayed and treatment suffered severe limitations because of the stage at which the disease was discovered and the stringency of the thoracic surgical services available The National Health Service has done much to remedy these deficiencies, particularly in backward areas, and the introduction of effective chemotherapeutic agents has contributed to an unprecedented fall in the death rate , so much so that there is a tendency in some responsible quarters to assume that this break through is equivalent to final victory You, Sir, have previously drawn attention (*Lancet*, Oct 22, 1955, p 857) to the prematurity of this assumption and to the need for strengthening the emphasis on prevention (*Lancet*, Nov 26, 1955, p 1125) But to appreciate the situation fully, attention must be accorded to the chest clinic service

The key position of the chest clinic in present circumstances has arisen simply and naturally from the resources which modern technology has placed at its disposal , in addition to ordinary large film radiography, the miniature camera has brought about in some clinics a fourfold increase in the number of persons sent for X-ray examination by general practitioners, and many of the abnormalities detected by mass radiography are referred to the clinic physician for investigation and treatment While still fulfilling his considerable responsibilities with regard to tuberculosis, the clinic physician, as a direct result of modern advances in equipment, now finds himself overwhelmed with cases of non-tuberculous respiratory ailments of every conceivable kind for which treatment facilities are inadequate and preventive measures rudimentary The training in environmental medicine which tuberculosis has given him prompts him to do his best for these patients—of all ages—who come to him with non tuberculous lung disease, many of whom present sociomedical problems similar to those met with in tuberculosis and to deal with which the chest clinic possesses the appropriate organisational nucleus in the form of health visitors and social workers

But present circumstances often preclude the chest physician from undertaking more than a fraction of what requires to be done , and pleas to his administrators are too often countered with the argument that as tuberculosis is declining and economy a prime consideration, demands for additional staff would appear to be ridiculous But it is no economy to have men who should be engaged in industry on sick benefit for months on end or to allow a child to develop into a chronic bronchitic or bronchiectatic

The unpalatable truth is that the people of this country suffer more from chronic respiratory disease than those of any other country in the world, that present arrangements for dealing with the situation are insufficient and lack coördination, and that we have barely begun to think about the problem of prevention The decline in tuberculosis has helped to unmask this long existent menace to the national health, which now faces us in the grisly reality of 30,000 deaths per annum from " bronchitis " (nearly four times the mortality from tuberculosis), over 16,000 deaths from bronchial carcinoma (more than twice that of tuberculosis), an increase in deaths from certified pneumoconiosis in miners from 232 in 1940 to 1016 in 1953 (McLaughlin, A I G *J R Inst publ Hlth*, 1955, 18, 218 (see table III, p 227)), and an untold morbidity amongst the childhood population which will seriously affect their health in later years

The problem is far from insoluble but it is apparent that if the massive subject of chronic respiratory illness in this country is to be seriously tackled a considerable reorientation of outlook is required Early consideration could well be given to increasing—even doubling—the number of consultant appointments in chest disease in industrial areas, where the morbidity from tuberculosis remains high and the incidence of other respiratory diseases is significantly greater than elsewhere , not only would this relieve the present situation in a field which has an excessive proportion of S H M O appointments, but it would encourage young men to enter a broadened specialty where indeed their services will be required for many years to come

Finally, there is a great need for closer cooperation between the medical specialists dealing with the different aspects of respiratory illness Besides physicians in chest clinics, and physicians and surgeons in chest hospitals, there is much that can be done by general physicians, pædiatricians, geriatricians, ear, nose, and throat specialists, respiratory physiologists, physical medicine experts, industrial medical officers, medical officers of health, statisticians, and general practitioners The help of all these—and more will emerge—is required to deal adequately with the problem of chest illness as it exists in this country today , and the integration of the various specialties to provide a fully functional chest service is clearly an administrative problem of the first importance Such a service should include all who have something to contribute, and existing barriers to coöperation should be removed —NORMAN MACDONALD, F R C P E (Clare Hall Hospital, South Mimms, Barnet)

Mass Radiography —On Feb 11 you reported Prof A P Thomson as saying that " among the patients in the Birmingham area examined by mass radiography in 1954, tuberculosis was found nearly seven times more frequently in those referred by general practitioners than in those in all the other groups This suggested that doctors did not neglect to examine their patients before referring them for radiography " May I point out that mass radiography is radiography without a prior medical examination—not an aid to clinical medicine, but a substitute for it The practitioners were not in fact using mass radiography at all , they were using the unit in the way I suggested when the mass radiography scheme was found to be unsatisfactory, as I had predicted (*Postgrad med J* 1944, 20, 135 , *Med Wld*, March 31 1944) The 31,249 patients sent by practitioners were examined and then referred for radiography to confirm the clinical findings The practitioners use the mass radiography unit because they cannot, as in private, refer cases direct to the radiologist but must send them to an intermediary physician or surgeon at a hospital, who alone has the right to refer them to the X ray department

Of the 364,033 other persons, examined by radiography, no fewer than 3371 (I quote from Dr McDowell's report in *Tubercle*, 1955, 36, 122) came forward individually–because they had symptoms or feared infection from contact–instead of reporting to a general practitioner Why then have any physicians at all ? Surely, as dean of the medical faculty, Professor Thomson does not consider this sound medical practice ? Of all the objections to mass radiography, the most serious is that it leads to students being taught that active progressive tuberculosis can be present without signs or symptoms It has led to neglect of the clinical examination At an inquest in this area it was reported that a patient who had repeatedly complained of his chest received no treatment , he died on the

DECORTICATION IN PULMONARY TUBERCULOSIS

DECORTICATION of the lung has proved less successful in pulmonary tuberculosis than in traumatic hæmothorax. In tuberculosis involvement of the underlying lung gives rise to difficulty in removing the "peel," and thus to subsequent air-leaks which may prevent expansion of the lung; failure may also result from hæmorrhage or infection.[1] Yet as experience grows, the results are becoming more encouraging. Thus Savage and Fleming[2] report from Sully Hospital that the majority of their tuberculous patients who underwent decortication of the lung showed significant functional improvement. In each of 34 cases where a persistent pleural space, infected or uninfected, was present, this was obliterated without inducing mediastinal shift; indeed where mediastinal shift was present preoperatively, it was at least partly reduced by the operation. In only 2 instances was thoracoplasty required to aid obliteration; but in 3 other instances thoracoplasty was carried out to control disease in the lung after the space had been obliterated by decortication. One woman, aged 47, in whom thickened pleura had been present for twenty years, and who had shortness of breath on the slightest exertion and severe œdema of the ankles, was able to continue her life as a school teacher with much improved exercise tolerance as a result of freeing her constricted left lung and restoring her displaced mediastinum to a more central position.

Such spectacular results are exceptional. Nevertheless, of 24 patients who complained of shortness of breath on mild to moderate exertion, all showed some improvement in effort tolerance after operation. No doubt in some instances this was partly psychogenic, but respiratory function studies indicated improvement, ranging from moderate to striking, in all except 2 of the 25 cases investigated. In the early period after decortication pulmonary angiograms demonstrated a poor flow through the branches of the pulmonary artery; later this flow improved with corresponding increase in oxygen uptake. Patton et al.,[3] who studied lung function in a series of patients up to three years after decortication, also found steady improvement; the final result was not closely related to the duration of the condition before operation, but where parenchymal disease is extensive, little improvement in function can be expected.

Where the extent of parenchymal disease is slight and the remainder of the lung is healthy, Savage and Fleming confidently expect a good result, provided due attention is paid to management. Preoperatively chemotherapy and physiotherapy are important, and great care is necessary during the operation to avoid damaging the thoracic duct and the vagus and phrenic nerves. Mistakes in postoperative management can nullify the best efforts of the surgeon, and it is in this respect that the Sully contribution is chiefly helpful. Savage and Fleming suggest that, if disease is not widely scattered through the lung, its failure to expand after decortication is due to inability to deal with the air-leaks and the fluid which collects in the pleural space in the early postoperative days. The lung should be fully expanded at the earliest possible moment and kept so until all air leaks have ceased. Continuous suction is applied to the drainage tubes through water seal bottles as soon as the patient returns to the ward, and the tubes are not removed till they have ceased functioning. The patient is nursed on the unoperated side, and on the second or third day is put into a special hyperextension plaster which has been made for him preoperatively; in this position the mediastinum tends to fall to the opposite side, the diaphragm is carried caudally, and the ribs are stretched apart—the reverse of the situation before operation. The patient continues to lie in the plaster cast, except for meals, for three to six weeks until chest expansion is equal on both sides or has reached its maximum; thereafter it is used for sleeping until three to six months have elapsed. Breathing exercises are begun on the first postoperative day and are continued for six months; all postoperative care is guided by frequent radiographs taken, with portable apparatus, at least twelve hourly in the early stages.

There were no deaths in the series, and the few complications were not serious; tension pneumothorax and extensive surgical emphysema were not met with, having been prevented by multiple drainage tubes with suction. The results, indeed, are encouraging enough for Savage and Fleming to state: "There is no doubt that functional improvement of significant degree can be achieved in most cases, and we are prepared to recommend operation on that ground alone." Postoperative care is the keynote to success. The management of thoracic surgical patients demands a high level of training and team-work, which nowadays, owing to shortage of skilled personnel, is not easily maintained. Attention to this vital factor is urgently required at many chest hospitals if they are to continue to meet their obligations as competently as they would like.

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[1] *Lancet*, 1954, i, 34.
[2] Savage, T., Fleming, H. A. *Thorax*, 1955, 10, 293.
[3] Patton, W. E., Watson, T. R., Gaensler, E. A. *Surg. Gynec. Obstet.* 1952, 95, 477.

DIURESIS AND DIURETICS

AT the Royal Society of Medicine on Feb. 28, Dr D. A. K. Black defined the fundamental differences between water diuresis, in which solute excretion is slightly if at all increased, and osmotic diuresis, in which urinary solute is always increased. In diuretic therapy it is essential to enhance the output of sodium, and therefore all effective diuretics must cause osmotic diuresis. Diuretics can be used with advantage in states where oliguria and œdema are combined. Dr T. Hanley said that he has found acetazolamide ('Diamox') inferior to mercurials; its efficacy diminishes with continued use, owing to reduction of plasma-bicarbonate and acidosis. Dr M. D. Milne agreed with this view, and reviewed means of augmenting the effectiveness of mercurial diuretics. He recommended measures to increase plasma chloride (e.g., ammonium and potassium chloride by mouth, ion exchange resins in the ammonium cycle, or acetazolamide itself) and to increase the glomerular filtration rate (e.g., intravenous aminophylline given about two to three hours after injection of the mercurial). Cases have recently been reported in which a nephrotic syndrome has developed during prolonged therapy with mercurials. It is difficult to be certain that the renal damage is actually due to mercurial toxicity, but therapy should certainly be discontinued if proteinuria steadily increases.

CANCER AND THE PUBLIC

INSTRUCTION of the public about cancer has no stronger advocate or exponent than Mr Malcolm Donaldson, who believes that suitable explanation allays more apprehension than it causes[1] and is likely to bring patients to their doctor at an earlier and more curable stage of their disease. The effect of "cancer education" on the time of diagnosis of "accessible" cancers—i.e., those usually causing symptoms fairly early in their course—is examined in his report on a survey he made in 1954-55 on behalf of the Yorkshire Council of the British Empire Cancer Campaign.[2]

In an area comprising York, Hull, and the East Riding with a population of about 600,000, 210 lectures on cancer were given to the lay public during two years. At the end of most of these lectures ballot papers were distributed asking the audiences whether the lectures had relieved their anxiety or increased it, and whether they thought more should be given. Of more than 6000 votes 99% were in favour and only 0.2% against. In addition, more than 50,000 pamphlets were distributed, articles were published in the press, posters advertising the campaign were displayed, and diagrams explaining cancer and its treatment were shown in local health exhibitions. Nurses, health visitors, and midwives were given special lectures to enable them to discuss cancer with patients. The value of these measures appeared most convincing in cancer of the rectum, where the proportion of patients reporting symptoms with less than a month's delay rose from 16.9% to 33.7% and 43.8% during successive six-monthly periods. There was a slight rise in the equivalent figures for cancer of the breast, which were 35%, 37.7%, and 39%; but those for the uterus showed no material improvement—partly because patients found it hard to distinguish physiological from pathological bleeding. There were so few cases of cancer of the larynx, mouth, tongue, and bladder that the results were inconclusive, and in cancers of the skin early diagnosis is relatively unimportant.

As Donaldson says, this Yorkshire experiment, and the Manchester survey[3], "should prove to be of real value to any other local health authorities who are proposing to carry out cancer education of the public, which is so stongly advocated by the Ministry of Health." The results of the two pilot

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[1] *Lancet*, 1955, i, 959.
[2] Report of Pilot Experiment in Cancer Education of the Public. By Malcolm Donaldson, F.R.C.S., F.R.C.O.G. Obtainable from the author at 337, Woodstock Road, Oxford. Pp. 34. 5s.
[3] Paterson, R., Aitken Swan, J. *Lancet*, 1954, ii, 857.

Notes and News

On Feb 1 the Joint Consultants Committee considered a document embodying the Ministry of Health's proposals on the medical staffing of hospitals (This was the Ministry's reply to the proposals—based broadly on the Strachan report—which the committee submitted last July) After a general discussion it was referred to a subcommittee for detailed examination Pending any changes in the structure of hospital medical staffing the Ministry is being asked to continue the present transitional arrangements to safeguard the position of senior registrars

The epidemic of influenza in Suffolk (see *Lancet*, Jan 28 p 200) was largely due to virus A *Of the specimens sent for examination*, the great majority showed a high titre of A antibodies There has been a considerable increase in mild influenza like illness in many parts of the country Outbreaks are reported from places as far apart as Bristol Guisborough, West Hartlepool, Great Yarmouth, Dover, and Hastings

The net cost of the National Health Service in England, Wales and Scotland in 1956–57 is estimated at £502,715 130 The cost in 1955–56, with the supplementary estimate, is put at £479,337,405 In the coming financial year the social services are to receive altogether an additional £99 million including an increase of £32 million *for the* education services (1956–57 Vote on Account Civil Estimates *H M Stationery Office 6d*)

On Feb 11 the degree of M B of the University of Cambridge was conferred on Rosemary C Hayball, and (by proxy) *on* Mary R Glyn-John

Dr E Stengel has been appointed professor of psychiatry in the University of Sheffield

Dr Andrew Curran deputy medical officer of health for West Ham has been appointed senior lecturer in public health and social medicine in the University of Glasgow

On Feb 11, the Charter Day of the Royal College of Surgeons in Ireland the honorary fellowship was conferred on Dr R B Cattell and Sir Clement Price Thomas

A Chadwick Trust prize of £100 together with a silver medal, has been awarded to Group Captain Christopher Crowley for his contribution "in organising and administering measures for promoting health in the R.A F Maintenance Command "

At the annual dinner of the Hunterian Society on Feb 16 the Lord Mayor of London Alderman Cuthbert L Ackroyd replied to the toast of the Lord Mayor and Corporation, proposed by Dr J Y Dent The toast of The Society was proposed by Sir John Maud and the president Mr A Dickson Wright, responded Sir Heneage Ogilvie welcomed the guests for whom Mr Douglas Fairbanks replied

The trustees of the Lady Tata Memorial Fund invite applications for grants scholarships, or fellowships for research on blood diseases, with special reference to leukæmia in the academic year beginning next October Programmes of research on any aspect of malignant disease which may throw light on problems of leukæmia will be considered and awards may be made to investigators of any nationality, working in any country where payment can be made Particulars and application forms may be had from the secretary of the (European) Scientific Advisory Committee Lady Tata Memorial Trust, Chester Beatty Research Institute, Fulham Road London S W 3 Applications must be submitted before March 31

The proceedings of the Fifth International Congress of Blood Tranfusion held in 1954 have been published in Paris The 1200 pages cover the four sections—immunohæmatology clinical problems, preparation and preservation of blood and its constituents and organisation The book is obtainable for 5000 francs from the secretary-general of the congress 58, Boulevard d Auteuil, Bologne sur Seine France

The following doctors have been appointed to the Scottish Health Services Council Dr J C Macarthur, Prof W A Mackay, Prof W M Millar, Dr Eric G Oastler, and Dr I B L Weir Dr C W Clayson and Prof J L Henderson have been reappointed

The first publication of the College of General Practitioners to be offered for sale to the medical profession is a report of their conference on general practitioner obstetrics held last November Copies (3s 6d) may be had from the college, 14, Black Friars Lane, London, E C 4

Four countries—Cambodia, Laos, Thailand and Vietnam—have decided to merge their malaria control programmes in an effort to rid the Indo Chinese peninsula of this disease

Air Commodore A F Cook has been appointed an honorary physician to the Queen in succession to Air Vice Marshal R H Stanbridge who has retired from the R.A.F

A Food Standards Committee *report on copper (H M* Stationery Office, 6d) recommends limits for the copper content of soft drink concentrates, certain non alcoholic beverages, yeast and yeast products, and solid pectin The report does not advise giving statutory effect to these limits as has been done for the limits recommended *for edible gelatin and tomato ketchup*

The report of the Marie Curie Memorial Foundation for 1954–55 records an increase in annual income from £85,000 to £116 000 The Foundation hopes presently to open a fifth home to serve the north-eastern counties

The British Council for Rehabilitation in conjunction with Queen's University Belfast, is holding in Belfast from March 21 to 23 a residential conference on the Development of Rehabilitation Services in Northern Ireland A public meeting will be held at the City Hall on March 20 and there will be an exhibition of aids for the disabled in daily life The council s address is Tavistock House (South), Tavistock Square, London, W C 1

To try to keep together at home families where children might otherwise have to be received into care the health committee of the London County Council propose to employ some 50 additional whole-time home helps The committee also propose to provide selected home helps to work with and teach housecraft to mothers who need help of this kind Five days training will be given in the first instance to some 85 home helps who will work in families under the guidance of health visitors Basic kitchen equipment will be lent to families when necessary

The first issue has appeared of the *German Medical Journal*, a monthly English language edition of the *Deutsche medizinische Wochenschrift* This edition edited by G R Graham is obtainable from the publishers, Georg Thieme Verlag, Herdweg 63 Stuttgart, Germany for £1 10*s* per annum

Appointments

BROWN, GEORGE M B Edin appointed factory doctor, New Tredegar, Monmouth
CAMERON, A H, M D Durh whole time consultant pathologist Children s Hospital, Birmingham
CLARKE N P G M B, B SC N U I registrar in pathology St Kevin's Hospital, Dublin
GUNN ANNE C, M B Glasg, D P H whole time medical asst bacteriologist Glasgow Corporation
MCLEAN CHRISTINA J, M B Edin county psychiatrist, Staffordshire
MITCHELL EVELYN J, M B Camb asst resident M O, Tadworth Court branch The Hospital for Sick Children Great Ormond Street London
MONKHOUSE J P, M B Lond F R C S part time consultant in Royal National Orthopædic Hospital, London E N T surgery,
NICHOLSON B C M D Camb M R C P D P H consultant in medicine, Chapel Allerton Hospital Leeds
NIXON H H M B Camb F R C S part time consultant surgeon, The Hospital for Sick Children Great Ormond Street London
PARKES P W, M R C S appointed factory doctor Tamworth Stafford
TOVEY J E M B Brist registrar, department of pathology Southmead Hospital, Bristol
WETHERELL G A M CH ORTH Lpool, F R C.S whole time asst orthopædic surgeon, Clatterbridge General Hospital
WHITAKER WILLIAM M D, B SC Leeds M R C P consultant asst United Leeds Hospitals and Leeds R H B physician (cardiology)
WHITE CLEON M B Birm school M O, Birmingham
WILSON, E H, M D Lpool asst physician (S H M O) geriatrics, Newcastle upon Tyne H M C

Vacancies

ACADEMIC AND EDUCATIONAL
Hosp for Sick Child W C 1 Research Fellow (Histochemistry)
Bristol University Refresher Course for G P 's (Obst & Gyn), 9th 14th July
Cambridge Gonville & Caius College Berkeley Bye F'ship
Durham University & Newcastle United Hosps Prof of Med (Cons)
Glasgow University Admissions—Session 1956/7
Inst of Laryngology & Otology Courses for M O H 's, Endoscopy & Aural Surgery, Mar Apl
Leeds University Temp Lecturer (Dept Obst & Gyn)
Manchester University Fortnight's Course from 28th May, Industrial M O s
Medical Research Council M O
Edinburgh University Physical Anthropologist
Oxford University Asst. Graduate in Path
Tancred s Studentships (Divinity Medicine Law)
Saskatchewan University, Canada Lecturer in Bact
Sheffield University Lecturer in Path

ANÆSTHETICS
Hackney Group H M C Sr H O
Enfield Chase Farm Sr H O
North West Met. R H B Cons
Bristol United Hosps & South Western R H B Reg
Manchester R H B P t Cons & Sr H M O
Plymouth South Devon & East Cornwall Sr H O
Redhill County Locum Reg
Scotland Eastern R H B Sr Reg
Stafford H M C Sr H O
Tasmania Royal Hobart Specialist
U S A Cambridge Mass Residencies
Wolverhampton Royal Sr H O

CASUALTY
Hackney E 9 H O
Wanstead, E 11 Sr H O
Whipps Cross, E 11 Sr H O

Chesterfield Royal H O
Hemel Hempstead West Herts Jr H.M.O
Hertford County Sr H O
Plymouth South Devon & East Cornwall Sr H O
Reading Battle H O
Sheffield R.H B Sr Casualty Officer
Weston super Mare Gen Sr H O
Windsor King Edward VII Sr H O

CHEST AND TUBERCULOSIS
Brompton S W 3 H O s
Grove Park, S E 12 Sr H O

Aberdeen Deeside Sanatoria Reg & Sr H O
Benenden San M O
Birmingham R.H B Reg
Bristol Ham Green Jr H M O

We do not claim that the use of high-potency vitamins provides the whole—or even the most effective—method of treatment but we do suggest that the striking clinical results which we have observed can be accounted for in terms of known enzyme chemistry

The interest shown by clinical psychiatrists in this field should not come as a matter of surprise, in view not only of the rapidly increasing use of barbiturates in attemped suicide but also of the interesting psychiatric syndromes resulting from the use of barbiturates as sedative drugs during the day and hypnotics at night over long periods In my department these syndromes—often unrecognised—have come to be known unofficialy as "chronic subclinical barbiturate intoxication"

These considerations make the continued collaboration of clinicians and biochemists a matter of urgency to meet what may without exaggeration be regarded as a social menace —E B STRAUSS, F R C P (St Bartholomew's Hospital, London E C 1)

Tuberculosis and Liver biopsy —Dr Engstedt suggests (Feb 25) bone marrow aspiration in cases of tuberculosis In 1952 Mr *Barton and I reported on examination of rib* bone marrow in patients undergoing surgical treatment (*Lancet*, 1952, ii, 1059) We were unable to demonstrate tubercle bacilli either by smear or culture We suggested that the ribs removed in thoracic operations could be used in orthopædic units for grafting But subsequently Dr Lack pointed out that he knew of two cases of tuberculosis which had occurred when ribs from tuberculous patients had been used for spinal fusion for scoliosis (*Lancet*, 1952, ii 1182) He suggested that if the aspirated bone marrow had been placed in a muscle pouch of the guineapig our results might have been different, but we have had no opportunity to carry out this work —KENNETH MARSH, D M (Chest Clinic, Camberwell, London, S E 5)

The Future of the Chest Service —Dr Macdonald (Feb 25) has pointed the right way for the future

Despite the moans about "splitting" of the old tuberculosis service, the chest services have have been one of the successes of the National Health Service Thanks to improved diagnostic and therapeutic facilities, pulmonary tuberculosis is being brought under control It is, however, far too little recognised that many clinics and sanatoria have been doing increasing amounts of non-tuberculosis chest work and penetrating an unexplored field of chronic invalidism Much of this invalidism is preventable, and, as Dr Macdonald says, the sociomedical problems of, say, chronic bronchitis are strikingly similar to those of the patient with tuberculosis

The chest services, with their staffs of physicians, health visitors, and almoners, and using the welfare facilities of the local authorities through the medical officers of health, are in an exellent position to launch an all out attack on chronic respiratory disease The indications are for expansion, not contraction, and for progressive integration with the general hospital services Initial expenditure would not be high and dividends would very soon come in —GWYN HOWELLS, M R C P (Littleover, Derby)

Gluten to Blame?—Your annotation (Feb 25) suggests that at the Royal Society of Medicine I attributed the "precœliac syndrome" to agene In fact I was as careful to avoid such a specific imputation as I was in my letter of Feb 18 *Observations on my cases suggest* that the "staling" *process* of flour may be connected with the cause of this syndrome Flour may become stale through being kept too long, or it may attain similar properties as the result of treatment by the various "improving" processes to which it is usually subjected

In the past three years at a residential nursery school here I have seen no case of the precœliac syndrome, notwithstanding a number of epidemics including measles The reason may be that the bread, biscuits, and cakes included in the children's diet are made only from fresh untreated stone ground flour

Recent research has shown that when flour becomes stale there is a progressive loss of its vitamin E content, and this vitamin is quickly and completely destroyed when the flour is treated by agene or chlorine dioxide This might suggest that a vitamin E antimetabolite plays a part in the ætiology of the precœliac syndrome

The patient to patient *variation in the manifestations* of cœliac disease was brought forward as an argument against the connection between this disease and the syndrome I have described There is considerable variation from patient to patient also in the precœliac syndrome when symptons have been present for two months or more, it is only in the early weeks that the signs are so consistent

Your annotation suggests that there is little resemblance between canine hysteria and cœliac disease Veterinary workers recognise that canine hysteria can occur when a dog eats no agenised bread, thus methionine sulphoximine is not the only cause of this condition in dogs, and I have never suggested that it was the only cause of the precœliac syndrome Canine hysteria due to causes other than agene, after having been present for a few months, resembles cœliac disease quite closely, apart from the fits The dogs lose weight, have distended abdomens, have poor appetites, are bad tempered and unfriendly, and may have pale, bulky, foul smelling stools Also as in cœliac disease, these symptoms are greatly aggravated by infections

Clearly much further research is needed to elucidate the cause of this syndrome, whatever this may prove to be, at least we have in the gluten free diet a valuable symptomatic treatment to speed convalescence after infections, which will be appreciated by both *patients and parents* —GUY DAYNES, M R C S (Hove, Sussex)

***Production of Codeine*—*I agree with Dr Williams* (Jan** 21) that the amount of codeine in tab codein co does not enhance the analgesic value It does, however, produce side-effects, in particular constipation, which limits its continued use in such common conditions as the chronic rheumatic diseases

Recently I have compared the effect of a new analgesic *n* acetyl *p* aminophenol ('Panadol,' Bayer Products) with tab codein co in 20 cases of chronic rheumatic disease found in my general practice Side effects developed in 12 cases on tab codein co, but in only 1 on panadol It appears that this new drug has an analgesic value equal to that of tab codein co with the advantage of having fewer side effects

In my opinion the only effect of stopping the production of codeine would be, as Dr Williams implies, to reduce the consumption of laxatives —R R HAMILTON M B (Hawick Roxburghshire)

Prevention of Hay-fever —At this time of year, when hay fever sufferers are beginning some form of prophylactic treatment, my experience with a patient who has had hay fever for over thirty years may be of interest

Using 'Pollacine' vaccine (Parke, Davis), in fourteen doses I have advanced from 500 units to 30,000 units by administering, as an adjunct to the vaccine, chlorpromazine maleate ('Piriton Maleate', Allen & Hanburys) 10 mg in 1 ml This is added to the recommended dose of pollacine with a small amount of lignocaine to reduce the absorption and the pain from a 2 ml injection into the deltoid muscle The patient has had no untoward reaction He carries with him as a safety measure tablets of piriton, with instructions to take two (8 mg) at once if there is any delayed reaction To date this has not been necessary He is inclined to be drowsy by early afternoon, and this is overcome by his taking one tablet of 'Preludin' (Pfizer) during the morning At this rate the total course of some sixty injections, ranging from 500 to 150,000 units, can be reduced by two thirds, with a substantial saving of both doctor's and patient's time

The advantage of piriton over other anti histamine substances which have been administered to this patient is the very slight reaction —DOUGLAS STATHERS, M R C S (*Caterham,* Surrey)

New Kidneys for Old —I agree with your views as to the possible importance of kidney transplantation as an eventual therapeutic goal It would seem unfortunate, however, that you apparently remain ignorant of the work in this field carried out in this country May I draw attention to some of the errors in your leading article of Feb 18

(1) The problem of renal homotransplantation was not discussed at the Ciba symposim in 1954 (Preservation and Transplantation of normal tissues London, 1954)

(2) Your reference for the evidence of common antigenicity of skin and kidney cites a paper (R E Billingham et al *Ann N Y Acad Sci* 1955, 59, 409) which does not consider this problem let alone give any evidence The two relevant publications are as follows M Simonsen, F Sorensen, *Acta chir scand 1949, 99, 61* W J *Dempster, Brit J plast Surg* 1953 5, 228

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Printing of The Lancet

Outside London, normal printing has been resumed pending the decisions of the Industrial Courts But in London the printing houses remain paralysed, and several periodicals have ceased to appear in any form We trust that an early settlement may enable us to make up for some of the deficiencies of our current issues

B C G

A report by the Medical Research Council published last week[1] confirms that vaccination with B C G or vole-bacillus vaccine can prevent the clinical manifestations of tuberculous infection particularly miliary tuberculosis and meningitis The investigation, which involved 56,700 fourteen-year old children living in English cities and towns, was well planned, carefully executed, and clearly reported the results are unequivocal It is estimated that a general vaccination scheme of children of this age should reduce tuberculous morbidity between the ages of fourteen and seventeen by about half and the more serious types of disease might be reduced even more, for in the M R C investigation meningitis or miliary tuberculosis developed in none of the vaccinated children but in 6 of the unvaccinated

This investigation will provide valuable information and encouragement to those concerned with the public health, both in this country and (which is more important) in the less highly developed countries where vaccination is the only effective measure that can at present be applied Yet, as the report points out, "although it is now more than thirty years since B C G vaccine was first used in man" this "is the first controlled trial of the vaccine to be undertaken in Great Britain," and many of us will long regret that we did not press for such a trial sooner When it was eventually undertaken in 1950, B C G had already been in use in many countries since its introduction in France twenty six years previously[2] and though much of the published evidence of its value was invalid, and justified the initial scepticism with which it was regarded, there had also been several extensive planned investigations almost all of which suggested very strongly that B C G was useful None was unassailable close critical examination showed possible sources of error in each But it now seems that too much attention was paid to the fact that bias had been introduced into these trials, and not enough attention was given to the possibility that this bias had not materially affected the results Prof **JOHN FRANCIS**, who insisted in 1949 that what was needed was not so much an adequate trial of B C G as a campaign for its use, argued that exceptionally severe criteria of efficacy were being applied, in Great Britain, to this vaccine "the evidence supporting the value of B C G," he said, was "better than the evidence supporting the value of any *other* immunological procedure used in man"[3] Certainly, it has long been better than the evidence in favour of the poliomyelitis vaccine shortly to be offered to the public

In 1949 the Ministry of Health who control the manufacture and distribution of B C G vaccine, allowed it to be used routinely in those exposed to special risks, and later they permitted vaccination of school-children not exposed to special risks—stating, however, that, in order not to interfere with the M R C trial "any extension of the present B C G vaccination scheme should not include young adolescents aged 15 to 18"[4] But, as we pointed out,[5] vaccination of children and adolescents will not prevent infants dying from tuberculous meningitis Of the children in the M R C trial 40% had already been infected by the time they were fourteen Even at thirteen—the age at which school children are now vaccinated—it is likely that at least 1 in 5 will already be infected at birth none are infected Last year we suggested that B C G vaccination should be made available to all who wanted it and that the practising doctor, who bears a more direct responsibility than public-health authorities for the health of those under his care should be free to decide whether his patients should have B C G[6] We hope that vaccination has now been offered to the unvaccinated volunteers in the M R C trial who are still uninfected

Iron Foundries

REGULATIONS which should promote health, safety, and welfare in iron and steel foundries[7] came fully into operation at the beginning of this year, and the first report[8] of the Joint Standing Committee on Conditions in Iron Foundries is timely, because it makes practical suggestions about the control of dust and fume

The founding of metal is an ancient craft—so ancient that, under the weight of tradition, both employers and workers have regarded the hot, dusty, and dangerous conditions as inevitable, and the campaign for better working conditions did not begin in this country until the late 1930s A leading article which we published at that time[9] was based partly on American experience and partly on observations by doctors in the Factory Department and the Silicosis and Asbestosis Medical Board Ever since then the Factory Department has kept up steady pressure, and during the war the Chief Inspector set up two joint advisory committees, one for steel and the other for iron foundries About the same time a survey of the health risks of iron and steel foundry workers was begun by the Factory Department in conjunction with the Medical Research Council's department for research in industrial medicine directed by Dr. **DONALD HUNTER** at the London Hospital The results of this survey,[10] of which Dr A I G **MCLAUGHLIN** was in charge, were published in 1950 In 1947 a very thorough report[11] from the Joint Advisory Committee

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[1] *Brit med J* Feb 25 1956 413

[2] Calmette L C A Guérin C Weill-Hallé B *Bull Acad Méd Paris* 1924 91, 787

[3] *Lancet* 1949 ii 549 1105

[4] Memorandum 324/B C G, Nov 5, 1953

[5] *Lancet*, 1954, ii, 178

[6] *Ibid*, 1955, i, 757

[7] The Iron and Steel Foundries Regulations S I 1953, no 1464

[8] First Report of Joint Standing Committee on Conditions in Iron Foundries, 1956 H.M. Stationery Office Pp 73 *4s 6d*

[9] *Lancet* 1938, ii 629

[10] McLaughlin A I G et al Industrial Lung Diseases of Iron and Steel Foundry Workers 1950 H.M Stationery Office, see *Lancet* 1950, ii 576

[11] Report of Joint Advisory Committee on Conditions in Iron Foundries H.M Stationery Office 1947

ANÆSTHETICS
King Edward Mem , W Sr H O
Prince of Wales's Gen N 15 Sr H O
Barrow & Furness H M C Jr H M O
Birmingham Dudley Road Sr H O
Ethiopia Princess Tsahai Mem Addis Ababa Anæs
Kettering & Dist H M C Sr H O
Manchester R H B & United Hosps P -t Cons
Northampton Gen H O
Oxford United Hosps Sr H O
Stafford H M C Sr H O
U S A Cambridge Mass Residencies
Welsh R H B. Cons

CASUALTY
Hackney E 9 H O
Lambeth, S E 11 Sr H O or H O
West London W 6 Sr H O
Brighton Royal Sussex County H O 's
Canterbury Kent & Canterbury Sr H O
Cardiff St David's Sr H O
Cheltenham Gen & Eye Sr H.O
Chesterfield Royal H O
Dudley, Stourbridge & Dist Sr H O
Northampton Gen Sr H O & H O
Reading Battle H O
Weston-super Mare Gen Sr H O

CHEST AND TUBERCULOSIS
North West Met R H B Reg
Birmingham R.H B Reg
Cardiff Glan Ely Sr H O
Chelmsford Broomfield Locum Sr H M O
Driffield Northfield San Sr H O
Ipswich St Helen's H O
Manchester R H B Reg
Scotland Eastern R H B Reg

DERMATOLOGY
Royal Free Hosp Group P t Cons
Glasgow Stobhill Gen Pre reg H O

EAR, NOSE, AND THROAT
Hosp for Sick Child W C 1 Reg
Metropolitan E N & T , W 8 H O
Royal National T N & E & Inst of Laryngology & Otology Sr Reg
Blackpool Victoria Sr H O
Doncaster Royal Infy Sr H O
Hull Victoria Hosp for Sick Child Locum Sr H O
Northampton Gen Sr H O
Portsmouth Group H.M C Sr H O
Reading Royal Berks H O
Southampton Royal South Hants & Gen Sr H O

GERIATRICS
East Anglian R.H B Sr H M O
Glasgow Stobhill Gen Pre reg H O

INFECTIOUS DISEASES
Portslade Foredown Jr H M O

MEDICINE
Bethnal Green, E 2 H O
Fulham, W 6 Reg
Queen Mary's Hosp for East End, E 15 H O
South Lodge, N 21 H O
St Leonard's, N 1 Sr H O
Birmingham Dudley Road H O
Birmingham R H B P t Cons
Birmingham R H B Reg
Bournemouth Christchurch Reg
Bournemouth Royal Victoria H O
East Anglian R H B Reg
Enfield Chase Farm Sr H O
Enfield War Mem Sr H O
Glasgow Royal Infy Sr H O
Huntingdon County H O
Ilford King George Pre reg H O
Ipswich & East Suffolk Sr H O
Luton & Dunstable Reg
Maidenhead H O
Manchester R H B Reg
Portsmouth Group H M C Sr H O
Scunthorpe War Mem Pre reg H O or Sr H O
Stoke on Trent City Gen H O
Swansea Mount Pleasant Jr H M O
Torquay Torbay Sr H O
Tredegar, Mon St James H O

NEUROLOGY
National Hosp for Nervous Diseases Reg
South West Met R H B Cons

OBSTETRICS AND GYNÆCOLOGY
Hackney, E 9 H O
South London Hosp for Women S W 4 H O s
St Bartholomew's E C 1 Reg
Birmingham Marston Green Maty H O
Birmingham R H B Regs
Birmingham United Hosps Reg & H O 's
Bromsgrove Gen Pre reg H O
Canterbury, Kent & Canterbury H O
Cheltenham Maternity H O
Croydon Group H M C Locum Cons
Doncaster Western Reg
Halifax Area Hosps M C Sr H O
Hastings Buchanan H O
Manchester R H B Reg
Manchester United Hosps Sr H O & H O
Nottingham Firs Maternity Sr H O
Portsmouth Group H M C Pre-Reg H O
Reading Combined Hosps H O 's
Rochford, Essex Gen H O
Romford Oldchurch Sr H O
Sheffield R H B Sr Reg
Swansea Sr H O

OPHTHALMOLOGY
Manchester United Hosps Sr H M O
Newcastle upon-Tyne H M C Sr H O
Oxford United Hosps H O

ORTHOPÆDICS
Royal National Orthopædic W 1 Sr H O
South-East Met R H B P -t Cons
Alton Lord Mayor Treloar Orthopædic Locum Reg
Bebington Clatterbridge Locum Jr H M O
Birmingham R H B Reg
Braintree Black Notley H O
Bridge of Earn, Perthshire Sr H O & H O
Brighton Gen H O
Durham County H O
Isleworth West Middlesex Sr H O
Medway & Gravesend H M C Locum Reg
Northampton Gen H O
Oxford R H B Reg
Portsmouth Group H M C Pre reg H O
Romford Oldchurch H O
Southampton Royal South Hants Sr H O
Swansea Sr H O
Wigan Royal Albert Edward Infy Sr H O

PÆDIATRICS
Hosp for Sick Child , W C 1 Sr H O
St James's, S W 12 Sr H O
Birmingham United Hosps Sr Reg
Chelmsford St John's H O
Luton & Dunstable H O
Manchester Duchess of York Hosp for Babies H O
Northampton Gen H O
Reading Royal Berks H O
Canada Child's Hosp , Vancouver Residents

PATHOLOGY
Royal Marsden S W 3 Locum Sr H M O or Sr Reg
St Bartholomew's E C 1 Sr H M O
Birmingham R H B Regs
Leeds R H B Sr H M O
Macclesfield Sr H O
Manchester West Manchester H M C Sr H O
Northwood, Middx Mount Vernon Sr H O
Oxford R H B Reg
Oxford United Hosps Locum Sr H O
Rochford Essex Gen Locum Reg & Sr H O
Sheffield United Hosps Reg or Sr H O

PSYCHIATRY
Friern H M C N 11 Jr H M O
Marlborough Day, N W 8 P t Reg
North West Met R H B P t Sr H M O
South East Met R H B P t Cons & Sr H M O
St George's S W 1 Reg
Aylesbury St John's Jr H.M O
Birmingham R H B Reg
Brentwood Warley Sr H O
Exeter Digby/Wonford Jr H M O
Nottingham Saxondale Reg
Oxford R H B Sr H.M O
St Alban's Hill End Reg
Wallingford, Berks Fair Mile Jr H M O
Wickford, Essex Runwell Sr H O

RADIOLOGY
South West Met R H B P -t Cons
St Bartholomew's, E C 1 Sr Reg
Portsmouth Group H M C Reg
Sheffield R H B P t Cons
Southend on Sea Gen Temp P t Cons or Temp Sr H.M O
Watford & Dist Peace Mem Reg.
Welsh R H B Locum Cons
Welsh R H B Cons

SURGERY
Bethnal Green E 2 H O
Hammersmith Hosp & Postgrad Med School, W 12 H O
Hosp for Sick Child , W C 1 P t Sr Reg
Royal Marsden S W 3 H O
South East Met. R H B P t Con
South East Met R H B Reg
South Western, S W 9 Sr H O
St George in the East, E 1 H O
St James's S W 12 Reg
St Leonard's, N 1 H O
Wanstead, E 11 H O
Barrow-in Furness North Lonsdale H O
Batley, Yorks Gen Pre reg H O s
Blackburn & Dist H M C H O 's
Birmingham Accident Hosp & Rehab Centre Sr H O 's
Brighton Royal Sussex County H O 's
Canterbury, Kent & Canterbury H O
Carlisle Cumberland Infy H O s
Carlisle Cumberland Infy Sr, H O
Carshalton. Queen Mary's Hosp for Child Reg
Chelmsford & Essex Locum Reg
Chelmsford & Essex Pre reg H O 's
Chesterfield Royal H O
Derby Derbyshire Royal Infy Pre-reg H O or Sr H O
Doncaster Royal Infy Sr H O
Dudley, Stourbridge & Dist Sr H O
Enfield Chase Farm H O
Halifax Gen H O
Haslemere & Dist H O or Locum
Hastings Royal East Sussex Pre reg H O s
Hastings St Helen's Pre reg H O
Huddersfield Royal Infy H O
Isleworth South Middlesex Pre reg H O
Leeds United Hosps R H B Sr Reg
Lincoln County Pre reg H O
Liverpool Mossley Hill Jr H M O
Louth County Infy Sr H O
Maidenhead Reg
Manchester R H B Reg
Manchester West Manchester H M C Pre reg H O s
Manchester Wythenshawe Sr H O
Northampton Gen H O
Nottingham Gen Pre reg H O
Nottingham Highbury Sr H O
Peterborough Mem H O
Plymouth S Devon & E Cornwall Gen Pre reg H O
Porth & Dist Jr H M O
Portsmouth Group H M C Sr H O & Pre reg H O
Preston Royal Infy Reg
Richmond, Surrey Royal Sr H O
St Alban's City Locum Reg
Stoke on Trent City Gen H O
Welsh R H B Reg
Welsh R H B Cons

THORACIC SURGERY
Ilkley Middleton Sr H O

VENEREOLOGY
London, E 1 P t Cons

GENERAL
Oxford United Hosps Sr H O

PUBLIC APPOINTMENTS
National Coal Board (South Western Div) Asst Area M O
National Coal Board (North Eastern Div) Area M O
Cheshire C C Asst County M O
Ministry of Health H Q M O 's
Gold Coast Local Civil Service Specialist Anæs
British Guiana Govt Lady Health Officer
H M Overseas Service Kenya M O 's
Glasgow Corp A M O (Maty & C W)
Staffordshire C C Asst County M.O & School M O
West Hartlepool County Borough Deputy M O H & Deputy Principal School M O

(Further particulars of above vacancies available on request to Advertisement Manager)

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Annotations

RESTRICTION OF ANTIBIOTICS ?

On Jan 28 we discussed the New Zealand government's decision to restrict the use of erythromycin so as to conserve its efficacy against infections resistant to all other antibiotics In considering what policy might be evolved to ensure the best use of antibiotics, we made no mention of one important interest—that of the manufacturers Some manufacturers have done their utmost to ensure wise use of the powerful drugs they introduce, and they have sometimes done the public and the profession a service also by refraining from putting a new drug on the market when the medical evidence was not entirely in its favour By maintaining high standards in these matters a firm may lose a lot of money, and full credit should be given likewise to those who do not over optimistically broaden their claims for antibiotics, or hint (with the help of quotations from medically qualified but uncritical observers) that there is scarcely an infection in which their product is not worth a trial Equally we should be grateful to firms who act with restraint when they find themselves in possession of "new" antibiotics whose claims to novelty may be slight Some of the drugs which have appeared under new names have in fact so much in common with established antibiotics that there is no real justification for bringing them forward Indeed they may do actual harm by increasing the number of organisms resistant to drugs already in use There is some evidence, for example, that this may be happening in France with a drug which closely resembles erythromycin and has no clear advantages over it Fortunately, this antibiotic has not appeared on the market in this country, for our manufacturers have wisely stayed their hand

The drug firms, perhaps, can do more than anyone else to teach doctors how best to use antibiotics, and they certainly have the information necessary to regulate the supply in such a way as to discourage the emergence of resistant organisms Such regulation, however, could involve heavy financial sacrifice, and if certain antibiotics are to be "rested" by agreement, from time to time, arrangements will have to be devised for compensating the firms thus penalised in the public interest

VENOUS ULCERS

It is custom to label as "venous" those ulcers which persist or recur above the inner malleolus and which are surrounded by pigmented and atrophic skin Often a cause for the ulceration is readily found—for example, a previous "white leg" or grossly incompetent varicose veins But sometimes the cause is uncertain or is presumed to be a silent phlebitis or venous incompetence due to deficient valves

Why these ulcers develop almost exclusively around the internal malleolus has never been very convincingly explained Cockett[1] believes the venous anatomy of this region may offer a clue From his studies on cadaver dissections he describes a large constant "posterior arch" vein which winds from the internal saphenous vein down the posterior aspects of the inner calf, *superficial* to the deep fascia, to anastomose *finally* with a series of small venous arches These small arches feed into three perforating veins which pass through the deep fascia above the internal malleolus and empty directly into the posterior tibial veins Although there is some variation in his dissected specimens, the perforating veins are short and reasonably large vessels, whose valves are so arranged that blood normally flows inwards from the subcutaneous tissues through to the subfascial veins but not in the reverse direction It is thus suggested that in the erect position the major venous outflow from the ulcer bearing area is directly into the deep veins via the perforating veins and not, as holds for the rest of the skin of the leg, into the saphenous system It follows that the small vein arches may be distended via the "posterior arch" vein from an incompetent internal saphenous vein or from the deep venous system, should the valves in the perforating veins become inefficient

Cockett's thesis is that venous ulcers and associated induration of the lower leg are usually due to destruction of the valves of these ankle perforating veins, and an operation designed to interrupt them is a logical step in the treatment of these ulcers Patients should be carefully selected the older patients and those with long standing ulcers in whom the whole of the lower third of the leg is strangled in a mass of indurated fibrous tissue are excluded and treated by the well established methods of supportive bandage and massage

In the 200 "selected" patients on whom Cockett has operated, a straight incision was made one finger's breadth behind the posterior margin of the tibia from midway between the knee and ankle down to 1 in above the internal malleolus This included an excision of the ulcer and any doubtful skin Any large subcutaneous veins were dissected out and followed up and down They led to one or other of the perforating veins and most commonly the upper and middle ones were found enlarged These were then ligated flush with the deep fascia and the whole plexus of subcutaneous veins excised Any large veins which diverged from the area of the incision to join the saphenous system or other perforators were followed and removed if necessary through separate incisions Excessive undercutting of the skin was avoided since this leads to extensive skin necrosis, a complication which may take longer to heal than the original ulcer In 135 operations for ulcers unassociated with superficial varicose veins, incompetent ankle perforators were present in 96 In 54 cases in which the ulcer was associated with varicose veins, an incompetent perforating vein which contributed to the persistence of the ulcer was present in 36

In a condition where many methods of treatment have been advanced only to disappoint, Cockett is commendably cautious about his results The follow up period is still short but the early results are promising

ALCOHOLISM ON THE CONTINENT

In its second number,[1] the *International Journal on Alcohol and Alcoholism* includes two contributions which throw important light on the extent of and the reasons for the recent increase in alcoholism on the Continent

An article by Hans Seidel discusses the development of alcoholism in the German Federal Republic since the war and shows that alcohol consumption in Western Germany, especially consumption of Branntwein (the German brandy product), has once again almost reached the high figures of the immediate pre war years under the Nazi régime In the past few years in the wake of the spectacular economic recovery of the country, "a kind of forced, hothouse alcoholism has come to the fore" Seidel regards this to some extent as a consequence of the systematic drinking during the war in the Army, as well as in other National Socialist organisations Large quantities of French hard liquor were sent to the German army during the Russian winter campaigns He also mentions the accumulated demand for stimulants after post-war shortages and privations Above all, however, he explains the present "hasty, unquiet and ostentatious form of drinking" as an expression of widespread inferiority feelings arising out of the social and political upheavals following the war

Alcoholism, Seidel suggests, is closely connected with the appalling figures of road accidents in Western Germany, as high a proportion as 25% of road deaths has been attributed by some experts directly or indirectly to alcohol consumption The number of habitual alcoholics in Western Germany is placed at between 180,000 and 200,000 or something over 4 per 1000 of the population But it seems that little effort is being made to tackle the situation Modern methods of treatment are said to be little used and difficult to enforce, the number of beds in non mental hospitals is described as hopelessly inadequate for systematic treatment, and social-insurance authorities are extremely reluctant to meet the cost of lengthy treatment

Dr Gabriel Mouchot gives some of the background to recent steps by the French government to combat alcoholism,[2] and he assesses their scope and prospect of success in a rather sarcastic way "It is easy,' he declares, "to drive a coach and four through recent liquor legislation," for the law cannot do much unless backed by public opinion, and "almost everyone in France thinks that wine, or brandy, or whatever he drinks is good for him!" Alcohol producers moreover, are numerous, rich, and powerful Several million Frenchmen depend on drink for their daily bread, millions of acres are covered by vineyards In the circumstances, few politicians and certainly no government which hopes to remain in power are likely to possess the hardihood to tackle the root problem —over production "So long as we have no precise ideas," may be suppressed, and be replaced by no more than the equivalent amount of exogenous hormone In theory the only advantages to the patient would be the substitution of a regular supply of hormone for the varying output of his own glands (the maximum secretion during a twenty-four hour period may be ten times greater than the minimum) or the very hypothetical suppression of a harmful adrenocortical hormone Before adopting a policy of "safe" maintenance therapy we must try to establish whether we are, in fact, using an expensive drug to any good purpose

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[1] Cockett F B *Brit J Surg* 1955, 43 260

[1] October, 1955

[2] See *Lancet*, 1955, ii, 1083

Clean Meat?

THE importance of meat as a source of food-poisoning, to which we lately called attention,[1] is not peculiar to this country or this age As long ago as 1880 BOLLINGER collected details of 17 outbreaks of food-poisoning due to meat and affecting 2400 people[2] In 1888 GAERTNER[3] described the organism which for so long bore his name and which we now call *Salmonella enteritidis* he recovered it from the carcass of a cow, and, post mortem, from a man who had eaten the meat The Aertrycke bacillus (now *S typhimurium*) owed its name to the Belgian village where it was first detected by DE NOBELE[4] under like circumstances Though we owe much to our own Durham and the reports of the Local Government Board, it was the German bacteriologists who paid most attention to food-poisoning in those early days One reason for this was the national habit of eating undercooked meat, and one result, a system of meat inspection which should be the envy of every country

The report of a joint committee of the Food and Agriculture Organisation and the World Health Organisation emphasises that our most valuable source of protein has its dangers[5] The list of meat-borne diseases is intimidating, though some of them—brucellosis, tuberculosis, and erysipeloid, for example—threaten the butcher rather than his customers (In some parts of the United States undulant fever has become principally an occupational disease of slaughterers[6]) Even if the problem is limited to salmonella infections alone, the difficulties in offering the housewife food free from all possible risk are very considerable In this country at any rate, bovine infection with *S typhimurium* and *S dublin* is not uncommon, and diagnosis, in life or after death, must depend upon a bacteriological examination which is seldom made Conditions in the best run abattoir are seldom such that contamination of clean meat by infected viscera or fæces is impossible Even in this enlightened land the design and practice of too many abattoirs are archaic of conditions in some of our Colonies the less said the better Nevertheless experience and the statistics of the Public Health Laboratory Service shows that "a cut off the joint" is seldom the origin of salmonella infection The commonest source is processed meat in one of its various forms A list which did not claim to be comprehensive mentioned 61 varieties cooked before sale and another 4 (including the domestic sausage) which are sold raw in this country[7] Not even the makers would claim that the meat which goes into these succulent foodstuffs is the same as that on the butcher's slab These dishes are in fact a sensible way of using up all those parts of the animals' anatomy which are in their pristine state repellant to our squeamish tastes But liver, spleen, and lymph glands can be reservoirs of bacterial infection, and an inside view of the trade will reveal other components, both native and imported, sufficiently bizarre to encourage further inquiry

If all this is true of Great Britain it is likely that the practice of hygiene is even more difficult in countries where meat is preferred when it has been ripened by decay or where a chronic shortage of protein gives every scrap of a carcass added value This report does not concern itself with the details of practice but lays down general principles which are hard to fault Two new developments are mentioned which have not had much attention here There is probably little cruelty in a well run abattoir, but the preliminary stunning of pigs with carbon dioxide points to further improvement in this direction Some process by which meat might be sterilised cheaply and without danger of taint might well remove many troubles in the meat trade Some trials of irradiation for this purpose are so promising that the subject is recommended for further study by the committee Their report is said to be the first of a series, and we look forward to its successors

Chest Radiography in Pneumoconiosis

To certify a miner as having pneumoconiosis is a grave responsibility apart from his natural dread of the disease, he and his family will inevitably suffer hardship, and the mining industry may lose a skilled worker who is badly needed According to the Ministry of National Insurance[1] the diagnosis of pneumoconiosis depends primarily on radiography, but how reliable is this?

On the results of a survey made in 1950-51 in four Durham coalmines,[2,3] Professor BROWNE and his associates now question the value of radiography in assessing pneumoconiosis Of the 5118 men examined (89% of all those working in the four coalmines) 30-35% showed radiological evidence of the disease, and for men who had worked at the coalface for twenty years or more the figure was 65% A little over 2% of all men had radiological evidence of complicated pneumoconiosis (progressive massive fibrosis) When allowance is made for Durham miners going to the coalface ten years earlier than their Welsh colleagues, these figures agree closely with those recorded by the M R C workers for four coal mines in South Wales, in the Rhondda Fach[4]

But in the Durham survey NEWELL and BROWNE[2] recognised, in uncomplicated pneumoconiosis, no association between symptoms and radiological category A man with symptoms might or might not have had an abnormal radiograph Hence they believe that "many men who have no symptoms may be classified as having radiological pneumoconiosis, while many who are disabled cannot be so classified and compensated, as there is no abnormality in their radiographs", and they point out that dyspnœa, cough, and spit, which are disabling to the patient, cannot be detected radiologically Their general conclusion is that whereas radiological category is influenced by the degree of dust exposure, the disability of coalface workers is a function of age They suggest that, if their findings are supported by those in other coalfields, the compensating machinery for miners' pneumoconiosis should be reconsidered

> "Disability (as measured by inability to continue the present job) in a coalface worker might well entitle a man to compensation Let the chest radiograph be boldly omitted At present many men are being refused compensation because their chest radiographs are normal, even though they are grossly disabled, and vice versa"

McCALLUM and BROWNE[3] hold that, in the interests of both the men and the coalmining industry, it would be

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1 *Lancet*, 1956, i, 87
2 Edelmann, R, Mohler J R Eichhorn, A Textbook of Meat Hygiene London, 1925 p 383
3 Gaertner, A *KorrespBl ärztl Thüringen* 1888
4 de Nobele *Ann Soc Méd Gand* 1899
5 *Tech Rep Wld Hlth Org* 1955, no 99
6 Hendricks, S L *Amer J publ Hlth*, 1955 45, 1282
7 Report of the Manufactured Meat Products Working Party H M Stationery Office 1950

1 Notes on the Diagnosis of Occupational Diseases Ministry of National Insurance 1950 H M Stationery Office
2 Newell, D J, Browne R C *J Fac Radiol Lond* 1955 7, 20
3 McCallum, R I, Browne, R C *Brit J industr Med* 1955 12 279
4 Cochrane A L Cox J G Jarman T F *Brit med J* 1952 ii 843

Letters to the Editor

Poliomyelitis Vaccination —Since I began to work on poliomyelitis vaccine, I have often been asked whether I would have my own children injected with the current type of vaccine In spite of the official information which has been given, there is still a surprising degree of ignorance of the basic facts about this vaccine, perhaps because its practical development has preceded the publication in this country of the scientific data necessary for its appraisal It rests therefore with those "in the know to give what reassurances they can

I hope that my children, at least those that are eligible, will receive poliomyelitis vaccine this spring I am satisfied that the vaccine can do no possible harm Since the revised safety regulations were introduced last summer, reactions and side effects have been virtually nil in over 10 million children vaccinated in the United States and elsewhere The safety margin of the vaccine has been widened enormously in the last year and in this country in three different ways (1) by using the very much larger volumes of sample for the safety tests, as introduced in the United States last summer, (2) by doing the safety tests in duplicate and independently in two different laboratories, and (3) by using attenuated strains of virus to prepare the vaccine

Much less certain is the amount of good the vaccine will do It is hoped to produce vaccine of a standard at least equivalent to that of current American production, which, to judge by the most recent figures, has a protective effect of between 70% and 80% That is to say, the risk of contracting *paralytic* poliomyelitis for a vaccinated child is about a quarter or a fifth of that for an unvaccinated child It may be argued that the risk of contracting paralytic poliomyelitis in this country is pretty small For children aged 2 5 years the chance is about 1 in 3000 in a year that is about average for poliomyelitis incidence But those who are familiar with the consequences to the individual and to the family of a crippling and fatal illness will wish to lessen that risk for their own family And thus is the advice I think doctors should be giving to their patients and friends —ALAN GOFFE, M B (Wellcome Research Laboratories, Beckenham, Kent)

Remuneration of Doctors —As a country practitioner I am rather tired of the pious horror with which some of my prosperous colleagues greet our proposals for an increase of pay Let us be realistic We are not taking the first plunge into an antisocial debauch of inflation Instead, we are bringing up the rear in a rather sorry race, which we did not want to start Does Professor Davis (Feb 18) really believe that our example, at this late stage, will influence electricians, teachers, or railwaymen one way or the other ? It seems to me that the true position of our high minded critics is revealed by a sentence in the last paragraph of Professor Davis s letter "instead of pressing salary claims obtaining a modification of the present taxation system " I should like to ask which of the two measures would more accelerate inflation—increase of doctors' remuneration, or a general relaxation of taxes for higher income groups ?—M A FENTON B M (Moreton in Marsh, Gloucestershire)

We should like to support the opinion, expressed by the Royal College of Physicians of Edinburgh (Feb 18, p 296), that no claim for increased remuneration be submitted at present We feel that it is the duty of the medical profession, as a responsible section of the community, to give a lead which, we hope, others may follow —E G HALL, M B , F P HUDSON, F.R C.P.E , A E MCCANDLESS, M.R C P , R M.TODD, M.R C.P (Alder Hey Children's Hospital, Liverpool)

I should like to add my voice to that of those who consider the present time inappropriate for claiming increased remuneration —R.D REID, M B (West Mersea, Essex)

Factory in a Hospital —I would agree with Dr Rollin and Dr Watkin (Feb 18) if I had claimed that the factory had cured any of our patients, or that it would, by itself, lead to the discharge of any number I made no such claim My intention was to provoke discussion of the issues which the factory project, with other social changes, raises Many of our long stay patients are harmless, and if they can be trained to be self supporting it would seem unnecessary for them to remain in hospital Changes in the law and the recent introduction of non statutory beds together with the open-door ' policy, have helped to show the public that the psychotic patient rarely needs isolation because of dangerous behaviour If we can show that even the deteriorated patient can be useful to the community, yet another source of prejudice will be removed

Most psychiatrists working in mental hospitals complain of the overcrowding, and this has led to a damand for new building and more hospitals Schizophrenia is a chronic illness with frequent relapses, but so are peptic ulcer, bronchitis, and rheumatoid arthritis If patients with these diseases were kept in hospital for fear of relapses and because of the risk of "accidents if they left, the general hospital, too, would soon be overcrowded

More patients will leave the mental hospital only if there is a change in the attitude of society so that room is made for them in the community Our factory may help to stimulate such a change—A A BAKER, M D (Banstead Hospital, Sutton, Surrey)

Too Much Barbiturate ?—We also have encountered some of the complications mentioned by Miss Brooke (Jan 21), such as chronic barbiturate intoxication, barbiturate addiction, and severe withdrawal manifestations, including grand mal seizures and a picture closely resembling delirium tremens We have in the last few years investigated new types of hypnotic sedative drugs unrelated to the barbiturates These included methylpentynol, α phenyl α ethyl glutarimide, 2, 4 dioxo 3, 3 diethyl methyl piperidine and 1 ethinylcyclohexyl carbamate So far we have found these drugs quite satisfactory, although the observation period is obviously much too short to make any definite claims Exercise of restraint in the prescription of any hypnotic is obviously the most satisfactory solution , but it is important that the use of these new compounds has enabled us to dispense with barbiturates (for insomnia) altogether in the ward concerned for the past eighteen months —M M GLATT, M D (Warlingham Park Hospital, Warlingham, Surrey)

Protophrenia—Dr Bourne's letter (Feb 4) is an astonishing mixture of misquotations and fantastic distortions of statements I made in earlier letters According to him, I said that ' only feckless parents would seek hospital care for an imbecile child if he looks anatomically normal " What I really said was " few parents of a normal looking child below school age who can walk and can control his sphincters will agree to have him certified as a mental defective " I concluded that this circumstance " may explain why almost all Dr Bourne's residual ' cases have feckless or otherwise unsuitable parents " Not I, but Dr Bourne, showed that almost all his ' residual " cases had " feckless or otherwise unsuitable parents " He continues " *Plainly from this, she knows nothing of the burden such a misfortune may bring to a working class home* " I have in fact first hand knowledge of the burden such a misfortune may bring to people who have to work for their living , I have also discussed this problem with many parents from the Association for Mentally Retarded Children in the U S A and from the Society for Mentally Handicapped Children (S M H C) in England—many of them ' working-class "—who, like me, steadfastly declined to apply for institutional care for their pre school age children Regarding Dr Bourne's refutation of my second " extravagant ' assertion—that his proportion of residual cases was unduly small—I can only advise him to visit a few outside children's parties arranged by groups of parents in the S.M.H C He will then see that a high proportion of the under-fives (or sixes) look completely normal His question " which outpatients ? " is thus easily answered

Dr *Bourne* says that my theories directly contradict my previous statement Why ? Because I stated that these children look normal but that most of them reveal to the expert signs of neurological disturbances ? I did not say " all," as Dr Bourne asserts He goes on to say that my clinical signs of organic disease " are only to be found by the esoteric methods of neurological examination prescribed in her unpublished papers " I described several of these well-known signs in my letter and referred to others published in two English journals accessible to everybody Finally Dr Bourne declares that he has read my other letters to the medical press But when reading his comments I started wondering how he could possibly have read them Where did he take it from that " A single child's case was enough to convince her that defect arises not from inadequacy of the rest, its position did not alter on deep inspiration followed by the Valsalva manœuvre, whereas in patients with lung hernia this caused the apex to bulge upwards. Although some of Fenichel and Epstein's patients were alarmed at the appearance of supraclavicular swelling, they suffered no inconvenience and, as is usually the case, no treatment was necessary. Exceptionally, however, the condition has given rise to severe pain,[10] and Rigden[11] described a patient in whom surgical repair of an intermittent cervical hernia had to be undertaken partly because of local discomfort, but mainly because protrusion of the lung was accompanied by throbbing in the head and neck.

MORBIDITY AFTER PROSTATECTOMY

Since surgical treatment was first used for benign enlargement of the prostate, it has undergone many modifications. The primary aim has always been to ensure permanent relief from the threatened dangers of urinary obstruction and to do so by an operation of low mortality. This objective can now be attained by suitable selection of cases and careful attention to technique, and the problem of reducing postoperative discomfort and morbidity now commands greater attention. In a symposium on morbidity following prostatectomy held in Melbourne last year, a number of leading Australian urologists recorded their experience with particular operations. Basically all agreed on the need for complete removal of obstructing tissue, the control of hæmorrhage, and avoidance of infection; and when these conditions had been fulfilled, methods dispensing with suprapubic drainage and its inconvenience could be adopted with advantage.

Discussing the transvesical operation devised by S. H. Harris, R. G. S. Harris[1] stressed the importance of "clean intracapsular removal" of the adenomatous tissue. Positive hæmostasis by suture and plastic reconstruction of the cavity went far to prevent postoperative sequelæ, and urinary fistula and incontinence were said to be rare. Mortensen[2] described transurethral prostatectomy and dealt with the untoward events which followed any form of prostatectomy and also with those specifically related to the operation of resection. The latter included urethral stricture, hæmolysis (from leakage of irrigating fluid into open venous sinuses), and persistent postoperative infection; but they were uncommon in expert hands. Contrasting the technique of retropubic prostatectomy with the transvesical operation, Kirkland[3] made some interesting comments on the comparative freedom from risk in opening up the prevesical space and interfering with the prostatic venous plexus. The particular Australian bogy of osteitis pubis in relation to the retropubic operation was largely discounted at the symposium; and the short period of catheter drainage required after this operation was regarded as a contribution to the early restoration of urinary continence.

It is hard to draw any very significant comparative conclusions from the views of these Australian surgeons. As Caine[4] pointed out in a recent review of the late results and sequelæ of prostatectomy, the surgeon of today has a choice of many technical procedures, all of them well tried and each with its distinguished advocates. Each has produced good results in the hands of those familiar with it, and the patient with prostatic trouble may now reasonably expect both relief from his symptoms and freedom from postoperative distress.

MORPHINE-LIKE DRUGS

Few drugs have been more closely studied from the point of view of the relationship between molecular structure and pharmacological activity than morphine. When the structural formula of morphine was established, many simpler structures could be identified within its complex molecule. For many years potent analgesics were sought by synthesising phenanthrene derivatives, but the results were very disappointing. The discovery of pethidine's analgesic properties was a big advance which focused attention on the resemblance of this apparently unrelated compound to morphine. Other types of compound were synthesised, including methadone, isomethadone, and the dithienylbutenylamines. In all, many hundreds of synthetic chemicals were prepared and tested for analgesic activity. All of these bore some structural relation to the natural prototype, morphine. Braenden et al.[5] have lately collected and summarised a mass of detail about the way in which alterations in the chemical constitution of several groups of compounds related to morphine modifies their analgesic potency. This valuable work shows that it is now possible to point to certain chemical features which are shared by drugs with true morphine-like analgesic activity. This activity is associated with a tertiary nitrogen atom carrying a methyl group or another group which must be of low molecular weight. There is a central quaternary carbon atom, none of the valencies of which are connected with hydrogen; and the carbon atom bears on one valency either a phenyl group or a group which is isosteric with phenyl. Maximum analgesic activity seems to be achieved when the tertiary nitrogen atom is separated from the quaternary carbon atom by a chain of two carbon atoms. Yet some compounds with these very features have no morphine-like properties and it is still not possible to predict with confidence that a particular chemical configuration will act in this way. The picture is obviously incomplete, and it becomes a very preliminary sketch when we realise that though in time we may be able to identify analgesic properties in a molecule from an examination of its chemical and physicochemical properties we still know little or nothing about the receptors with which it combines and reacts.

INTERSTITIAL MYOCARDITIS

Interstitial non-rheumatic non-suppurative myocarditis was well known to pathologists of the 19th century. It was considered to be a complication of bacterial infections, usually typhoid fever and streptococcal infections. In 1899 Fiedler[1] considered that the isolated form of acute interstitial myocarditis was a special disease, to which his name is now often attached. Saphir,[2] after a thorough examination of his own material and of the literature, concluded that isolated myocarditis was not a specific disease but the outcome of various infective and toxic processes.

Because there are seldom any characteristic gross anatomical findings, the condition may have been often overlooked at necropsy. When such changes are present, they consist of enlargement of the heart due to eccentric hypertrophy or to dilatation alone, mottling of the myocardium by pale purple or pinkish grey spots, and occasional red spots of hæmorrhage. But usually only the histological examination reveals the real nature of the disease. The characteristic finding is interstitial cellular infiltration, with predominance of round cells. The infiltration is more often focal than diffuse. The clinical picture was well described by Williams et al.,[3] who studied 14 patients of ages ranging from twelve days to five years, and by van Creveld et al.,[4] who recorded 11 examples of this condition in childhood. There is acute circulatory and respiratory distress (without significant fever), cyanosis, extreme tachycardia with a very small, weak, thready pulse, no murmurs, sometimes gallop rhythm, and usually enlargement of the heart. The electrocardiogram shows a low voltage, RST segment, flat or inverted T wave, and supraventricular tachycardia. The disease may be confused with glycogen storage disease of the heart, with one form of fibroelastosis, and with the disease of the coronary arteries of the newborn that is known by various names (that recently proposed by Zischka[5] is "arteriopathia calcificans infantum").

Important progress in the understanding of these form
myocarditis came from experiments which show the
relation between interstitial myocard no h
anoxæmia plus virus infection on t
been reviewed by Pearce.[6] An ac
when blood was taken from rabbit
few minutes before the animals we
The injection of virus led to severe
typical intranuclear inclusion bodi
tion. In later experiments, rabbit
venous injection of pitressin or gu
with a virus such as vaccinia, pseud
strains of fibroma virus. A high p
had cardiac lesions, particularly
Similar results followed when rabb
were later given an intravenous in
adrenaline, pitressin, or gum acacia
of reducing the oxygen supply to th

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1. Harris, R. G. S. Med. J. Aust. 1955, ii, 917.
2. Mortensen, H. Ibid, p. 919.
3. Kirkland, K. Ibid, p. 921.
4. Caine, M. Brit. J. Urol. 1954, 26, 205.
5. Braenden, O. J., Eddy, N. B., Halbach, H. Bull. World Hlth Org. 1955, 13, 937.

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1. Quoted by Saphir (ref. 2).
2. Saphir, O. Arch. Path. 1941, 32, 1000.
3. Williams, H., O'Reilly, R. N., Willi
   28, 271.
4. van Creveld, S., de Groot, J. W. C. J.
   Ann. Paediat. 1954, 183, 193.
5. Zischka, W. Beitr. path. Anat. 1955, 1
6. Pearce, J. M. In the Pathogenes
   Disease. New York, 1950.

In England Now

There is nothing like being a patient in your own hospital to solve the mysteries of your work For years I have been puzzled by the regular, if rare, arrival in the anæsthetic room of a patient with a full stomach Elucidation came to me as I was lying in bed pleasantly drowsy from my premedication awaiting the arrival of the theatre trolley A cheerful patient appeared round the curtain

'Here y are guv, a nice cuppa tea with sugar an all" -

'No thanks I replied, I m just going to the theatre and they don t let you drink

Now look 'ere chum", the tempter persisted ' It ain t the surgeons who are keen on this no food racket it s only the anæsthetists and no one takes any notice of them

Too true, ' I agreed sleepily, I am one '

* * *

Our hospital general typists office is typical of the Welfare State—no pen and no inkpots but two teapots, one coffee-pot and countless milk bottles

Parliament

At the standing committee on the Clean Air Bill on Feb 21 Mr Enoch Powell, parliamentary secretary to the Ministry of Housing and Local Government said it was proposed that the appointed day for the prohibition of " dark smoke " from any chimney should be early in 1958 The Bill provides that for seven years after legislation is passed exemptions shall be given when smoke is caused by the nature of a building or its equipment and not by failure to maintain them properly Mr A L Blenkinsop felt that with this exemption there would be little or no sense of urgency in the campaign to end air pollution but an Opposition amendment to reduce the period to three years was turned down

The Secretary of State for Scotland announced that as part of a two year campaign against tuberculosis he had invited Glasgow Corporation to conduct a city wide survey by mass radiography in March, 1957 Besides the 10 mass radiography units normally in use in Scotland 20 more would (he hoped) be lent by England and Wales for five weeks The other three Scottish cities and many areas in the industrial belt, would later be offered facilities for similar surveys

The Minister of Labour has announced that, on the advice of the Industrial Health Advisory Committee, a pilot industrial health survey is to be made of the pottery industry Last year it was announced (see *Lancet*, 1955, ii 610) that a similar pilot survey would be made at Halifax

News

Prof. A C Frazer s Oliver-Sharpey lectures at 5 p m. on March 13 and 15, to the Royal College of Physicians of London will deal with Intestinal Absorption in Man

The fellowship of the Royal College of Surgeons in Ireland has been conferred on A F O Williams

The honorary fellowship of the Royal College of Obstetricians and Gynæcologists is to be conferred on Viscount Nuffield and Sir Ronald Weeks

Dr W S Walton medical officer of health for Newcastle upon Tyne and lecturer in charge of the department of public health in the University of Durham has been appointed to the University of London chair of public health at the London School of Hygiene and Tropical Medicine

Dr D V Bates first assistant in the medical unit of St Bartholomew's Hospital London has been appointed associate professor of medicine at McGill University and assistant physician to the Royal Victoria Hospital Montreal

Appointments

ELLIS D D M B Belf, D P M whole time asst psychiatrist Winwick Hospital, Warrington, Lancs

FRASER, R J A M B Aberd, F R.C.S E. consultant neurosurgeon Scottish North Eastern R.H B

FOLEY MARY M M D N U I, D P H, D C H whole time tuberculosis M O, Ormskirk H M C area

HOLLAND, H W M B Lond M R.C P D.M R consultant radiologist Addenbrooke s Hospital, Cambridge

KERRIGAN MONICA M B Belf D P H. senior asst M O H and school M O, Dudley

KINNISH, R. V, M B Lpool whole time asst. anæsthetist Doncaster hospitals

MARSDEN A. J, M B Lpool, F R C.S part time consultant general surgeon Ormskirk group

TAYLOR, MAVIS B M R C.S school M O, York/Northallerton area

WISEMAN ARIANE G M M B St And D.P H asst M O H and school M O Salford

Births, Marriages, and Deaths

BIRTHS

PERRY —On Feb 20 at the County Hospital, Haverfordwest to Dr Elizabeth Perry (formerly Thomas), wife of Dr C Lynn Perry —a son brother for William

DEATHS

NELIGAN —On Feb 24 at the Royal Victoria Hospital, Folkestone George Ernest Neligan M C, F R C.S, consulting surgeon The London Hospital aged 71

Vacancies

ACADEMIC AND EDUCATIONAL

Inst of Psychiatry Lecturer in Clin Neurophysiology

University of London Lectures " Biology Corpus Luteum 5th & 8th March.

Oxford University Sr Research Officer Lab of Human Nutrition

St Andrew's University Refresher Course for G P s. 18th–29th June

Sheffield University Lecturer in Med.

Sheffield University Lecturer & Demonstrators in Anatomy

Royal College of Physicians of London. Oliver-Sharpey lectures 13th–15th March.

Royal College of Surgeons of England Faculty of Dental Surgery Examinership

University College London. Public Lecture 'Present Status of Enzyme-Forming Mechanism 5th March.

Hosp for Sick Child W C 1 Research Fellow (Histochemistry)

Cambridge Gonville & Caius College Berkeley Bye-F ship

Durham University & Newcastle United Hosps Prof. of Med (Cons)

Manchester University Fortnight s Course from 28th May Industrial M.O s

Oxford University Asst Graduate in Path

Royal Inst of P H & Hygiene Course of Instruction (C P H) 16th March.

University of London Lectures "Future of Pharmacy in Relation to World Needs 7th & 15th March

University of London Chair of Medicine

Edinburgh University Lecturer (Dept Physiology)

ANÆSTHETICS

North West Met R H B Cons
North East Met R H B P t Cons
Barrow & Furness H.M.C Jr H M O
Birmingham Dudley Road Sr H O
Birmingham R.H B Cons & P-t Cons
Birmingham United Hosps. Sr H O
Edinburgh Northern Group of Hosps H.O
Hitchin Hosps Locum Sr H O
Manchester R H B P t Cons
Northampton Gen. H O
Oxford United Hosps, Sr H.O
Scotland. Western R.H B Sr Reg
Stafford H.M C Sr H O
U S A Cambridge Mass Residencies
Worthing Group H.M.C Reg

CARDIOLOGY

Westminster S W 1 Reg

CASUALTY

Hackney E 9 H O
Royal Northern, N 7 Sr H O

Canterbury Kent & Canterbury Sr H O
Cardiff St David s Sr H O
Chertsey St. Peter s Sr H O
Chichester St. Richard s Sr H.O
Hemel Hempstead West Herts Jr H.M O
Northampton Gen. Sr H O & H O
Reading Battle H O
Weston-super-Mare Gen. Sr H O
Windsor King Edward VII. Sr H O

CHEST AND TUBERCULOSIS

Brompton, S W 3 H O s
North East Met R H B Reg
Paddington Group H.M C. Reg
Alton. Henry Gauvain Sr H O
Benenden San M O
Bristol Ham Green Sr H O
Cardiff Glan Ely Sr H O
Chelmsford Broomfield Locum Sr R M O
Driffield. Northfield San. Sr H O
Dublin National B C G Committee Vaccinator
Grimsby Springfield Reg
Leeds R H B Sr Reg
Manchester R H.B Reg
Scotland Western R.H B Sr H M.O

DENTAL SURGERY

Leeds United Hosps P t Cons

DERMATOLOGY

Sheffield United Hosps Sr Reg

There can be few of us who would not shrink from such a task. When Bernard Shaw wrote of *The Doctor's Dilemma* he could scarcely have guessed the reality of the plot. You will remember, the choice between the deserving colleague and the undeserving genius was not made lightly. Your choice, made from the meagre data on a slip of paper, is all the harder. I do not blame you for making a compromise. What can be simpler than to share the chair?

For my part I've always thought it my duty to put relief of suffering before everything else—even before the saving of life. It comforts me to know that, however incurable the disease, there is always something I can do. But for once I am powerless.

Anæmia is not usually a distressing complaint. Mrs Neal, however, is elderly and her arteries are hard and narrow. Her lungs are emphysematous, her heart is weak, her eyesight is poor. Her gastric mucous membrane is atrophic, and her digestion is not good. When her hæmoglobin falls below 60% she begins to get angina, breathlessness, and cramp. She loses appetite and weight, and even medicine gives her indigestion. As her legs gradually swell, so her body slows and her mind becomes dull. Finally, her hæmoglobin 35%, she is reduced to the picture of abject misery that I know so well. She comes to us for help. And what do we do? We transfuse her till her hæmoglobin is 65%, and five days later the whole wretched story begins all over again. You have made your compromise.

I admit we are no nearer to a solution, although I hope I have convinced you that, of the possibilities, at least two are unacceptable. Surely there must be an answer to the problem that does not clash with one's ideals? I should willingly do anything in my power to help you find it.

Forgive me for taking you from your microscope.

Yours ever,
H. B.

Letters to the Editor

Vaccinia versus Poliomyelitis.—Colonel Morhouse (Feb 25) says that in the United States, though vaccination against smallpox has usually taken place by the age of 6–7, children of that age are regarded as particularly liable to contract poliomyelitis. Can he give us an idea of what proportion of these vaccinations are performed in infancy? If, as in this country, vaccination is commonly performed at 3–6 months, it could not be expected to give full protection against poliomyelitis at school age.

My own data suggest that, though smallpox vaccination several years previously *may not prevent poliomyelitis, it may* modify the illness so that paralysis is avoided. In 1955 in this area 35 children aged 4–7 years contracted poliomyelitis (paralytic or non paralytic). Of the 25 in whom there was no paralysis after the illness, 19 had been vaccinated in infancy, while 6 had never been vaccinated. Of the 10 with paralysis, 4 had been vaccinated in infancy while 6 had never been vaccinated, and it is noteworthy that in all 4 vaccinated children paralysis was slight, whereas in all 6 unvaccinated children it was severe.

Since in my area about half the children are vaccinated against smallpox, it may be asked why, of 25 children with non paralytic poliomyelitis, as many as 19 should prove to be vaccinated. A possible explanation is that children vaccinated in infancy are for several years so fully protected against poliomyelitis that they do not contract the disease in any form and therefore do not acquire any specific immunity to it. Hence, compared with children who have never been protected by smallpox vaccination, they may be more liable to contract poliomyelitis at school age—though the waning effect of the vaccination may still suffice to save them from paralysis.—D. P. MacIver, M.D. (Weybridge, Surrey.)

Leptospirosis.—As a veterinary surgeon I see many cases of leptospirosis in the dog, mostly due to *Leptospira canicola*, more infrequently to *L. icterohæmorrhagiæ*. My experience is perhaps relevant to the correspondence on the value of penicillin in the treatment of the disease in man (Feb 11 and 18).

I find that penicillin causes temporary remission of symptoms, lasting for about 36–48 hours, followed by relapse. Dark ground examination for the causal organism is often positive after several days' administration of penicillin in h- doses. I am inclined to think that acute cases responding to some degree to penicillin become chronic, usually show eventual nephritis with uræmia; a further acute attack is not uncommon. Administration of streptomycin and oxytetracycline concurrently produces very satisfactory, perman- results with gratifying speed.

Leptospirosis in the dog is far from uncommon, as many of my colleagues have found to their cost. It is surprising that more cases do not appear among those devoted to dogs at close quarters—children in particular. I make a point of handling suspect urine with care.—R. T. Dawson, M.R.C.V.S. (Ashington, Northumberland.)

Mass Radiography.—I have read with interest and no little amusement Dr Brailsford's letter (Feb 25). So far from being "the most serious" objection to mass radiography, I think it will be a great advantage if this method "leads to students being taught that active progressive tuberculosis can be present without signs or symptoms." This a hard fact which we, in the chest service, have all learnt by experience and I could only wish that it had been emphasised when I was a student.—G. I. Rees Jones, M.R.C.S., director, mass radiography units 7B and 7F (Oakwood Hospital, Maidstone.)

Production of Codeine.—I am glad Dr Hamilton (March 10) agrees with me that the codeine in tab codein co does not enhance the analgesic effect, but surely if his so-called new drug, *n* acetyl *p* aminophenol, is only of equal analgesic value why does he not stick to tab codein co without the codeine? At present a hundred (0.5 g.) tablets of *n* acetyl *p* aminophenol ('Panadol') cost 10*s.* 11½*d.*, which is the price of a thousand (gr 10) aspirin tablets.

There is, however, a far more important reason why Dr Hamilton should temper his present enthusiasm. *n* Acetyl *p* aminophenol is merely another way of saying *p* hydroxy acetanilide—a word full of sinister implication which conjures up memories of 'Antifebrin', 'Daisy Powders', and deaths from agranulocytosis.

Acetanilide was excluded from the 1954 *British Pharmaceutical Codex* because of its toxicity, and Daisy powders are no longer available. It will take much to convince me that Dr Hamilton's new hydroxylated "Daisy pill" is completely above suspicion.—Eirian Williams, M.R.C.P. (London Hospital, E.1.)

Streptonivicin.—May I comment on your annotation (March 3) reporting the common identity of streptonivicin ('Albamycin') cathomycin ('Cathocin'), crystallinic acid ('Cardelmycin'), and albomycin?

H. Welch and W. W. Wright (*Antibiot Chemother* 1955 5, 670) reported the common identity of streptonivicin, cathomycin, and crystallinic acid, based inter alia on unequivocal evidence—the infra red absorption spectra of the crystalline antibiotics. There is, however, no report that albomycin, first described by G. F. Gause and M. G. Brazhnikova (*Nov Med Mosk* 1951, 23, 3) is identical with these other three antibiotics, nor that the antibiotic strains *Streptomyces niveus* and *Actinomyces subtropicus* are identical.

Streptonivicin is a dibasic acid (H. Hoeksema et al. *J Amer chem Soc* 1956, 77, 6710) containing C, H, O, and N only, active predominantly against gram positive bacteria, inhibiting staphylococci at dilutions of 1/750,000 to 1,3,000,000. Streptonivicin by mouth can protect infected animals. Albomycin, on the other hand (G. F. Gause, *Brit med J* 1955, ii, 1177), is a cyclic polypeptide, thought to be an "imitation" of some iron containing respiratory enzyme in albomycin sensitive bacteria, contains 4.16% iron, is active against gram positive bacteria, in particular staphylococci at a dilution of 1/700,000,000, and is also active against certain gram negative bacteria. No report on the effectiveness of oral albomycin is available, and it is likely, in common with other "polypeptide" antibiotics, not to be absorbed from the alimentary tract.

It may be added that crystallinic acid (cardelmycin) has been previously known as antibiotic PA93 of the Pfizer Laboratories (H. Wright, W. W. Wright, *Antibiot Chemother* 1955 5, 670).

A further point of difference between the two antibiotics is their colour; streptonivicin is white, whereas albomycin (presumably on account of the iron content) is red.—K. A. Lees, F.P.S. (Glaxo Laboratories Ltd., Fermentation Research Division, Sefton Park, Stoke Poges, Bucks.)

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Hypofibrinogenæmia in Pregnancy

Serious loss of blood from the uterus after labour is one of the major complications of childbirth and one of the commonest causes of death of the mother The collection of incidents and information over the past ten years has led obstetricians to recognise that the immediate cause of the disastrous uterine hæmorrhage is often a temporary abnormality of the blood-clotting process, and furthermore, if treated in time, these hæmorrhages can be stopped and the patient saved by other than local methods Ratnoff et al[1] have recently reviewed the evidence and come to the conclusion that abnormal blood clotting is the usual cause of fatal uterine postpartum hæmorrhage

In normal pregnancy and labour blood-clotting processes are little changed There are no significant changes in the platelet count and no unusual fibrinolytic activity in the plasma The fibrinogen content of the plasma rises slowly by about one-third during the pregnancy After labour it is, as Barnes[2] pointed out, the contraction of the myometrium that ensures proper hæmostasis at the placental site, the most striking examples of this have been seen in patients with thrombocytopenic purpura[3] and in a young woman with hæmophilia[4] who have successfully completed labour without any unusual *immediate* blood-loss, subsequent blood-loss in these patients came from damage to other parts of the genital tract that are not supplied with such an efficient vasoconstrictor apparatus as the uterus The obstetric conditions especially liable to be followed by excessive uterine hæmorrhage, are premature separation of the placenta, amniotic-fluid embolism, missed abortion with retention of a dead fœtus, and eclampsia It has been discovered that, except in eclampsia, the blood-clotting abnormality in all these conditions is a gross deficiency of fibrinogen, and the explanation proposed is that thromboplastic material reaches the maternal circulation Experimental evidence for this hypothesis has been known for some time Ratnoff et al[1] quote experiments by Mills in 1921 which showed that intravenous injection of tissue-thromboplastin caused a decrease of plasma fibrinogen, and in fact gradual infusion of thromboplastin led to complete defibrination of the animal, the fibrinogen level in the plasma returned to normal twenty-four hours after the infusion ceased There is also evidence that amniotic fluid and placental tissue have considerable thromboplastic activity Hæmorrhagic symptoms appear when the plasma-fibrinogen level falls below 100 mg per 100 ml there is often bleeding from venepuncture sites and subcutaneous hæmorrhage, and postpartum uterine bleeding may be severe and prolonged and the consequences grave

Premature separation of the placenta is the commonest cause of uterine bleeding in pregnancy and is said to occur in from 1 in 85 to 1 in 250 pregnancies The condition has been known for twenty years to be associated with hypofibrinogenæmia, but only lately has this point received much attention The cause is thought to be the passage of thromboplastic material from the placenta into the maternal blood-vessels, where intravascular clotting takes place, and this continuing process uses up the plasma-fibrinogen, but this explanation is not accepted by all authorities In amniotic fluid embolism, the sudden onset of labour and its rapid course is sometimes followed by severe uterine hæmorrhage, and hypofibrinogenæmia is often found, Jackson et al[5] have recorded 8 such cases The latest syndrome to be associated with plasma-fibrinogen depletion is missed abortion with retention of a dead fœtus in the uterus Weiner et al[6] described 3 cases of severe uterine hæmorrhage following spontaneous delivery of a dead fœtus, in which hypofibrinogenæmia was found in the mother, they thought that rhesus incompatibility was also concerned, but subsequent findings do not support this view Pritchard and Ratnoff[7] studied 31 patients who remained undelivered for three or more weeks after apparent intra-uterine fœtal death in 23 there was no evidence of critical depletion of fibrinogen (i e, a level below 150 mg per 100 ml), though in 7 patients the fibrinogen level fell steadily throughout the pregnancy, in the remaining 8 patients the fibrinogen levels became dangerously low After delivery the plasma-fibrinogen rose rapidly to normal in forty-eight hours Experience has shown that hypofibrinogenæmia does not develop when the fœtus dies before the fourth month of gestation, and it does not appear until at least five weeks after the apparent death of the fœtus

Lately cases of hypofibrinogenæmia in pregnancy have been reported in this country Barnett and Cussen[8] described 2 cases of concealed accidental hæmorrhage causing precipitate labour, qualitative tests showed a low fibrinogen level Barry et al[9] gave details of 6 cases of complications of pregnancy associated with hypofibrinogenæmia, and in 1 of them none of the recognised syndrome was present Kelsey and Muirhead[10] also described fibrinogen deficiency in an apparently uncomplicated case of postpartum hæmorrhage O'Driscoll and Lavelle[11] had a patient with a retained dead fœtus and low plasma fibrinogen, low platelet-count, and an active fibrinolysin in the plasma. When induction by an oxytocin drip failed, a hysterectomy was carried out, and it is interesting that no large retroplacental hæmatoma was found, because such a hæmatoma has been suggested as the source of the thromboplastin which reduces the plasma-fibrinogen Kimbell and Ghosh[12] found afibrinogenæmia associated with massive postpartum hæmorrhage after a lower-segment cæsarean section

In the matter of treatment, Ratnoff and his colleagues agree with Moloney et al[13] that human fibrinogen

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[1] Ratnoff O D Pritchard J A Colopy J E *New Engl J Med.* 1955 253 63 97
[2] Barnes, A. C *Amer J med Sci* 1947 213 463
[3] Epstein R D Lozner E L Cobbey, T S Davidson, C D *Amer J Med* 1950 9, 44
[4] Israels M C G Lempert H Gilbertson E *Lancet* 1951 i 1375
[5] Jackson D P, Hartmann R C, Busby T *Obstet. Gynec* 1955 5 223
[6] Weiner, A E, Reid D E Roby C C Diamond L K *Amer J Obstet Gynec* 1950 60 1015
[7] Pritchard J A., Ratnoff, O D *Surg Gynec Obstet* 1955 101, 467
[8] Barnett V H Cussen, C A *Brit med J* 1954 ii, 676
[9] Barry, A P Geoghegan F Shea S M *Ibid* 1955 ii 287
[10] Kelsey, H A., Muirhead J M. B *Lancet* 1955, ii, 705
[11] O Driscoll D T Lavelle S M. *Ibid* p 1169
[12] Kimbell N Ghosh, A K *Ibid* Jan 14, 1956, p 82
[13] Moloney W C, Egan W J, Gorman A J *New Engl J. Med* 1949, 240, 596

Newcastle R H B Sr Casualty Officer
Northampton Gen Sr H O & H O
Swansea Jr H M O
Swindon Hosp Group Sr H O s
Weston super Mare Gen Sr H O
Weymouth & Dist Sr H O

CHEST AND TUBERCULOSIS

Glasgow, Robroyston Jr H M O
Ipswich St Helen s H O
Lanchester Co Durham Maiden Law Jr H M O
Liverpool Walton Sr H O
Paisley & Dist Hosps B O M Jr H M O
Welsh R H B Locum Sr H M O

DERMATOLOGY

St John's Hosp for Diseases of the Skin W C 2 Reg
Guy s S E 1 P t Reg
Aberdeen Gen Hosps B O M Locum H O

EAR NOSE, AND THROAT

Birmingham & Midland Ear & Throat H O 's or Sr H O s
Brighton & Lewes H M C Sr H O
Carlisle Cumberland Infy Sr H O
Glasgow Victoria Infy Pre reg H O
Northampton Gen Sr H O
Portsmouth Group H M C Sr H O
Reading Royal Berks H O
Scotland Western R H B Sr Reg or Locum
Southampton Royal South Hants & Gen Sr H O
Welsh R H B Cons

HÆMATOLOGY

Brentwood North East Met Regional Blood Transfusion Centre Jr H M O
South Western R H B National Blood Transfusion Service Sessional M O 's

INFECTIOUS DISEASES

Neasden, N W 10 Reg

MEDICINE

Dreadnought Seamen's S E 10 Pre reg H O
Nelson, S W 20 Sr H O
Queen Mary s Hosp for East End, E 15 H O
South Lodge N 21 H O
Birmingham R H B Reg
Bristol United Hosps & South Western R H B Reg
Chichester Royal West Sussex Reg & Locum
East Anglian R H B Reg
Gainsborough John Coupland Jr H M O
Huddersfield St Luke s Jr H M O & Sr H O
Ipswich & East Suffolk Sr H O
Kirkcaldy Group of Hosps Reg
Medway & Gravesend H M C Sr H O
Portsmouth Group H M C Sr H O
Portsmouth Group H M C Reg
Romford Victoria H O
Scotland South Eastern R H B Sr Reg or Reg
Scotland Western R H B Cons
Scunthorpe War Mem Pre reg H O or Sr H O
Sheffield United Hosps Sr H O
Southampton Royal South Hants H O s
Stoke on Trent City Gen H O
Torquay Torbay Sr H O

NEUROLOGY

National Hosp for Nervous Diseases Reg

NEUROSURGERY

Guy 's—Maudsley Neurosurgical Unit Reg

OBSTETRICS AND GYNÆCOLOGY

Hackney E 9 H O
North Middlesex N 18 H O & Pre reg H O
Birmingham United Hosps Reg
Bristol United Hosps & South Western R H B Reg
Bromsgrove Gen Pre reg H O & Locum
Bury & Rosendale H M C Sr H O
Carshalton St Helier Sr H O
Cheltenham Maternity H O
Hastings Buchanan H O
Hitchin North Herts Reg
Manchester R H B Reg
Marie Curie S W 3 H O
Mid-Worcestershire H M C Reg
Newcastle Gen H O
Newcastle R H B Reg
Portsmouth Group H M C Pre Reg H O
Reading Combined Hosps H O
Romford Oldchurch Sr H O
Scotland Eastern R H B Reg
Scotland Western R H B. Reg
Sutton & Cheam Hosp Maty Annexe P t G P
Swansea Sr H O
Welsh R H B Reg

OPHTHALMOLOGY

Manchester United Hosps Sr H M O
Birmingham R H B Reg
Australia Victorian Eye & Ear, East Melbourne Permanent Med Supt

ORTHOPÆDICS

Ascot Heatherwood Orthopædic Locum Reg
Ashford, Middx H O
Braintree Black Notley H O
Carlisle Cumberland Infy Sr H O
Carmarthen West Wales Gen Sr H O
Derby Derbyshire Royal Infy Reg
Leeds R H B Reg
Louth County Infy Reg
Northampton Gen H O
Newcastle R H B Reg
Paisley & Dist Hosps B O M Jr H M O
Portsmouth Group H M C Pre reg H O
Romford Oldchurch H O
St Bartholomew s, E C 1 Reg
Sheffield City Gen Reg
Southampton. Royal South Hants Sr H O
Swansea Sr H O

PÆDIATRICS

Ashton Hyde & Glossop H M C Sr H O or Jr H M O
Birmingham United Hosps Sr H O & H O
Hereford County H O
Kettering Gen Sr H O
Luton & Dunstable H O
Nottingham City Sr H O
Southampton Child s H O

PATHOLOGY

Group Pathological Lab , W 5 Sr H O
Royal Marsden S W 3 Cons
Royal Marsden, S W 3 Locum Sr H M O or Sr Reg
Northwood, Middx Mount Vernon Sr H O
Oxford United Hosps Sr H O

PHYSICAL MEDICINE

Whittington N 19 Reg
Royal Free, W C 1 Sr Reg

PLASTIC SURGERY

Welsh R H B Reg

PSYCHIATRY

Abbots Langley Leavesden Jr H M O
Birmingham R H B Reg
Brentwood Warley Locum Sr Reg
Bromsgrove Barnsley Hall Jr H M O
Dartford H M C Sr H O & Locum Sr H O
Devizes Roundway Jr H M O
East Anglian R H B Cons
Greenock Ravenscraig Jr H M O
Huddersfield Storthes Hall Jr H M O
Leeds R H B Reg
Macclesfield Parkside Mental Jr H M O
Newcastle upon Tyne H M C H O
Northern Ireland Hosps Auth Jr H M O
North West Met R H B Cons
Scotland Eastern R H B (Dundee Royal Mental Hosp) Cons Phys Supt & Prof Psych
Scotland Western R H B Regs
South Western R H B Deputy Med Supt (Sr H M O)
South Western R H B Sr H M O
South West Met R H B Sr H M O
St Alban s Napsbury Mental Jr H M O

RADIOLOGY

East Anglian R H B Reg
Sheffield R H B Cons
Scotland Western R H B Reg
Sheffield R H B Sr H M O
Watford & Dist Peace Mem Reg

RADIOTHERAPY

Leeds United Hosps Cons

SURGERY

Battersea Gen S W 11 H O
Bolingbroke, S W 11 H O
Central Middlesex, N W 10 H O
London Jewish E 1 Sr H O
North Middlesex N 18 H O
Royal Marsden, S W 3 H O
St George in the East E 1 H O
St Leonard s N 1 H O
Wanstead, E 11 H O
Aberdeen Gen Hosps B O M Locum H O 's
Barrow-in Furness North Lonsdale H O
Birmingham R H B Reg
Bishop Auckland Gen H O
Brighton Royal Sussex County H O 's
Burton upon Trent Gen H O
Chelmsford & Essex Locum Reg
Chelmsford & Essex Pre reg H O s
Cheltenham Gen H O
Chesterfield Royal H O
Crewe & Dist Mem Sr H O
Derby Derbyshire Royal Infy Pre reg H O or Sr H O
Doncaster Royal Infy Sr H O
Halifax Gen H O
Hastings Royal East Sussex Pre reg H O 's
Hastings St Helen s Pre reg H O
Hereford County H O
Hitchin Lister H O
Huddersfield Royal Infy H O
Kirkcaldy Gen H O 's
Leeds R H B Reg
Louth County Infy Sr H O
Macclesfield & Dist H M C Pre reg H O
Manchester Booth Hall Child s Reg
Manchester R H B Reg
Manchester West Manchester H M C Pre reg H O 's
Manchester Wythenshawe Sr H O
Mildmay Mission E 2 Sr H O
Newcastle United Hosps Reg
Northampton Gen H O
Northern Ireland Hosps Auth Reg
Nottingham Gen Pre reg H O
Nottingham Highbury Sr H O
Peterborough, Mem H O
Plymouth S Devon & E Cornwall Gen Pre reg H O
Perth & Dist Jr H M O
Portsmouth Group H M C Sr H O & Pre reg H O
Redhill County Reg
Romford Oldchurch H O
Romford Victoria Temp Reg
Scotland Western R H B Reg
Sheffield Wharncliffe Reg
Stoke on Trent City Gen H O
Taunton & Somerset H O

THORACIC SURGERY

Birmingham Yardley Green Sr H O

UROLOGY

St Peter s St Paul s & St Philip s Sr Reg

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Whitley Bay Northumberland Urban List approx 1260
Leeds Rothwell Urban Dist List 5431

PUBLIC APPOINTMENTS

National Coal Board (North Eastern Div) Area M O
Gold Coast Local Civil Service M O 's & M O H s
Staffordshire C C Asst County M O & School M O
London County Council M O (P H Dept)
Govt of Eastern Region of Nigeria Specialist (Orth Surg)
Buckinghamshire C C Asst County M O
Peterborough Joint Education Board School M O & Asst M O H
Malaya Federation Specialist Radiologist
Barbados Gen Hosp M O s
Gold Coast Local Civil Service M O s

(Further particulars of above vacancies available on request to Advertisement Manager)

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ar hypertrophy An apical diastolic murmur which ometimes confuses the diagnosis, and which may indeed e due to coincidental abnormalities of the mitral valve sually indicates a large shunt with an excessive blood-low through the left heart The shunt is usually small, ut in the more severe cases, with pulse-pressures between 0 and 100 mm Hg, it may amount to 50–70% of the left entricular output There is general agreement that urgical closure of a patent ductus is almost always advisable both because of the risk of bacterial endocarditis and because of the natural history of the disease Admittedly, large shunts can be tolerated for a surprisingly long time, and spontaneous closure is possible even after the age of thirty, but deterioration with heart-failure is to be expected, as CAMPBELL has found in the third or fourth decade[1]

An important and peculiar complication of patent ductus arteriosus is pulmonary hypertension[2-5] It is perhaps less common with patent ductus arteriosus than with other congenital communications such as atrial or ventricular septal defects[6], but there is evidence to suggest that at least 1 case in 10 may be affected Two forms can be recognised one which develops gradually and is usually mild, and the other which begins early and is severe Its effect is to reduce or abolish the shunt or even reverse its usual direction, and the clinical signs are modified accordingly In the mild form the continuous murmur may persist, although it is usually shortened to a systolic murmur, and it often disappears altogether in the severe form The pulse-pressure tends to remain large, but symptoms and signs of pulmonary hypertension develop and may even predominate Attacks of respiratory infection, with cough dyspnœa, and hæmoptysis, are common, and ultimately there is right sided heart-failure The pulmonary second sound is loud and accentuated, and it is accompanied by a palpable impulse in the second left intercostal space The characteristic parasternal lift of a hypertrophied right ventricle can usually be found, and the electrocardiogram often indicates right ventricular or combined right and left ventricular strain Giant *a* waves can sometimes be seen in the jugular pulse, and a Graham Steel diastolic murmur of pulmonary incompetence may suggest a diagnosis of aortic incompetence unless the significance of the other signs is appreciated Reversal of the shunt usually causes cyanosis, which can be generalised but is often more pronounced in the lower limbs because of the entry of the ductus into the aorta beyond the left subclavian artery

Recognition of a patent ductus arteriosus combined with pulmonary hypertension can be difficult Where the continuous murmur persists the diagnosis should be possible clinically, but when the signs of pulmonary hypertension predominate, the diagnosis from other lesions, such as atrial and ventricular septal defects and primary pulmonary hypertension, can be made only after catheterisation and angiocardiography Indeed the possibility of an underlying patent ductus arteriosus makes such investigations essential in any patient with unexplained pulmonary hypertension, whether cyanosed or not, particularly in children Catheterisation by itself will sometimes be enough, for the catheter often passes easily through the ductus, especially if the shunt is reversed In uncyanosed cases there should be a higher oxygen saturation in the pulmonary artery than in the right ventricle, and an angiocardiogram may show simultaneous filling of the pulmonary artery and the descending aorta

The cause of pulmonary hypertension in patent ductus arteriosus is debatable Mild hypertension coming on in middle life may be due to an increase in pulmonary blood flow, but this can hardly account for severe hypertension, since shunts amounting to 50% of the left ventricular outflow often persist uncomplicated for a number of years Pulmonary resistance is always increased when the shunt is reversed, and this increase is almost certainly what produces severe pulmonary hypertension Why resistance should increase is not clear histological studies have suggested that repeated pulmonary embolism and even acute pulmonary arteriolitis are occasionally responsible but persistence of a fœtal pattern of thick-walled and muscular arteries has been suggested by EDWARDS[8, 9] as a more likely explanation On the other hand, widespread arterial occlusion by fibrous tissue, associated with the formation of new and probably anastomotic vessels, as recently described by BREWER[10] suggests that the vascular abnormality is sometimes acquired as the late result of an earlier functional change

Opinion varies about the treatment of patent ductus arteriosus with hypertension The need for operation is clearly increased by slight hypertension, but it is debatable in the severer grades Where there is cyanosis indicating a reversed shunt, operation is contra-indicated since the ductus seems to act as a safety valve Some people advocate ligation in all cases with left-to-right shunt, claiming that its effects are beneficial even some time afterwards Others prefer to be guided by the effects on the pulmonary pressure of digital compression of the ductus at the time of operation, since success depends upon the reversibility of the hypertension The technical difficulties may be formidable because the ductus is often short and wide and may contain calcium, which can spread on to the pulmonary artery or the aorta and make them liable to tear

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Annotations

BRITISH POLIOMYELITIS VACCINES

THE department of biological standards of the National Institute for Medical Research is responsible for carrying out the safety tests on the poliomyelitis vaccines soon to be used in this country, and the director of the department, Dr W L M Perry, has sent us some detailed technical information about the vaccines In our present difficulties it is impossible to publish this information in full but Dr Perry s text will be found in this week s *British Medical Journal* The most important modification from the strains of virus used in the United States is the adoption of an alternative type 1 virus which is considerably less virulent than the original strain, a change which should greatly increase the safety of the vaccines The method of vaccine production and formalin treatment are similar to those used elsewhere, and the British vaccines will be subjected in duplicate to all the safety tests adopted in the U S.A, including the use of cortisone treated monkeys As Dr Goffe emphasised in our last issue the American vaccine which has met these new requirements has been given to some 10 million children without any detectable ill effects It is hoped that British vaccines will be at least as potent as American vaccines and Dr Perry calls for the support of the medical profession in this first step towards the safe and effective control of poliomyelitis in this country

In the past few days general practitioners received from the Ministry of Health a note giving information about poliomyelitis vaccination. The Medical Research Council has been invited by the Ministry to assess the efficacy of the British vaccines and medical officers of health will be asked to make a brief report on each notified case paralytic or non paralytic, in their areas in children born in 1947-54 type, once the specific antiserum became available, and both found it in babies outside the hospitals in which they worked ROGERS commented on his good fortune in having specific serum so quickly available, since TAYLOR had already prepared it against a strain isolated a few months earlier

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[1] Campbell M *Brit Heart J* 1955 17 511
[2] Cosh J A *Ibid*, 1953 15 423
[3] Damman J F, Sell, C G R *Circulation* 1952 6 110
[4] Johnson R E Werner P, Kerschner M, Cournand A *Ibid* 1950 1 1293
[5] Wood P St Cyres Lecture, 1951
[6] Shephard R J *Brit Heart J* 1954 16 361
[7] Whitaker W Heath D Brown J W *Ibid* 1955 17 121
[8] Edwards E *Amer Heart J* 1948 28 206
[9] Hultgren H Selzer A Purdy A Holman E Gerbode F. *Circulation* 1953 8 15
[10] Brewer, D B *J Path Bact* 1955 70 299

This recent work illustrates the importance of continuing the search for new serotypes SMITH[7] has described how these various types have been prevalent in different areas at different times and it is certain that in the future more serotypes will be identified and added to the list of those which are known to be pathogenic in babies

Visiting In Mental Hospitals

To be happy, we all need to feel secure, and insecurity has long been recognised as one of the most potent causes of illness The overt causes of personal insecurity are plain to see, and, given the means, easy to treat But, just as social reformers have learnt that money is no substitute for employment, so psychiatrists know that their patients' emotional troubles are seldom cured, though they may be eased, by the relief of practical difficulties

Whether we like it or not, we all start life as members of a group, and most of us are fortunate enough to spend at any rate the first years of life in the smallest unit of that group—the family As the nucleus of personal security, there seems to be no adequate substitute for the family, and we have abundant evidence of the ill effects of the absence of family ties We know too, how much support these ties can give in illness—and especially mental illness, when the sense of security is so often lost It is a pity, therefore, that the psychiatrist in a mental hospital, though he is well aware of his patient's family and often of their need for his advice, should often have difficulty in meeting them In so far as mental hospitals remain geographically and spiritually isolated, their doctors must deal with the patients' social problems by artificial methods group treatment is only a substitute for family treatment The promising results in the treatment of all types of mental illness in day hospitals and small units in urban areas may well be due as much to the closer contacts between the doctor and the family as to the preservation of the patient's social ties brought about by the ease of association with relatives and friends In other mental hospitals, for their contacts with the patient's family, the doctors must largely rely on visiting days The easier it is made for relatives and friends to visit a patient, the easier it is for the doctors to establish contact with them

Frequent visiting is also directly helpful to the patient A child who refuses to "settle down" in hospital was formerly considered neurotic, but the need to maintain family contacts has now been accepted, and by permitting daily visiting much has been done to mitigate the harm caused by separating children from their parents But, as Mr WOODLEY points out on another page, it is equally important that the adult patient in a mental hospital should not lose touch with home Other considerations apart, the experience of illness changes a patient, and relatives should have the time and opportunity to adjust to this change while he is still in hospital

The gravest problem in the modern mental hospital is the reablement of the patient who has lost touch with the outside world Modern methods of treatment have so far reduced the length of stay of the average patient that "settling down" is no longer essential to recovery indeed for not a few it is a danger to be avoided Daily contact with friends and relatives, whether for social or therapeutic reasons, can do little harm and may do much good An increasing number of mental hospitals already allow, or even encourage, daily visits from relatives, and there are no insurmountable reasons why all should not do so

Annotations

FORCES' MEDICAL AND DENTAL SERVICES

IN 1953 the Minister of Defence appointed a committee under the chairmanship of Viscount Waverley, to report on the medical and dental services of the Armed Forces The committee, whose medical members are Sir Harold Boldero and Sir Arthur Porritt, has now reported[1]

The question whether the three medical branches should be amalgamated the committee answers with an emphatic No, but, it says, joint use of hospitals should be extended, in the United Kingdom unnecessary duplication should be avoided, and the Services should consider establishing a specialist hospital for traumatic surgery Both the Army and the Air Force should have specialist sections in which officers would continue in their specialist work for their whole career, with the chance of attaining the rank of at least colonel (or group captain) The dental branches should be further coördinated, and the prospects for dental specialists improved The pay of lieutenant and captain medical officers should be increased to conform with the scales lately announced for combatant officers (this involves increases of from 5s 6d to 7s 0d a day) Increases for higher ranks are also proposed The pay of dental officers should be the same, rank for rank, as that of medical officers

The committee's many recommendations would have the effect of enhancing the professional and financial attractions of the Services, and thus of stimulating recruitment

INFECTION IN HOSPITAL

CLEAN air, clean food, clean instruments this is Dr Maurice Mitman's recipe for averting infection in hospital In his presidential address to the section of epidemiology and preventive medicine of the Royal Society of Medicine on March 16, he showed that this is no cheap recipe, but he also questioned whether hospitals are making the fullest use of the ingredients at their command Nowadays of the infectious diseases only smallpox calls for rigid isolation in a separate hospital, other infections can be treated side by side in the modern isolation hospital with proper nursing techniques General hospitals do not apply the principles of isolation rigorously enough Cases of non tuberculosis respiratory infection should be classified and, like the tuberculous, segregated Likewise patients with early poliomyelitis should be isolated These and other infectious diseases Dr Mitman pictured as being handled increasingly in infectious disease units attached to general hospitals Concerned at the difficulty in keeping the air clean in general hospitals, Dr Mitman is attracted to the idea of wards as domitory units (an idea made more practicable by early ambulation) This involves an increase in ancillary rooms which, by adaptation, should be extended at the expense of beds Among such rooms should be an examination room and a treatment suite, on the lines of an operating theatre suite, including clean and dirty utility rooms Soiled dressings could, if dry, be incinerated in the ward, if wet, enclosed in destructible waterproof containers To prevent losses, soiled linen is still sorted in wards—a practice conducive to infection Infant feeds should be prepared under aseptic conditions in a formula room In hygienic standards, notably in the kitchen hospitals should give a lead to industry hitherto such a lead has been lacking Dr Mitman emphasised that both staff and patients are especially liable to infection in the ward and the kitchen, for the staff the laundry is a special hazard

WOUND HEALING

IT now seems that epithelium is the prime mover in the the healing of an incised wound In demonstrating that epidermal cells pour downwards into the wound long before connective tissue regeneration has started, Gillman et al[1] have upset the view that connective tissue repair precedes epithelial regeneration Their work has been extended to excised wounds in areas from which split skin grafts have been taken Here again the raw surface is covered at the out experiments justify, in his view a far larger investigation in an area with a population of at least a million and lasting five to ten years so that patients may be adequately followed up

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[7] Smith J The Etiology of Epidemic Infantile Gastro-enteritis Royal College of Physicians of Edinburgh Publications 195, no 5, see Lancet 1955 ii 1182

[1] Forces Medical and Dental Services Committee First Report H M Stationery Office [illegible]

NON-EXPLOSIVE ANÆSTHETICS

It seems that the risk of an explosion during an operation is of the order of 1 in 485,870 [1] This very occasional hazard can be eliminated only by the routine use of non explosive anæsthetic agents There are many such drugs, but usually several must be administered in combination

In 1951 Cullen and Gross [2] reported that the non explosive gas, xenon, was an efficient anæsthetic agent in man, being a little more potent than nitrous oxide Cullen et al [3] have shown that it produces only very slight biochemical and physiological disturbances during clinical anæsthesia maintained for as long as 2 hours 21 minutes Now Bracken et al [4] have confirmed experimentally the safety of brief administration of xenon and have designed an apparatus for investigating the long term effects of this and other rare gases No toxic effects were found macroscopically or microscopically in a rabbit which breathed xenon for 48 hours

Xenon is extremely expensive and is not potent enough to be of practical value as an anæthetic, but pilot investigations of this sort are important since there is a definite need for an all purpose, non explosive inhalational anæsthetic

HEROIN

The case against banning heroin was presented fully to the Society for the Study of Addiction on Feb 21 Mr Lawrence Abel said that in treating cancer one needs as many drugs as possible so as to ring the changes 10–15% of people cannot tolerate morphine, and when a patient needs heroin he does need it Morphine can cause spasm of the bile ducts so that pressure is built up, and he thought the high incidence of trouble after cholecystectomy in the United States may be due to using morphine instead of heroin Dr A H Douthwaite said that, unlike *morphine*, heroin does *not* cloud the mind and allows people to attend to their affairs to find a drug which relieves pain, produces euphoria, and does not impair the intellect, yet does not produce addiction, would be impossible Because morphine so often induces vomiting, he has forbidden its use in his wards in cases of gastric hæmorrhage Dr Reginald Hale White pointed out that in incurable disease euphoria may be as valuable as freedom from physical pain when heroin is given the whole household cheers up Dr J A Hobson believed that if heroin ceases to be obtainable from medical sources the price will rise to a level at which professional drug pedlars will be attracted, they will smuggle in more of the drug and it will be worth their while to produce more addicts Prof A D Macdonald concluded that as analgesics, none of the substitutes are quite in the same class as heroin, and there is no really well established case for suppressing it

Two of the advertised speakers being absent, Prof P O Wolff, formerly of the World Health Organisation, was left almost unaided to state the case in favour of the ban[5] In answer to questions he explained that by its constitution W H O, as an essentially medical body, has no responsibility for controlling the illicit drug traffic, and is concerned simply with drug addiction arising from medical practice Even the United Nations cannot impose a ban they can do no more than ask governments to coöperate Dr Wolff believes that doctors must be free to prescribe what they think necessary, and he said that governments which have banned heroin (including that of the U S A) do in fact keep small supplies which are obtainable by doctors who think the drug indispensable for a particular patient He believes too that a government should not impose a ban without the agreement of the medical profession But he pointed to the example of Switzerland, which in 1931 declared heroin indispensable, yet twenty years later abolished its use – not because Switzerland had an addiction problem of her own but because Swiss doctors no longer found heroin a necessity and the government wished to coöperate with other countries in suppressing the drug, in order to "fulfil a humanitarian task which is in keeping with its traditions" Apart from the United Kingdom, only four countries out of some eighty members of W H O have not declared their willingness to dispense with heroin, and Professor Wolff hoped that on further consideration the profession in this country too will find heroin "ripe for replacement" Among the substitutes for it he drew attention particularly to the usefulness of dextromethorphan for cough and of levorphan for pain, which he thought worth further trial here

Mr Abel seemed to resent any suggestion that British doctors may be less than fully informed on anything that might benefit their patients, but Sir Weldon Dalrymple Champneys felt that they have at any rate shown regrettably little interest in the treatment of intractable pain with cobra venom, which in some cases gives remarkable relief Dr Jeffrey Bishop regarded the proposed international ban on heroin as an attempt to bolster up the policy of the head of the (non medical) American Narcotics Bureau—a policy which he said was increasingly discredited at home To which Professor Wolff replied (1) that each delegation at the Commision of Narcotic Drugs of the Economic and Social Council of the United Nations acts on the instructions of its own government; and (2) that the American Medical Association, a body which certainly does not take orders from the Narcotics Bureau has not opposed the Congressional prohibition of heroin in medical practice

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[1] Report of the Ministry of Health 1954 Part II p 168 H M Stationery Office 1955

[2] Cullen S C Gross E G *Science* 1951, 113, 580

[3] Pittinger, C B, Moyers J Cullen S C Featherstone R M, Gross, E G *Anesthesiology*, 1953 14 10

[4] Bracken, A Burns, T H S, Newland D S *Anæsthesia* 1956 11, 40

[5] We hope later to publish extracts from his paper

Letters to the Editor

Poliomyelitis Vaccination —Dr Goffe, in his letter last week, estimates the chance of young children contracting paralytic poliomyelitis as 1 in 3000 per year, and hopes that the British Salk type vaccine will reduce this to 1 in 12,000 per year In order to prevent 3 paralytic cases 12,000 children must each be given two or more injections of inactivated virus This might be worth while if the protection lasted, but unfortunately it may only persist for a year or two What will be the situation after five years as regards the millions of American children who have been given the inactivated virus? Will the partial protection be maintained, lost, or even reversed? It seems to many that the long term prospects for those now being given the Salk type vaccine are so uncertain that the present American programme may be correctly described as a gigantic gamble —W RITCHIE RUSSELL, F R C P (Oxford)

Barbiturate Poisoning —Your leading article (Feb 18) encourages me to draw attention to Gould's work in the treatment of this condition His *article quoted in your leader* was the first of a series in which the clinical scope and physiological rationale of the treatment of acute barbiturate intoxication and allied conditions were discussed (J Gould *Lancet*, 1953, i, 570, *Brit J Addict*, 1954, No 1, *Proc. R Soc Med* 1954, 47, 215 R W Armstrong, J Gould, *J ment Sci* 1955, 101, 70 J Gould B S Cooper, *Med Pr* 1955, 234, 138) Gould maintains that intracellular brain katabolism is impeded in these states, and the later work of R A Hunter et al on vitamin B_1 (*Lancet*, 1955, ii, 1353) supports his clinical deductions Novelli and Soodak suggest that, for the reconstitution of dissociated enzyme and co enzyme systems, up to 1000 times the normal tissue concentrations of co enzyme —usually a B vitamin—may be required (Biochemistry and Physiology of Nutrition, vol 2, p 328) This is in close conformity with Gould's clinical observations and practice

Physicians unfamiliar with these ideas are necessarily puzzled by the enormous doses of vitamins recommended by Gould *and his co workers in my department*, but the high dosages are clinically demanded and would appear to be scientifically justified by the work of Novelli et al In other words, in the treatment of barbiturate intoxication by high potency vitamins we are no longer thinking of these in terms of normal nutritional needs, but are using them as powerful biochemical agents

Another feature of the technique which has bothered critics is the continued administration of large amounts of balanced vitamins after the initial injection The reason for this becomes clear when it is remembered that the gut and tissue fluids remain for a very long time reservoirs of absorbable barbiturate which can only be exhausted by gradual absorption into the blood stream

"Conservative' methods of treatment were advocated by S Locket and J Angus (*Lancet*, 1952, i, 380), but it is surely desirable on physiological grounds to reduce the time during which brain cells are subjected to biochemical insult gitic. In striking contrast to Ingraham's experience,[11] Desmit found no subdural effusions.

When powerful antibiotics were first introduced, the problem of purulent meningitis seemed to be solved, but plainly there is as yet no agreement about the course, treatment, and outcome of these infections. Ounsted[12] has pointed out that the number of children with brains mutilated by meningitis is increasing rapidly. Such children are prone to gross forms of epilepsy and disordered behaviour, and quite apart from the personal tragedies involved, the community must bear this costly burden for many years. There is a clear indication for a carefully planned and well controlled study of the treatment and outcome of purulent meningitis.

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11 McKay, R J, Ingraham, F D, Matson D D *J Amer med Ass* 1953 152, 357

12 Ounsted, C *Lancet*, 1955, ii 303

Occasional Survey

GASTRO-INTESTINAL COMPLICATIONS OF ORAL ANTIBIOTICS *

MINOR intestinal symptoms are not uncommon when antibiotics are given by mouth. Any part of the alimentary tract may be affected—sore tongue and mouth, nausea, occasional vomiting, abdominal distension, diarrhœa, and the so called *anorectal syndrome*, which, incidentally, may persist for weeks after the antibiotic is stopped.[1 2]

PREDISPOSING FACTORS

The frequency of these complications, which may be as high as 30% or more,[3-8] depends on a number of factors. The most important of these is the breadth of the drug's antibacterial spectrum. The tetracyclines are therefore the worst offenders. Oral penicillin gives less trouble because it leaves coliform bacilli unaffected. Injected penicillin and streptomycin, singly or in combination, very rarely produce alimentary symptoms since very *little of either penetrates the intestinal lumen*.

The antibacterial spectrum, however, cannot be the only factor involved, since the spectrum of all the tetracycline drugs is virtually the same, yet it is generally agreed *that tetracycline itself is less likely to give rise* to complications than either chlortetracycline or oxytetracycline[7]; it is probable that chloramphenicol and neomycin, which have similar antibacterial spectra, are still less likely to cause digestive disturbances.[8] It seems that the difference is due to chemical irritation of the gut. Certainly the tetracyclines are very irritant on injection, not infrequently causing thrombosis when injected intravenously and considerable pain when injected intramuscularly, even when given with procaine. Chemical purity may have been a factor in the past. It has been *claimed that thrice crystallised chlortetra*cycline is better tolerated than the original impure preparations.[9]

Finally, the incidence of enteral complications is closely related to the dose of the drug and its duration. Finland and others[5] showed that symptoms occurred twice as often with a dose of 250 mg of chlortetracycline given four hourly as with the same dose six hourly.

PREVENTION

It follows that alimentary side effects may be minimised by:

(1) Interfering with the gut flora as little as possible. This implies using sulphonamides or penicillin by injection when suitable. It is highly important that when sterilisation of the bowel is required, only drugs effective against any locally endemic staphylococci should be used. It is asking for trouble to remove all the normally resident non-pathogenic bacteria from the intestine in an environment where resistant staphylococci are prevalent.

(2) Nausea and diarrhœa can be reduced by giving milk with *each dose of oral antibiotic*. Alkalis such as aluminium hydroxide and magnesium trisilicate, though effective, should not be used for this purpose since they interfere with absorption.[9] Several authors have reported that yogurt given in doses of one cupful *three or four times a day is effective, both in prophylaxis* and treatment of antibiotic-induced diarrhœa.[10 11] Perhaps yoghurt should be made from an antibiotic-resistant strain of lactobacillus. Various vitamin-B preparations have been recommended for these purposes, *but it is doubtful whether they are of much value*.[11-13] Cathartics should be avoided.[5]

(3) The *dose and duration of treatment* must be kept down to the minimum that is effective.

SUPERINFECTION

The vast majority of alimentary complications are due to minor disturbances in bacterial ecology and to the irritant effect of the antibiotic on the intestinal wall. They subside rapidly when the drug is withdrawn. However, in the past few years there has been a disturbing number of reports of superinfection by resistant organisms such as monilia[14-17] and staphylococci,[13 18-19] *which may become widely disseminated throughout the* body. Usually one or more broad spectrum antibiotics have been given, but *staphylococcal superinfection has occasionally followed the use of intramuscular penicillin and streptomycin in combination*[20-22] and in one unpublished non fatal case it followed a week's course of intramuscular penicillin alone. In two of three cases mentioned by Barber and Burston[23] no antibiotic at all had been given.

Clinically the syndrome is very like that of pseudomembranous enteritis reported occasionally in pre-antibiotic days, usually associated with postoperative shock.[18 24] In the unpublished case mentioned above the enteritis did in fact follow a thigh *amputation*, and it is difficult to be sure of the part the administration *of penicillin played in its development*. Though both are excreted to a small extent in the bile,[25 26] it is inconceivable that injected penicillin and streptomycin alone or together, could sterilise the gut. A more likely explanation is that these antibiotics, especially in combination, may virtually sterilise the nose, throat and respiratory tract, so promoting their colonisation by resistant staphylococci which gain a *foothold* in the alimentary tract through the patient swallowing his own secretions.

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* Based on a contribution to a symposium on Staphylococcal Infections in Hospital held at the Whittington Hospital on Nov 30, 1955. I am indebted to Dr J M Alston and Dr A L Jacobs for information and advice.

1 Manheim, S D *N Y St J Med* 1951, 51 2740

2 Wilcox R R *Lancet* 1951 ii 154

3 Medical Research Council *Brit med J* 1951 ii 1361

4 Harris, H J *J Amer med Ass* 1950, 142 161

5 Finland, M et al *Arch intern Med* 1954, 93 23

6 Frei, E *New Engl J Med* 1955, 252 173

7 Welch H *Antibiot & Chemother* 1954 4 375

8 Spink, W W *J Amer med Ass* 1953 152 585

9 Welch H Principles and Practice of Antibiotic Therapy New York 1954

10 Polymenakos L G *Lancet* 1951 i, 732

11 Romansky M J, Kesler G A *J Amer med Ass* 1950 150 1147

12 Anderson, T *In* Dunlop, Davidson, and McNee's Textbook of Medical Treatment Edinburgh 1953 p 88

13 Hay P, McKenzie P *Lancet* 1954 i 915

14 Taylor, R Rundle, J A *Ibid* 1952, i, 1236

15 Wolff I W *Ibid*

16 Brown, C, Propp S, Guest C M, Beebe, R T, Early L *J Amer med Ass* 1953 152 206

17 Browne, S G *Lancet*, 1954 i, 393

18 Dearing W H, Heilman, F R *Proc Mayo Clin* 1953, 28 121

19 Gardner D L *Lancet* 1953 ii 1236

20 Todd A S Hopps, P O D *Ibid* 1955, ii 749

21 Fowler B J *Brit med J* 1955 i 1313

22 Fairlie C W, Kendall R E *J Amer med Ass* 1953 153, 90

23 Barber, M Burston, J *Lancet*, 1955 ii, 518

24 Penner, A Bernheim, A I *Arch Path* 1939 27 966

25 Florey, H W, et al Antibiotics London 1949 p 1300

26 Waksman, S A Streptomycin Baltimore, 1949 p 219

(3) Your reference to a paper by us (W J Dempster A M Joekes, *Quart J exp Physiol* 1953, 38, 11) as showing that transplanted kidneys with the ureters implanted into organs other than the bladder" deteriorate rapidly in function is inept This paper dealt exclusively with some problems of diuresis and antidiuresis in autotransplanted kidneys with skin ureterostomy

Work in this country has had as one of its major aims to confirm technical feasibility of transplanting kidneys, known since the turn of the century, and to establish the best site for long term survival and maintenance of function (W J Dempster A M Joekes, *Acta med scand* 1953, 147, 99 W J Dempster A M Joekes, N Oeconomos, *Ann R Coll Surg Engl* 1955, 16, 324) Reimplantation of the ureter into the bladder resulted in better function of transplanted kidneys, which showed indefinite survival times with normal function

It is surprising that you follow the paper from Boston (J P Merrill et al *J Amer med Ass* 1956, 160, 277) describing the successful homotransplantation of a kidney between identical twins, in failing to cite the only published work, done in this country, giving clear indications for the elective site for a kidney transplant —A M JOEKES, M R C P (London. W 1)

Obituary

Miss DIANA BECK

Miss Beck, neurosurgeon to Middlesex Hospital where she died on March 3 was one of the first women to be appointed to the consultant staff of a London teaching hospital which was not her own Born in 1902 in Chester of a family of Scottish descent, she qualified from the Royal Free Hospital London in 1925 Having taken the F R C S in 1930 she returned to the Royal Free as surgical registrar and lecturer in surgical anatomy, and she had already proved herself as a surgeon and teacher before she specialised in neurosurgery Shortly before the late war she began her apprenticeship in this exacting specialty with Hugh Cairns at Oxford In 1943 she was appointed neurosurgeon to the Royal Free Hospital She worked at Chase Farm and in Bristol where she had charge of an E.M.S neurosurgical unit She joined the staff of Middlesex Hospital in 1947

Prof L P GAMGEE

THE Gamgee family belong to the history of Birmingham surgery, and Professor Gamgee, who died on March 1 at the age of 87 belonged to the second generation His father Sampson Gamgee who joined the staff of the Queen s Hospital almost a century ago, will be remembered for his advocacy of dry infrequent dressing of wounds and also his promotion of the Hospital Saturday Fund Leonard Gamgee qualified in 1891 from Queen's College Birmingham and his first appointments were as assistant to the professor of surgery and as a resident at the Queen's Hospital He joined the staff of the Birmingham General Hospital in 1893 and later was appointed to the chair of surgery in the university His teaching was practical and effective He had the knack of setting out surgical principles clearly and entertainingly and the courage to set them out dogmatically, for he was unwilling to confuse his students with differing opinions and authorities As a colleague put it, his students were told what to do and when to do it and as often as not made to do it there and then" Gamgee belonged to the age of clinical rather than laboratory surgery and he was content to write little and practise much, treating patients rather than diseases

In England Now

O what can ail *The Lancet's* form
Alone and palely loitering?
The ink is wither'd from the page
And no printers print

News

Influenza like illnesses have been increasingly common in the past few weeks in many parts of the country In the north Cumberland Lancashire and Cheshire have been particularly affected Elsewhere the outer London area especially Kent and Sussex has been among the many areas involved Virus A has again been demonstrated in many outbreaks

On Feb 25 at a congregation of the University of Oxford the degree of D M was conferred on A W Frankland Margaret E H Turner Warwick and H A K Rowland and the degree of B M on Joyce Dutton

At recent examinations for the degree of M CHIR in the University of Cambridge the following were successful D A Bailey J M Davies C.O Henriques P F Jones D W T Roberts T M Robinson W F W Southwood

The University of Dublin is to confer the honorary degree of M D on Dr E R Boland and the honorary degree of M CH on Prof A K Henry

At recent examinations of the Royal Colleges of Physicians and Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow for the diploma of L R C P E L R C S E L R F P S G the following were successful S J Benjamin D A Blair K M Cohen W D Dodds Noorali Devji Dhanji William Irvine, Wah Lean Low Alan McEwan A H Macgregor Cheng Hooi Oie J I Robb, Chun Yuen Su

The late Dr Ethel Townend of Hull has left about £50 000 on trust for necessitous members of the medical and other professions

Mr John Anderson deputy secretary of the Scottish Home Department, has been appointed secretary of the Department of Health for Scotland

The fellowship of University College London has been conferred on Prof D V Davies, St Thomas s Hospital

The council of St Mary s Hospital Medical School gave a dinner on Feb 29 in honour of Mr Edgar E Lawley chairman of the medical school centenary fund council Mr Lawley said the fund now amounted to £185 000 and there were good hopes that it would eventually reach £200 000

The annual general meeting of the Hæmophilia Society will be held on March 18 at 3.30 P M at St Pancras Town Hall London N W 1 The president, Sir Lionel Whitby will give an address

Dr E J C Hewitt has been appointed a medical commissioner of the General Board of Control for Scotland.

International scholarships in anesthesiology for women doctors have been established at the New England Hospital Boston Massachusetts Candidates from English-speaking countries are eligible for a scholarship which includes a stipend of $1800 a year full maintenance and travelling expenses

Appointments

DOHERTY, J K L.R C P I D P H asst M O H. and school M O Oldham

EARLE, J H O, M D Lond clinical pathologist Royal Masonic Hospital London

FISCHER, EMANUEL, PH D Prague L.R C.P I D P.M consultant psychiatrist and deputy medical superintendent Little Plumstead mental deficiency group of hospitals

HOPE, MARGARET M.B Edm D C H asst M O Dumfriesshire

KELLOCK, W, F R C.S senior orthopædic registrar United Norwich Hospitals

LADELL, W S S M B Camb research physiologist Ministry of Supply

MCELROY R S, M B Dubl D P H D T.M M O H and area M O Meriden and Tamworth R D s.

Vacancies

ACADEMIC AND EDUCATIONAL

Sheffield University Lecturer in Med

Sheffield University Lecturer & Demonstrators in Anatomy

Oxford University Asst. Graduate in Path

University of London Lecture Some New Aspects of Action of Morphine-like Analgesics 14th March

Royal College of Surgeons of England Annual Examinerships

Royal College of Surgeons of England Election of Professors and Lecturers

Royal College of Surgeons of England Sir William Lister Award in Ophthalmology (Travelling Scholarship)

Middlesex Hosp Med School Prize in Applied Pharmacology

British Psycho-Analytical Society Freud Centenary Lectures

Glasgow University Lectureship in Medicine

Johannesburg S Africa University Witwatersrand (Pathology Dept) 2 Full time Chairs

Nuffield Foundation, N W 1 Travelling F'ships in Med

Sheffield University Course of Instruction (D.P H) 1st Oct

Chester Beatty Research Inst. Royal Cancer Hosp S W 3 Sr Tech

Liverpool University (Biochem Dept.) Asst Lecturers or Lecturers

Leeds University I C I Research F'ships

They can be minimised by attention to certain well-established principles

Occasionally superinfection with resistant organisms develops In recent years the staphylococcus has overshadowed the others in importance It may produce diarrhœa which, if urgent measures are not taken, may become choleriform and rapidly fatal

Emphasis is laid on the danger of disturbing the normal intestinal flora in an environment where resistant staphylococci are prevalent

T B BINNS
M R C P, M R C P E, D C H

Preliminary Communication

RITALIN AS AN ANTAGONIST TO RESERPINE IN MONKEYS

RESERPINE ('Serpasil'), an alkaloid originally made from *Rauwolfia serpentina*, has been given with benefit to many patients both in this country and in America, but there have been many reports of undesirable side-effects, including diarrhœa, nightmares, agitated depression, giddiness, anxiety, parkinsonian like tremor, asthma, and facilitation of convulsions Furthermore, it has been estimated that serious mental effects arise in about 5% of patients treated with reserpine—a finding that may cause some hesitation to prescribe the drug

We have found experimentally that the effects of large doses of reserpine are dramatically reversed by subcutaneous injection of 'Ritalin' (the hydrochloride of phenyl [α-piperidyl] acetic acid methyl ester), a new synthetic compound with a specific central stimulating component The interaction of ritalin and reserpine was observed *during studies on the effect of reserpine in monkeys*

We have so far used in our experiments nine monkeys—four *Macaca nemestrina* and five *Macaca mulatta*—adolescent or pre-adolescent animals, weighing 2 5–3 5 kg In each experiment 5 mg (2 ml) of reserpine was injected intramuscularly About three hours later, when the drug had produced a catatonic-like state, 20 mg (1 ml) of ritalin was injected subcutaneously

The result of injecting 5 mg of reserpine varied singularly little between different animals, except that in some the onset of symptoms occurred after about one hour and in others after nearly two hours When the reserpine was fully effective, the animals sat in a fœtal-like position with a parkinsonian like tremor and flushed hands, feet, and face Food was ignored or, if placed in the mouth, held between the teeth but not chewed Patellar and plantar reflexes remained present, and a very strong grasp reflex was established in all four extremities It was possible to place the monkey's body and limbs in bizarre positions, which were held Spontaneous activity was abolished, but response to strong stimuli such as a needle prick remained When an animal in this catatonic-like state was given 20 mg (1 ml) of ritalin, a striking change ensued in three *and a half to six minutes* First, eye movements occurred as if the animal were looking around, then the ears and the limbs moved, and finally the animal suddenly "woke up," sat in a normal position, and ate voraciously any *food* within reach Within fifteen seconds of "waking up" an animal can leap across a gap of three feet between a table and its cage, and catch the cage bars in a completely normal way, *thus demonstrating perfect* oculomotor coordination and control of movement After about six hours, some of the reserpine signs, such as the clenched feet and the fœtal position, reappear, and the monkey's motor activity is depressed, but with only one exception the animals roused themselves when they were offered food This partial return of "reserpine syndrome" is completely abolished by a further subcutaneous injection of 10 mg (0 5 ml) of ritalin—i e, half the previous dose

So dramatic is the *effect of ritalin* that there is little doubt that in these animals it acts as an antagonist to reserpine

Our observation that the completely abolished "reserpine *syndrome*" *tends to build up again*, though to a lesser degree, about six hours after the administration of ritalin suggests that this drug does not "neutralise" nor "wash out" the reserpine

Bein et al[2] *suggest that the action* of reserpine resembles the effects of diencephalic stimulation, and they conclude from their observation of the cat's retracted nictitating membrane that reserpine inhibits the sympathetic *outflow and does not stimulate the* parasympathetic component of the hypothalamus A syndrome similar to that observed by us after a large dose of reserpine has been reported in monkeys by Collins[3] *following* lesions in the posterior hypothalamus reaching into the rostral portion of the midbrain Hess[4] also observed in cats with mid-hypothalamic lesions a type of behaviour, "adynamia," which closely resembles what we have observed in monkeys

We therefore assume that reserpine acts at hypothalamic level, favouring the parasympathetic centres either by stimulating them or by depressing the sympathetic centres *The antagonistic effect of ritalin* could then be the result either of removal of this depressant effect or of increase in the sympathetic output of the hypothalamus, thus in either case re establishing a balanced hypothalamic function

The effects fo amphetamine and bemegride administered after reserpine are also being investigated The effects of amphetamine closely resemble those of ritalin, with the addition of increased motor activity The effects of bemegride are very different

We thank Prof E G T Liddell for his support, Dr C D Falconer for his interest in this work, and Ciba Ltd for supplying 'Serpasil' and 'Ritalin'

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Letters to the Editor

Visiting in Mental Hospitals—Today there is some talk of improved facilities for those who visit patients in general hospitals, but though in their evidence to the Royal Commission the representatives of the Royal Medico Psychological Association claimed that progress had also been made in mental hospitals, the lack of imagination shown by some medical superintendents is regrettable

Whether a patient in a general hospital receives visits from friends and relatives is, *comparatively, immaterial*, for he is conscious of his condition and aware of his surroundings But for the mental patient—because of the disturbance of judgment wrought by his illness, and his consequent inability to appreciate his predicament—unrestricted visits from friends and relatives are essential He finds himself suddenly, and perhaps violently, uprooted from everyday life, and cast into the confusion and indignity of a mental hospital ward—there to wage unequal combat with the unspoken suggestion that he *has done something* that he *ought* not to have done, and to regard himself as the object of an accusation, against which he is required to defend himself Realising that something has occurred to set him apart from other men, he instinctively gropes for that sympathy and understanding which must come first from his friends and relatives, *and secondly* from psychiatry Unhappily, however, and all too often, his grasp closes on thin air, for, though half our mental hospitals wisely permit visitors at any reasonable hour on any and every day, the rest limit visits to certain days and specified times

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1 *Lancet* 1955, ii, 1326

2 Bein H J Gross F Tripod J Meier R *Schweiz med Wschr* 1953, 83, 1007

3 Collins E H *J comp Neurol* 1954 100 661

4 Hess W R Das Zwischenhirn Basle, 1954

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Cortisone versus Aspirin

IN early rheumatoid arthritis cortisone relieves symptoms no more effectively than aspirin This conclusion, recalled some weeks ago by Dr BAYLISS,[1] was the utcome of a carefully controlled trial conducted by the Medical Research Council and the Nuffield Foundation[2] The investigation was confined to early cases, and to many it seemed possible that this group, in which a high proportion of spontaneous remissions was to be expected was not best calculated to reveal any difference between the two methods of treatment Accordingly the Empire Rheumatism Council designed a comparison of the same two drugs in patients with disease of varying duration—selected only in so far that anatomical changes were not too advanced to preclude measurable improvement in function A novel feature of this trial, the first results of which have now been reported,[3] was an attempt to assess the progress of changes in the radiographic appearances of the joints Nine centres contributed patients, who were allocated centrally and at random to the two treatment groups In the cortisone group treatment started with a total daily dose of 75 mg, and the dose was later adjusted to the smallest which would keep the patient largely free from symptoms To avoid the dangers of high dosage it was decided that treatment with cortisone should be abandoned if symptoms could be controlled only by a daily dose as great as 100 mg The absence of serious complications is probably due to this precaution, and to the exclusion from the trial of patients with gastric disease mental instability, or hypertension At the end of a year (the trial is to continue for three years in all) there was no significant difference between the two groups in functional capacity, number of joints affected, hæmoglobin value, erythrocyte sedimentation rate, or progress of lesions demonstrated radiographically In the cortisone group the mean sedimentation-rate was normal at the end of the first and second months (thus differing very distinctly from the aspirin cases), but the rate then rose rapidly, and from the fifth month there was no difference between the two groups, in each of which the mean rate slowly fell till the end of the year Hæmoglobin values were higher on the average in the cortisone group at the end of six months, but after a year this difference too had disappeared Serial radiographs, which were inspected particularly for the development or enlargement of juxta articular erosions in the wrists and hands, gave a hint of greater deterioration in the aspirin group, but statistically the difference was not quite significant

Thus in rheumatoid arthritis of varying duration, as in early cases (as well as in rheumatic fever[4]), salicylate or aspirin emerges from the rigours of controlled comparison in no way inferior to cortisone The crucial question whether either drug fundamentally alters the progress of the disease remains unanswered Ethically it would be unjustifiable to withhold all treatment from a control group of patients, but some information might be gleaned from a comparison of treatment with large amounts of aspirin and with minimal analgesic doses Meanwhile, the evidence from this and earlier trials raises the question whether cortisone, with its acknowledged dangers, is ever indicated in rheumatoid arthritis As regards prolonged administration in largely unselected cases, the Empire Rheumatism Council investigation (at any rate at the stage of this first annual stocktaking) gives an answer as unequivocally negative as did the previous investigation of early cases Are there any situations, or is there any special group of cases, in which the potent effects of a short course of cortisone can be beneficial? BAYLISS[1] believes that such courses may sometimes help in reablement—an effect which is not easily proved—and in some acute febrile cases If it could be shown that cortisone diminishes the damage to joints, which advances rapidly in some of these cases, its use during the active phase, which is often short, would certainly be correct In severe and unrelentingly progressive cases the temptation to try cortisone is great, but there is no good evidence that it improves the outcome The second and third years of the Empire Rheumatism Council's trial may produce different conclusions, but this seems unlikely and clinicians will be more anxious to hear how prednisone and prednisolone have fared under similar conditions of test

Clinical trials of this sort have become a necessary accompaniment to the introduction of new and potent drugs The comparison of corticotrophin, cortisone, and aspirin in the treatment of rheumatic fever, sponsored by the Medical Research Council and the American Heart Association[4] was a notable instance of international collaboration in this field Prompted by this trial, the American Rheumatism Association considered the feasibility of a similar study in rheumatoid arthritis, but as a preliminary it undertook a retrospective analysis of the experience of several clinics with cortisone in rheumatoid arthritis—a study which necessarily did not include a control group of patients[5] The limitations of this type of survey were recognised by its organisers, and have been analysed by MAINLAND[6] The difficulties are exemplified by the wide range of results reported by different clinics the proportion of satisfactory results after a year of treatment with cortisone ranged from nil to 70% Nevertheless some useful facts were collected The major undesirable effects in 314 patients who received more than 50 mg of cortisone daily included pathological fractures in 5 1%, psychosis in 2 5%, peptic ulcer in 8 3%, and infection in 13 4% In patients with psoriasis and arthritis the skin condition did not seem to be influenced by cortisone Recognition of the direct relation of dosage to undesirable effects has led to increasing caution At a meeting of the American Rheumatism Association last year Dr HOWARD F POLLEY,[7] speaking of experience at the Mayo Clinic, set the highest tolerated maintenance dose of cortisone at 25–30 mg daily for postmenopausal women, 35–40 mg for premenopausal women, and 40–50 mg for men It was pointed out at the same meeting that with doses of this order output of endogenous hydrocortisone

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[1] Bayliss R I S *Lancet* 1955 ii, 1075

[2] *Brit med J* 1954 i 1223 *Ibid*, 1955 ii 695

[3] *Ann rheum Dis* 1955 14 353

[4] *Circulation* 1955 ii 343 *Brit med J* 1955 i 555

[5] *Ann rheum Dis* 1955 14 3[illegible]

[6] Mainland D *Ibid* p 337

[7] *Ibid* p 417

CASUALTY

Hackney E 9 H O
New End, N W 3 Jr H M O
Paddington Green Child's, W 2 Pre-reg H O
Birmingham R H B Sr Casualty Officer
Brighton Royal Sussex County H O s
Colchester Essex County Sr H O
Croydon Gen Sr H O
Dudley, Stourbridge & Dist Sr H O
Manchester Ancoats Sr H O
Northampton Gen Sr H O & H O
Swansea Jr H M O
Swindon Hosp Group Sr H O 's

CHEST AND TUBERCULOSIS

Brompton S W 3 H O 's
Central Middlesex N W 10 H O
Aberdeen Deeside Sanatoria Reg & Sr H O
Bristol Ham Green Sr H O
Chester Barrowmore Sr H O
Edgware Chest Clinic & Gen Hosp Reg
Ipswich St Helen s H O
Newcastle R H B Reg
Scotland Northern R H B Jr H M O
Skipton The Hosp Grassington Sr H O or Jr H M O

DERMATOLOGY

St John's Hosp for Diseases of the Skin W C 2 Reg
Guy's S E 1 P t Reg

EAR, NOSE, AND THROAT

Royal National T N & E & Inst of Laryngology & Otology Sr Reg
Birmingham & Midland Ear & Throat H O s or Sr H O 's
Blackpool Victoria Sr H O
Brighton & Lewes H M C Sr H O
Carlisle Cumberland Infy Sr H O
Derby Derbyshire Royal Infy Sr H O
Edinburgh Central Hosps B O M H O
Manchester R H B Reg
Northampton Gen Sr H O
Portsmouth Group H M C Sr H O
Reading Royal Berks H O
Southampton Royal South Hants & Gen Sr H O

GERIATRICS

Birmingham R H B P t Sr H M O
Leeds R H B Cons
Newcastle R H B P t Locum Cons
North East Met R H B Regs

HÆMATOLOGY

Adelaide S Australia Australian Red Cross Society Director of Blood Transfusion Services

INFECTIOUS DISEASES

Middlesbrough West Lane Jr H M O

MEDICINE

Central Middlesex N W 10 H O 's
Royal Free W C 1 Jr H M O
St Stephen's S W 10 Sr H O
Aberdeen Gen Hosps B O M Jr H M O
Chichester Royal West Sussex Reg & Locum
Edinburgh Northern Group of Hosps Jr H M O
Gainsborough John Coupland Jr H M O
Glasgow Victoria Infy Sr H O
Hove Gen Pre reg H O
Huddersfield St Luke s Jr H M O & Sr H O
Leeds R H B Pre reg H O 's
Medway & Gravesend H M C Sr H O
Newcastle R H B Cons
Plymouth South Devon & East Cornwall Sr H O
Portsmouth Group H M C Sr H O & Pre reg H O
Portsmouth Group H M C Reg
Scotland Northern R H B Jr H M O
Torquay Torbay Sr H O

NEUROLOGY

Leeds R H B Pre reg H O

NEUROSURGERY

Romford Oldchurch P t Locum Cons

OBSTETRICS AND GYNÆCOLOGY

Hosp for Women, W 1 Sr H O
Marie Curie, N W 3 H O
St James s S W 12 Sr H O
Westminster S W 1 Temp Sr Reg
Bedford Gen Sr H O
Birmingham R H B Sr Reg
Boston Gen Reg
Chesterfield Scarsdale Reg
Chichester Group H M C Reg
Croydon St Mary s Maternity H O
Doncaster H M C Sr H O or Pre reg H O
Harrogate & Dist Gen Sr H O
Hitchin North Herts Reg
Huddersfield Royal Infy Pre reg H O
Ipswich & East Suffolk Pre reg H O
Leeds R H B Pre reg H O 's
Manchester Northern Sr H O
North East Met R H B Sr Reg
Portsmouth Group H M C Pre Reg H O
Reading Combined Hosps H O
Romford Oldchurch Sr H O

OPHTHALMOLOGY

Brighton Sussex Eye H O
Leeds R H B Sr H M O
Manchester United Hosps Sr H M O
Scotland South Eastern R H B Sr Reg

ORTHOPÆDICS

Whittington N 19 Locum Reg
Ashford Middlesex H O
Brighton Gen H O
Cambridge Addenbrooke s Reg
Carlisle Cumberland Infy Sr H O
Chertsey St Peter s Sr H O or Pre reg H O
Exeter Royal Devon & Exeter Sr H O
Leeds R H B Reg
Northampton Gen H O
Portsmouth Group H M C Pre reg H O
Romford Oldchurch H O
Scotland Eastern R H B Sr Reg
Southampton Royal South Hants Sr H O
Stoke on-Trent North Staffs Royal Infy Sr H O
Welsh R H B Sr H M O
Welsh R H B Reg
Wigan Royal Albert Edward Infy Sr H O

PÆDIATRICS

St James s S W 12 H O
Birmingham United Hosps Sr H O or Reg
East Anglian R H B Reg
Kettering Gen Sr H O
Newcastle R H B Reg
Nottingham City Sr H O
Southampton *Child's* H O
South East Met R H B P t Cons

PATHOLOGY

Royal Marsden *S W 3* Cons
Newcastle R H B Sr Reg
Oxford United Hosps Sr H O
Royal Free Hosp Group Sr H O & H O
S Africa Prov Admin of Cape of Good Hope Med Pract , Grade E

PHYSICAL MEDICINE

Royal Free, W C 1 Sr Reg

PSYCHIATRY

Coulsdon Netherne Reg & Sr H O
Dumfries Crichton Royal Sr H O
East Anglian R H B Cons
East Anglian R H B Reg
Leeds R H B Reg
Leeds R H B Sr H M O
Manchester R H B P t Cons & Sr H M O
North East Met R H B Sr Reg & Reg
North West Met R H B Cons
St Alban s Hill End Sr Reg
Welsh R H B Reg
West Malling Leybourne Grange Colony for Mental Defectives Jr H M O

RADIOLOGY

East Anglian R H B Reg
National Hosps for Nervous Diseases Reg
North Gloucestershire Clin Area Cons
Sheffield R H B Sr H M O
S Africa Prov Admin of Cape of Good Hope Med Pract Grade D
Wolverhampton Royal Reg

RADIOTHERAPY

Leeds United Hosps Cons
South West Met R H B Sr H M O

RHEUMATOLOGY

Taplow Canadian Red Cross M Sr H O

SURGERY

Bolingbroke S W 11 H O
Colindale N W 9 Reg
Putney, S W 15 Reg
St Leonard s N 1 H O
St Stephen's, S W 10 Reg
Wanstead E 11 H O
Belfast Royal Victoria Sr H O
Birmingham Accident H O
Birmingham R H B P t Con
Birmingham Solihull Sr H O
Birmingham United Hosps Locum Reg
Bishop Auckland Gen H O
Blackpool Victoria Sr H O
Brighton Royal Sussex County H O 's
Bristol Southmead Gen Hosp Group M C Sr H O
Burton upon Trent Gen H O
Cardiff Royal Hamadryad Gen & Seamen s Sr H O
Carlisle Cumberland Infy Sr H O & H O 's
Carshalton Queen Mary s Hosp for Child H O
Chelmsford & Essex Pre reg H O s
Cheltenham Gen H O
Chesterfield Royal H O
Chichester Group H M C Locum Sr Reg
Chichester St Richard s Reg
Cuckfield Sussex Pre reg H O
Dublin St Laurence's Reg
Dudley, Stourbridge & Dist Sr H O
Edinburgh Central Hosps B O M H O 's
Exeter Royal Devon & Exeter H O
Hasting Royal East Sussex Pre reg H O 's
Hitchin Lister H O
Huddersfield Royal Infy H O
Leeds R H B Pre reg H O 's
Leeds R H B Reg
Leeds United Hosps Locum H O or Sr H O
Louth County Infy Sr H O
Manchester Booth Hall Child s Locum Reg
Manchester Christie Hosp & Holt Radium Inst Sr H O
Manchester R H B Reg
Newcastle R H B Sr Reg
Newcastle R H B Sr Reg & Locum Reg
Northampton Gen H O
North East Met R H B Reg
Nottingham City H O
Nottingham Gen Pre reg H O
Nottingham Highbury Sr H O
Plymouth S Devon & E Cornwall *Gen* *Pre reg H O*
Portsmouth Group H M C Sr H O & Pre reg H O
Slough Upton Locum H O
Stockton & Thornaby H O

THORACIC SURGERY

Birmingham Yardley Green Sr H O
Leeds R H B Pre reg H O

UROLOGY

St Peter's St Paul's & St Philip s Sr Reg

GENERAL PRACTICE

(Executive *Councils Form* E C 16A)
Leeds Rothwell Urban Dist List 5431

PUBLIC APPOINTMENTS

Buckinghamshire C C Asst County M O
Barbados Gen Hosp M O s
Devon C C County Psych
British Guiana Govt M O 's
H M Oversea Civil Service, Western Samoa Surgeon
Birmingham City Education Committee School M O
Mauritius Govt Jr Path
All India Inst for Med Sciences New Delhi Asst Prof of Orthopædics
Meath C C Ireland Lab Tech

NON-MEDICAL

Birmingham Dudley Road Biochemist

(Further particulars of above vacancies available on request to Advertisement Manager)

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etter to allow pneumoconiotics to continue to work at he coalface if they want to, while keeping them under edical supervision Every effort should of course be ade to get rid of dust from the air in the mines

In a Medical Research Council report[5] just published, ILSON and HUGH-JONES record their investigations at he M R C Pneumoconiosis Research Unit in South ales Among their important results (to which we ope to refer in more detail in a later issue), they find hat "it is a man's age rather than the radiological egree of simple pneumoconiosis which is important in redicting his disability" Miners with no radiological neumoconiosis were, on the average, as breathless or their age as men with simple pneumoconiosis and more breathless than non-miners, especially in the elderly, "this suggests," GILSON and HUGH-JONES add, "that such miners might logically receive benefit for their disability"

Annotations

TREATMENT OF EPILEPSY WITH ACETAZOLAMIDE

IN a recent annotation[6] we discussed the effect of carbonic-anhydrase inhibition on electrically induced convulsions in mice[7] Lombroso and his colleagues from Harvard now describe[8] their experience with acetazolamide given to 126 young epileptics during the past three years Results were good or excellent in half their patients, and improvement was maintained for from three to thirty six months No patients deteriorated when acetazolamide was added to or substituted for previous treatment, and in a quarter of all cases the seizures were completely abolished These results were achieved with doses of about 500 mg or 750 mg daily Side effects were not troublesome and there were no serious toxic effects No striking difference was found in the response of different types of epilepsy, though results were rather better in patients with mixed types of seizures (usually a combination of grand mal and petit mal) than in those with petit mal alone, or with other seizure patterns alone Electroencephalographic analysis of the response indicated that results were best in patients who showed much spike wave activity, especially when hyperpnoea induced slowing of the waves and profuse spike wave discharges In such patients acetazolamide sometimes restored the E E G pattern to normal

In a letter in our issue of Feb 25 Professor Golla and Dr Sessions Hodge reported that they had added acetazolamide to the treatment of 70 patients suffering from petit mal The seizures were completely abolished in 25 of these patients during the first month of therapy, and only 2 of the 70 failed to show some improvement Professor Golla and Dr Sessions Hodge have not so far assessed the action of acetazolamide in major epilepsy

Like other drugs used in the treatment of epilepsy acetazolamide has apparently caused agranulocytosis[9], and thrombocytopenia[10] and renal lesions of sulphonamide type[11] have also been reported There may be other serious disadvantages in the prolonged inhibition of an enzyme so widely distributed as carbonic anhydrase But that does not mean that acetazolamide may not prove to be an important addition to the treatment of epilepsy

THE CHALLENGE OF MENTAL ILLNESS

THE Ford Foundation has given £75,000 to be spent over the next six years by the Mental Health Research Fund, which was founded four years ago by a group who believe that mental health and mental illness have not had the share of research which their immense importance demands[12] The tasks the Fund has set itself are to establish research fellowships, to encourage coöperation between workers in different fields, to support specific investigations, and to assist exchange of information, and the cost of the commitments it is now contemplating will be not less than £23,000 At its annual meeting on March 6 the chairman, Mr Ian Henderson, pointed out that through this Fund the friends and relatives of the mentally ill can give effective expression to their desire to help Sir Russell Brain spoke of the achievements of other voluntary agencies, such as the British Empire Cancer Campaign and the Empire Rheumatism Council, and said that these unofficial sevices are needed today every bit as much as in the past, when they so often led the way No money could be better spent, said Dr William Saigant, than that spent on the relief of intolerable mental suffering

RESTRICTION OF ANTIBIOTICS

ON Jan 28 and March 3 we discussed measures taken by the New Zealand government to conserve erythromycin for use only in infections resistant to all other antibiotics We said that from Feb 1 New Zealand doctors would be able to get erythromycin only through hospitals and only for the treatment of diseases which did not respond to other remedies This restriction applies to erythromycin supplied at the cost of the Social Security Fund, but not to other prescriptions for the drug We are indebted to Mr J R Hanan, New Zealand minister of health, for pointing out to us that the restriction is more limited than we supposed from the reports reaching us This important decision was however, based on the considerations we set out in our leading article of Jan 28, and, in reply to a point we raised, Mr Hanan adds that New Zealand hospitals have in fact been advised to go very carefully in their own use of erythromycin

CERVICAL LUNG HERNIA

HERNIATION of the lung is rare in 1946 Maurer and Blades[1] found 185 cases on record, and they were able to add only a few more The site of the hernia is variable, but most recent reports[2–11] have described cervical hernias, and Fenichel and Epstein[12] now suggest that this variety is commoner than the small number of reports would suggest, for in a short period they saw 19 patients with this condition Sometimes trauma or developmental defects have clearly been responsible, but Fenichel and Epstein consider that in their series the important cause was the strain of frequent coughing Their patients were elderly and they had all had coughs for years except 4 who, however, had emphysema like most of the others In 5 cases, there was a persistent, soft, resonant, supraclavicular swelling which distended on coughing, in the others, the bulging appeared only on coughing Usually the herniation was bilateral

The apex of the lung normally rises 2–5 cm above the level of the first costal cartilage, and expansion upwards and medially is limited by the pleura and the deep cervical fascia (Sibson's fascia) During the expiratory phase of coughing, when the contraction of the thoracic and abdominal muscles tends to thrust the apex of the lung further through the thoracic inlet, the pressure on Sibson's fascia must be considerable, and Fenichel and Epstein believe that in some patients with chronic cough the fascia may become so stretched and lax that the lung can bulge into the neck They think that emphysema may be another cause, because it tends to produce an upward tilting of the first rib with consequent widening of the thoracic inlet Supraclavicular bulging in emphysematous patients is probably well recognised, but it is not usually described as lung herniation In diagnosis, Fenichel and Epstein found that a lateral radiograph of the neck was of value In normal short necked people with heavy chests the cupola of the lung could not usually be seen, but it was visible in long lean individuals and also in patients with lung hernia In normal subjects, however, even when the apex of the lung could be seen in the neck at

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[5] Gilson, J C Hugh Jones, P *Spec Rep Ser med Res Coun Lond* 1955 no 290
[6] See *Lancet* Feb 11 1956 p 273
[7] Millichap J G, Woodbury D M, Goodman, L S *J Pharmacol* 1955, 115 251
[8] Lombroso L T Davidson D T Grossi Bianchi M L *J Amer med Ass* 1956 157, 268
[9] Pearson J R Binder C I Neber J *Ibid* 1955 157, 339
[10] Reisner E H jun, Morgan M C *Ibid* 1956, 160 206
[11] Glushien A S Fisher, E R *Ibid* p 204
[12] The Fund s address is 39 Queen Anne Street London W 1

[1] Maurer, E Blades B *J thorac Surg* 1946 15 77
[2] Pine I, Morganstern P *Amer Rev Tuberc* 1948 57, 580
[3] Meakins J F Wyatt C J, Aronovitch, M *Canad med Ass J* 1948 58 33
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[6] Bass, H E *N Y St J Med* 1950 50 1967
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[8] Fruitas E L, Vonfraenkel, P H *U S Forces med J* 1951, 2 219
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[11] Rigden, B G *Lancet*, 1955, ii, 803
[12] Fenichel, N M, Epstein B S *Arch intern Med* 1955 96, 747

It might be the result of the direct stimulus of the original infecting bacilli, or of dead bacilli, or of the growth of attenuated resistant bacilli present in small numbers in this inoculum, or of the growth, during the four weeks before the second challenge, of a few sensitive bacilli that survived treatment with isoniazid The number of bacilli in the initial challenge, however, was very much larger than would be expected in human infections, and none of these mechanisms would be likely when the infecting dose was smaller Thus, this experiment did not exclude the possibility that prophylactic isoniazid might hamper the development of immunity after an infection on the scale to be expected in man Though isoniazid might actually prevent the development of immunity, it would still succeed prophylactically if it killed all the bacilli, but there is evidence[2] that in mice infected with many bacilli isoniazid does not eliminate them all, though the number of organisms in the animal's tissues is much reduced One might suppose that, in infections with small numbers of bacilli, all the organisms would be killed, but there is no definite experimental evidence on this point Finally, it may be that the free use of isoniazid alone would encourage the emergence of resistant strains This seems unlik since the infecting dose of bacilli responsible for human tuberculosis would be small and would ver dom contain any of the rare resistant mutants that a present in sensitive strains

Much experimental and clinical evidence, includ the recent Medical Research Council trial,[3] has shown th B C G vaccination can provide a useful degree of immun —but not complete immunity Isoniazid, on the ot hand, apparently provided complete protection during period of treatment in the guineapigs Thus isoniaz *during the time it is given*, may be better than B C G, b later there may still be risks from lack of immunity a the occasional persistence of tubercle bacilli in the tis Nevertheless, B C G vaccination and prophylactic i azid might be combined with advantage For examp CANETTI[4] has suggested that isoniazid might be given a the same time as vaccination with an isoniazid re istar variant of B C G, thus combining considerable immedia protection with a lasting immunity Further anim experiments will enable us to judge these importa possibilities more fully

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2 McCune, R M, Tompsett R Muschenheim C, Organick, A, Batten, J, McDermott W Transactions of the 14th Conference on the Chemotherapy of Tuberculosis Veterans Administration, Washington, D C, 1955, p 66

3 *Brit med J* Feb 25, 1956, p 413

4 Canetti, G Symposium on Tuberculosis in Infancy and Chi hood National Jewish Hospital, Denver, Colorado, Novemb, 1955

Annotations

RESPONSIBILITY EVADED

THE growing disposition of patients to seek legal remedies for supposed medical negligence has caused hospitals to re examine their practices, and, where such revision abates the grounds for action, this will usually be to the advantage of both hospital and patient But the enhanced risk of actions should not lead hospitals to evade their own responsibilities Some months ago a patient who was to undergo "cold" appendicectomy received, with notification of the date when a bed would be free, the following notice

> There has been an outbreak of staphylococcal infection at the —— General Hospital
>
> *The outbreak is responding to the measures taken by the Hospital* Management Committee to limit the spread of infection However, it is felt that, where practicable patients should be aware before agreeing to come into Hospital that there is some increased risk of infection, and that the measures instituted must remain in force until conditions return to normal
>
> I have read the statement above and agree to enter the Hospital
>
> Signed

A patient receiving such a notice might take it to his own doctor, but the doctor could hardly advise the patient unless the hospital had informed him fully about the outbreak, and, even if he could give authoritative advice, this would not still the patient's uneasiness at such a chilly gesture from the place to which he looked for help Surely the hospital's duty was to obtain, possibly through the medical staff committee, the opinion of those best qualified to assess the outbreak, including the surgeons, the pathologist, and (we hope) the medical officer of health If, then, it had been decided that admissions for "cold" surgery should be continued, this course should have been followed with no word to the patient To require a patient to make up his own mind on an epidemiological issue is no way to retain confidence in the hospital service, and to call for his signature on an ill comprehended legalistic form is more likely to promote than to allay litigiousness

RABIES VACCINE

ONE of the disadvantages in using *animals for the* propagation of virus for rabies vaccine is the danger of allergic encephalomyelitis due to brain antigens in the vaccine It is of some interest therefore to study laboratory and clinical *tests*[1] *of vaccines made from* virus propagated on embryonated duck eggs The resulting vaccine was potent in animal tests and effectively evoked antibodies in humans Local reactions were mild and no systemic effects or neurological signs were found Hence it seems that vaccine made from virus propagated in embryonated duck eggs could often replace that produced in animal brains Since cross sensitivity may occur persons sensitive to hen egg albumen should not be given duck *embryo vaccine*

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1 Peck F B, Powell H M Culbertson C G *J Lab clin Med* 1955 45 679

TUBERCULOUS MENINGITIS OF SUDDEN ONSET

THE onset of tuberculous meningitis is nearly always in dious, but, now and then, the disease begins abruptly Taylo Smith, and Vollum[1] recorded an acute onset in about 4% of their large series of cases The abrupt onset is associated with three other features a tendency to spontaneous remission of *symptoms early in the disease*, *unusually high* cell counts in the cerebrospinal fluid obtained at diagnostic lumbar puncture, and a good clinical prognosis in the treated case

Diagnosis in such cases is difficult The illnesses in the Oxford series mimed, sometimes remarkably closely, a wide range of conditions subarachnoid hæmorrhage, poliomyelitis, intra cranial hæmorrhage, brain abscess, frontal sinusitis, hysteria, and benign choriolymphocytic meningitis The spontaneous remission of symptoms after an abrupt onset is a particularly disagreeable trick of the disease, for, as Trousseau pointed out in 1867,[2] it tempts the physician to change his first opinion —and that may be disastrous The Oxford workers described a case in which the remission of symptoms led them to change their diagnosis from tuberculous meningitis to *benign* choriolymphocytic meningitis They withheld chemotherapy until the diagnosis became unequivocal, and during these crucial days their patient received, it seems, permanent cerebral damage

The unusual clinical course is associated with an anomalous pleocytosis in the C S F The usual range of the cell count in the classical illness is 25 to 500 cells per c mm When the onset is abrupt, the count is uniformly higher, ranging from 500 to 1600 per c mm Smith and her colleagues have shown that intrathecal injection of a large dose of old tuberculin (P P D) generates in a tuberculin sensitive recipient clinical and C S F changes closely similar to those found in the abrupt onset type of true meningitis They suggest *that these acute* cases arise when a large caseous focus suddenly ruptures and floods the C S F with tuberculin loaded material, thus provoking a brisk intrathecal tuberculin reaction This antibody antigen reaction leads to the C S F *changes and* the clinical signs The reaction then subsides and the illness abates Bacteria have, however, seeded themselves within the subarachnoid system, they multiply, their lesions caseate, and finally *the march of the disease* continues

During the past six years Smith and her colleagues have done a great deal of work on the intrathecal tuberculin reaction Their results consistently point to one main conclusion

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1 Taylor K B, Smith, H V, Vollum R L *J Neurol Psychiat* 1955, 18, 165

2 Trousseau, A Lectures on Clinical Medicine London, 1867

considerable, proportion of myocarditis was found when inoculated rabbits were placed in a bell jar in which part of the oxygen was replaced by nitrogen

It was concluded that anoxæmia predisposes to myocardial infection by certain viruses This view is supported by the distribution of lesions in relation to the distribution of the coronary arteries In man interstitial myocarditis has often been noted in poliomyelitis Teloh [7] confirmed previous observations [8] that the prevalence of myocarditis varied considerably in different poliomyelitis epidemics suggesting that some strains of the virus were more prone to attack the heart than others Of special interest are the cases in which acute interstitial myocarditis was the only or main manifestation of a virus infection as illustrated in a recent report from Johannesburg [9] While they were in a maternity home or shortly after they had left it 10 infants became severely ill and 6 died The features of the illness were tachycardia cyanosis fever, tachypnœa and toxæmia Some of the babies had a relapsing type of fever like that seen in Bornholm disease Necropsy including microscopical examination was carried out in 3 cases Focal interstitial myocarditis was found in all 3, and in 1 case there was also a focus of encephalitis Thorough virus investigations including inoculation of young mice were performed in 4 patients of whom 1 recovered In all 4 infection with Coxsackie virus (group B) was proved

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Special Articles

CLAIM FOR BETTERMENT

On March 7 the Negotiating Committee which is to negotiate the claim for increased betterment for general practitioners and hospital medical staffs gave preliminary consideration to the preparation of the joint claim and authorised the use of the services of counsel in the drafting of the statement of claim It decided that the representation of the public health medical service on the committee should be increased by including two additional members to be nominated by the Public Health Committee of the British Medical Association The present membership is

Prof Ian Aird F R C S Sir Russell Brain P R C P Sir Harold Boldero, F R C P, Dr J D S Cameron Dr T Rowland Hill Mr Charles Read, P R C O G, and Mr T Holmes Sellers F R C S (representing the Joint Consultants Committee) Dr A Beauchamp Dr Guy Dain Dr A B Davies Dr F Gray Dr Talbot Rogers Dr C J Swanson and Dr S Wand (representing the General Medical Services Committee) and Dr J B Tilley (representing the Public Health Committee of the B M A) Sir Russell Brain and Dr Talbot Rogers preside at alternate meetings

Those present included Mr R G D Allen professor of statistics in the University of London and Mr N Leigh Taylor, solicitor to the B.M.A

GAMMA-GLOBULIN

GAMMA GLOBULIN prepared from pooled plasma from healthy adults is distributed through laboratories of the Public Health Laboratory Service for the protection of susceptible contacts of measles rubella and poliomyelitis as follows (see *Mon Bull Minist Hlth Lab Serv* 1956 15, 27)

Measles —(1) For control of hospital and institutional outbreaks (2) For persons with intercurrent illnesses or living in a poor environment for whom measles would be dangerous (3) For attenuation in children under 3 years of age

Rubella —For women exposed to infection in the first four months of pregnancy

Poliomyelitis —(1) For nurses and medical students closely associated with the care of early cases who have not been in known contact with the infection (2) For babies in a hospital or maternity home exposed to infection soon after birth (3) For children in a hospital ward where a case has developed—especially children who have recently undergone tonsillectomy

In addition gamma globulin prepared from the blood of persons recently vaccinated against smallpox is held for the treatment of generalised vaccinia or accidental vaccinial infections endangering the eye, and, in special circumstances for the protection of unvaccinated smallpox contacts

The Widdicombe File

XXXI—TOO LITTLE—AND LATE

DEAR HAWKE,

Mrs Neal has just gone out again This time she stayed in hospital for over two weeks, she had seven pints of blood, and her hæmoglobin rose from 34% to 65%

You may have good cause for satisfaction When somebody has had forty three pints of blood the uneventful transfusion of a further seven is an achievement on which the pathologist can justly look with pride Thanks to you and your colleagues a blood transfusion is probably the simplest and safest life saving operation in the whole of medicine The meticulous care taken in the collecting and in your grouping and matching, is almost enough to eliminate hazards at your end when the occasional mishap does occur, we all know that we must first look for the cause in ourselves Even the blood of Mrs Neal, with its antibodies and its hyperglobulins, is a poor challenge to your resourcefulness Your modest labels reading "Compatible Washed Cells do not deceive me as to the vast amount of work they conceal Mrs Neal has had her sixteenth transfusion without batting an eyelid

Yes you may well be satisfied But as her physician, I am not Seven pints is a lot of blood, but 65% is a long way from 100%, and two weeks is a long time

I have worked out that for her sixteen transfusions Mrs Neal has spent a total of close on five months in hospital Members of the committee might well throw up their hands in horror and weep over the £19 odd that it costs to maintain one bed in our hospital for one week but far more important considerations are at stake Often we have been very short of beds and have had to refuse admissions because Mrs Neal was taking up a bed For a time we tried taking her in when the blood was ready but you never sent enough and she still had to wait another week for the second instalment We tried giving her a few surreptitious bottles from our emergency stock but you found out and made a fuss We persuaded her relations to become donors but it has made no difference

Of course Mrs Neal is no less anxious to get out of hospital than we are to expedite her return home Last summer we tried to top her up for her summer holiday but you could not spare the blood in time We had to keep her in over Christmas for the same reason Your explanation for the delay is always the same Group O Rh negative blood is precious and the demand is heavy The need is more urgent elsewhere Sometimes there is an exchange transfusion for rhesus incompatibility and this must come first

So you see, this problem goes deeper and deeper, until it reaches our fundamental medical and other principles Is the life of this patient whose aplastic marrow renders her dependent on the blood of others any more or any less important than that of a jaundiced newborn babe? Are we to set ourselves up in judgment and say This life is worth preserving but that *one* is not "?

Mrs Neal is a simple soul She does not know what is wrong with her and would not understand if we told her She has no special gifts and her education leaves much to be desired. She has no hobbies and would be hard pressed to say what she does with herself all day At 60 she feels she has earned a rest and therefore lets the younger members of the family attend to the work Not that she appreciates her family any more than she appreciates all the medical attention she is having It would certainly never occur to her that fifty donors have given their blood freely to keep her alive for a year Instead she nurses a deep resentment against all of us because we cannot cure her at less inconvenience to herself Her simple mind cannot understand why she has to have transfusions when her friends and neighbours are revived by a few iron or vitamin pills

Many would say, here is a worthless life if ever Society could suffer no loss by her untimely end Her relations may well feel relieved of their burden A hospital bed would be freed

One can argue that when a man is struggling in the final stages of some fatal disease it is kindness to let him die peacefully There comes a time when penicillin may thoughtlessly deprive some age wracked body of its last friend It is as well if the infant imbecile need never open its eyes upon a cruel world

In all this I confess my guilt, but I cannot place Mrs. Neal in the same category Are you going to abandon someone who openly demands life as her birthright? Are you who hold the elixir of life, prepared to accept this terrible responsibility?

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[7] Teloh H. A. *Arch Path* 1953, 55 403

[8] Saphir, O Wile S A *Amer J med Sci* 1942 203 781 Ludden T E, Edwards, J E *Amer J Path* 1949 25 357 Jungeblut C W, Steenberg, E *Arch Path* 1950 49 574

[9] Javett, S N, Heymann S Mundel B Pepler W J Lurie H I, Gear J Measroch, V Kirsch, Z *J Pediat* 1956, 48, 1

and the instructors, and the subjects of discussion include absenteeism, lateness, difficulties with authority, and relations within the group. Present working problems are related to outside factory problems and this trial period allows the patients to analyse their attitude to work. One of the patients acts as secretary and each group reports back to the community meeting which all patients and staff attend. The work groups have come to take a new pride in their work, and their group consciousness has grown. They now assume responsibility for the absentee, the isolate, or the bad worker, and try to help him to understand the meaning of his antisocial behaviour and to work better. Pay is seldom discussed and is apparently not considered necessary.

AN APPROACH TO REAL LIFE

Work therapy, because it approaches real life, presents different problems for women than for men, since their social rôles outside the hospital are different. At first we encouraged the women to go to the handicraft shop, work in the needleroom, and help with the housework of the unit, and we organised discussion groups on infant care, beauty culture, and so on. Our ideas, however, were based on the middle class habits familiar to most of the staff, and here again we seemed to have paid too little attention to the patients' own views on their needs and their probable future. When we came to discuss this topic with the women patients themselves, we became aware of our ignorance of their place in society. Because of their personality difficulties many of the women patients of a unit such as ours do not expect to achieve the ordinary social goals. Marrying, having children, or even housekeeping may be difficult for the majority. Instead they will probably work in some relatively unskilled capacity, often alongside men, and live in relative isolation in one room. They expressed a wish to work with the men in the workshops, and when this was put into practice, most of them seemed to be much more interested than they had been in their previous occupation. Moreover, their presence was welcomed by the men.

In this way, handicrafts have ceased to exist as a female occupation in the unit. This change clearly shows one difference between occupation therapy (handicrafts) and work therapy. Many occupational therapy departments give much help to the more ill or dependent patients, but, when rehabilitation has reached the stage of preparing them for ordinary work, a group task involving production work of social value is to be preferred to individual tasks carried out in relative isolation in a handicrafts department. It is not enough to get patients to do something: they must be helped to identify themselves with the staff and the ward environment and given some choice in what they want to do. If the staff are willing and able to identify themselves with the patients a shared task and a social experience can be therapeutic.

PERMANENT SHELTER

Many patients, remaining in hospital, continue to work in laundry, farm, and so on for most of their lives. Ideally the same care should be taken over their placement and working conditions as is aimed at in the resettlement of patients in open employment. Work incentives, hours of work, and social conditions, will depend on the particular circumstances of the hospital, but there seems to be no serious objection to the establishment of a sheltered factory in or near a mental hospital, preferably under outside management, to which suitable cases could be referred.

Where the patient, though discharged from hospital, has a severe physical or mental disability, the sheltered workshop will often be the right solution. Britain is fortunate in having probably the best organisation to be found anywhere for the rehabilitation and resettlement of disabled persons in either open or shelter employment, and for this the Ministry of Labour a National Service deserve the main credit. Unfortunately, these services are too little known by doctors generally and it is a pity that the official booklet[1] is not mo widely read.

We should like to thank Dr. Louis Minski, physician superintendent of Belmont Hospital for his support. Also Mr. C. Brooks, Mr. F. Jaquest, Nurse P. Mateer, Mr. J. Sm and Mr. E. Taylor who have the major responsibility f the five work groups described in this paper. Dr. R. Rapop has given us much needed advice from the social point of view.

Before Our Time

DEATH UNDER CHARLES II

WHAT did our ancestors die of? Burial registers so seldom give any details that it is interesting to quote a rare exception.

For ten years from Oct. 14, 1653, to Nov. 28, 1663, the burial register of St. Michael's Church, Cornhill gives us the cause of death for most of the 250 people who died in that parish and were buried there. Starting with Michaell Earnley, a linendraper who died of a "feaver" on Oct. 14, 1653, we have on Nov. 10 John Turner "overlay'd" and Jane Hutcheson and Edward Paine who died on the 12th and 13th respectively of "ricketts" and "convultion." Analysing the detail for the ten years we find "consumption," usually spelt with two "s's," in the lead with 30 cases over "feaver" (unspecified) with 28. Smallpox accounts for 16 deaths and "aged" for 13. Infant mortality is deplorable. There are 12 deaths each from "teeth" and "convultions," 8 from "ricketts," and 4 from "thrush," with another unfortunate child who had "black thrush," whatever this may be. Yet "measles" causes only 3 deaths in the whole period. Amongst adults 4 died of "stoping of the stomack" and Mary Tomlinson, a widow, in March, 1662, of "timpany," which sounds like a musical instrument but is probably much the same thing. On the other hand, 6 people died of "scowring," whether therapeutic or not is unstated. Mrs. Elizabeth Payer, a doctor's wife, died on March 28, 1654, of "travell," and Elizabeth Golling, a barber's wife, of "griefe." There are 2 cases of murder and also a servant, Robert Butler, who was "casually shott." 4 women died from "childbed," and 2 sportsmen, Robert Brooks a merchant tailor, and Joseph Bannister an upholder (? upholsterer), from "surfetts." Kidney disease and "stone" account for 3 deaths and "dropsey" for 7 more. Only 1 case of "cancer" occurs in the series, but we have 2 from "palsy" and 1 from "gangrene" together with 2 each from "scurvey" and "jaundies."

Amongst other odd entries is that of John Smith, a hotpresser, who died of "tissick," which is rather baffling until we find a child, Jane Boyle, with the same complaint—almost certainly whooping cough. Three people died of "flox," which apart from the obvious misspelling has me puzzled, and the long list concludes with an anonymous maidservant of one John Harris a linendraper, who fell downstairs on Nov. 28, 1663—apparently the only fatal accident in the home or the streets throughout the entire period.

A comparison between this list and a cross section of a parish register in these days should prove extremely interesting, if only to note startling changes in our time.

JAMES S. HALL

Walmer, Kent. O.B.E., M.B. Lond., F.R.C.S.E.

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[1] Ministry of Labour and National Service. Services for the Disabled. H.M. Stationery Office, [illegible]

Remuneration of Doctors —It would be interesting to know the family status of those doctors who advise restraint in the matter of salaries To mention one financial problem alone—the fees at a public school famous for its medical affiliation amount to nearly £300 a year Those of us with three or more children find it impossible to contemplate such an outlay, even for one child

There is a large number of competent specialists in this country who have seen their share of war service and junior appointments, and who are making their contribution, in research and published work, to the widening of our professional frontiers Many of these are forced to take up S H M O appointments because of the paucity of consultant vacancies Their starting salary 12–14 years after qualifying is £1500 a year with an increment of £50

Could our more fortunate colleagues tell us whose children are entitled to these educational facilities if not our own ?—
M D , M.R C P

Obituary

Professor SAMSON WRIGHT

For 30 of his 57 years, Samson Wright's name was identified with his *Applied Physiology*, and up to the day of his death last Sunday he was working on its 10th edition. This famous book, which is said to be as much read in America as here, arose out of the courses for the primary F R C.S examination held at Middlesex Hospital where Wright had become assistant to the late Prof Swale Vincent soon after graduating M.B with the gold medal in 1922, and where (after an interlude at King s College) he has been Astor professor of physiology since 1930 In person and with the pen, he was a fine expositor, and a teacher who increased his pupils' wish to learn One reason for this was that his interest in medicine was by no means confined to his laboratory, and his interest in life by no means confined to medicine Deeply concerned by the distress of the Jews in Europe under Nazi regimes, he made himself a powerful helper and champion of our German and Austrian colleagues who escaped to this country, and latterly he has been one of the most useful British friends of the Hebrew University of Jerusalem, where a laboratory has been named after him If often critical he was direct, friendly, and sincere. Few men of our generation have taught so many so much and so well

Surgeon Captain W I GERRARD

Captain Gerrard, who died at his Aberdeenshire home on March 7, formerly held the chair of medicine at Hong-Kong After graduating at Aberdeen in 1909 he joined the medical inspectorate of schools During the 1914–18 war he served with the R N V R and he afterwards joined the R N Medical Service On retiring from the Navy he was appointed professor of medicine at Hong-Kong and physician to the government civil hospital He was elected F R C.P in 1936, and was appointed O.B.E For his services in the Navy during the late war he was promoted C B.E

News

On March 7 the Confederation of Health Service Employees asked the 10,000 nursing staff in 33 mental hospitals who are unofficially banning overtime work to abandon their action (*Times* March 8) If the negotiations on salary and conditions of work have not progressed satisfactorily the confederation will impose an official ban on May 1

Sir Ernest Finch has been appointed Hunterian orator of the Royal College of Surgeons of England for 1957 Mr R H Franklin and Mr Clifford Jones have been admitted to the court of examiners of the college and Dr Ronald Woolmer reader in anaesthetics at Bristol University, has been appointed director of the department of anaesthetics A diploma of fellowship has been granted to J Sunderman.

The National Institute of Industrial Psychology has awarded the Vernon prize for 1956 to Mr J S Weiner, PH D, honorary assistant director of the Medical Research Council unit at Oxford on climate and working efficiency

Sir Stewart Duke Elder will give the Thomas Young lecture on Thursday April 12 at 6 P M at St George s Hospital, London, S W 1 on the Eyes of Invertebrates

Dr R H M Stewart has been appointed senior administrative medical officer to the Newcastle Regional Hospital Board

Dr A. H Douthwaite will give the Croonian lectures to the Royal College of Physicians of London on Tuesday and Thursday, May 1 and 3 at 5 P M on Pitfalls in Medicine

On March 2 Mr R H Turton the Minister of Health opened a new villa at Fulbourn Hospital Cambridge The villa which is to be used as a social therapy unit will accommodate 40 women patients It contains wards recreation rooms a dining room with tables for four and a fully equipped kitchen

Appointments

BALME H W, M D Camb M R C P asst physician St Bartholomew s Hospital, London
CREERY R D G, M D Belf M R C P D C H consultant paediatrician South Shields H M C
HARTLEY MARY J, M B Leeds F F.A.R.C.S, D.A part time consultant anaesthetist, Sheffield No 1 H.M C group
HAYES BERNARD M B Durh D A. asst anaesthetist Blackpool and Fylde Hospitals
HOYLE THELMA B, M B Manc D A asst. anaesthetist, North Manchester hospitals and Booth Hall Hospital
MAITLAND, A I L M D M B Glasg F R C.S.E consultant surgeon Bridge of Earn Hospital
WHITE JAMES, M B B.SC Glasg D M R E consultant radiologist Stracathro Hospital, Brechin

Colonial Appointments

DREW G R H, M B Edin senior M O (administration), western region Nigeria
FURNESS J E, M B Lond senior M O (clinical) northern region Nigeria
GRIFFITH G V A M D Dubl A.D.M.S Hong-Kong
MOORE G W, M R C.S senior M O (administration), northern region Nigeria
MOORE S H, M B Dubl senior M O, Hong Kong
SNELL D G, M B Lond A M D S Uganda
TAYLOR J H M B Edin senior M O Kenya.
THOMSON I G, M B Aberd senior M O (administration) northern region Nigeria
WILLIAMS, F G M B Birm senior M O (administration), western region ,Nigeria

Vacancies

ACADEMIC AND EDUCATIONAL
Sheffield University Lecturer & Demonstrators in Anatomy
Glasgow University Lectureship in Medicine
Chester Beatty Research Inst Royal Cancer Hosp, S W 3 Sr Tech
Edinburgh University Chair of Surg Science
Inst of Neurology W C 1 Courses Clin Demonstrations Wed & Sat from 4th April–23rd June
Inst of Laryngology & Otology W C 1 Week-end Course Aural Surgery. 20th 21st and 22nd April
University of London P G Med School Symposium for Cons on Clinical Management of Hypertension. 12th & 13th April
University of London Lecture Recent Advances in the Study of Viral Growth in Cultivated Animal Cells." 23rd March 56
Assoc of Surgeons of Great Britian & Ireland Moynihan Prize
Inst of Cancer Research S W.3 Clin Research Path
Faculty of Anaesthetists of Royal College of Surgeons of England Examinerships
Oxford University Nuffield Dept of Orthopaedic Surgery Graduate Asst A
Australia Queensland University Sr Lecturer in Pharmacology
South Africa. Natal University Sr Lecturer in Bacteriology & Serology & Sr Lecturer in Chemical Pathology
New South Wales University of Technology Foundation Chair in Hosp Admin
London School of Hygiene & Tropical Med Scholarships 1956/57 D.P.H Course
ANÆSTHETICS
Hackney Group H.M.C Sr H O
Royal National T.N & E, W Reg
South West Met R.H B P t. Sr H.M O
Manchester R H B & United Hosps P t Cons
Manchester South Manchester H.M C Sr H O
Scotland North Eastern R H.B Sr Reg
Salisbury Group H.M C Reg
Sheffield R H B Cons
Winchester Royal Hants County H O
Northampton Gen H O
U S.A. Cambridge Mass Residencies
BACTERIOLOGY
Scotland Western R H B Reg
CASUALTY
Dreadnought Seamen s S E 10 Sr H O
Hackney E 9 H O
Poplar Hospital, E 14 Sr H O
Paddington Green Child s W 2 Pre reg H O
Brighton. Royal Sussex County H O's
Cheltenham Gen & Eye Sr H O
Colchester Essex County Sr H O

CONTROL OF YAWS

W H O Symposium in Nigeria

THE second W H O International Yaws Symposium was held at Enugu, Eastern Nigeria, on Nov 9–24, and it was attended by 53 participants from 30 countries One reason why this part of the world was chosen for the meeting was because it is the site of a particularly active anti-yaws campaign In the Nsukka Division alone from mid-February, 1954, to mid-May, 1955, no less than 383,769 persons were examined and treated, while in Nigeria as a whole more than 1,100,000 people had been examined by July, 1955

The first W H O symposium on yaws was held in Thailand, at Bangkok, in 1952 when much base line material was considered The various phases of a yaws campaign were then discussed and later it was possible to define certain technical principles to be followed in mass campaigns At Enugu, where much statistical evidence was studied, the soundness of these principles was found to have passed the test of time

The treponematoses include yaws, pinta, and endemic and venereal syphilis, all of which can be effectively treated with penicillin It was clear from the pooled experience of those at the symposium that endemic syphilis is much more general in Africa than had previously been supposed Earlier data had been largely confined to the *njovera* of Southern Rhodesia,[1] the *dichuchwa* of Bechuanaland,[2] certain foci in South[3] and East Africa,[4] the Sudan,[5] Gambia,[6] French Niger territory,[7] and Northern Nigeria[8] Reports at Enugu told of much endemic syphilis in French West Africa and adjoining territories and in areas bordering on the desert

In a yaws campaign it was agreed that the planning stage should take into consideration *all* phases of the campaign, including the consolidation phase and the ultimate integration of the anti-yaws measures into the permanent health structure of the country Unless this was done there was a danger that once yaws had been virtually eliminated, the success might be short-lived

The first essential in a mass campaign against treponematosis, be it yaws or endemic syphilis, is to treat an adequate proportion of the population less than 90% is considered inadequate

For the treatment of clinical cases, single injections of procaine penicillin with aluminium monostearate (P A M) (1 2 mega units for adults and half of this amount for children) have given excellent results from both the clinical and public-health aspects No-one now believes in the treatment of clinical cases only , there is abundant statistical proof that contacts must also be treated (half the dose of P A M for clinical cases is sufficient) to cover latent cases and those in the incubation period The only difference of opinion is in the definition of a contact

Total mass treatment—i e , the treatment of the entire examined population, as was witnessed in Nigeria (all persons without clinical yaws were regarded as contacts) —has been recommended when the prevalence of clinical cases, both infectious and non-infectious, exceeds 10% of the population *Juvenile mass treatment*—i e , the *treatment of clinical cases and all apparently non-infected* children under puberty—has been suggested when the prevalence of clinical cases is between 5 and 10% Finally, *selective mass treatment* has been used in areas where the prevalence of clinical cases is less than 5%, when only known infected persons and household contacts are treated The symposium favoured moving this upwards by discarding selective mass treatment and using total mass treatment more often

The conference was particularly impressed by the f that over 1700 cases of leprosy had been discovered Eastern Nigeria by the simple expedient of appoint a leprosy inspector to the yaws teams undertaking ma treatment A search for leprosy and other diseases be conveniently made during the initial mass treatme survey or during the subsequent re surveys which made every six to twelve months

Particular attention was paid to the possibility reintroduction of infection from outside the treated are This is less likely if the standards of living are sim taneously improved, but standards cannot usually be raised fast enough to prevent re entry of the dise unless it is also checked in adjacent infected areas Th is true not only of areas within a country but of who countries, and even continents. The need for yaw campaigns to develop simultaneously in all affected are is therefore an obvious corollary The conference therefore welcomed enthusiastically the proposal of Med Général Vaucel, of France, calling for an immedia planned offensive to eliminate yaws and other endem treponematoses from the continent of Africa

One way of improving living conditions would be to strengthen rural health services and so bring health education to the people It was realised that endemic syphilis could be revived in a treated area which remained underdeveloped, by the importation of venereal syphil from the towns In the planning of such a campaign therefore, the widespread control of venereal syphilis must also be considered

So far no less than 50 million people have been examined and 15 million treated in the W H O assisted campaigns against the treponematoses Very large numbers have been treated in a very short time in the campaign organised by the Eastern Region of Nigeria with W H O help The prevalence of yaws there has been much reduced and those who went to Enugu were impressed by the new health facilities which had rooted in the rural areas in the wake of the yaws teams If this pattern could be followed in a coordinated way throughout the whole of Africa, success would be certain

R R W

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In England Now

LAST week Princess Christina of Schleswig Holstein and her entourage attended the Hospitals Rugby Cup final between Guy's and Mary's Later certain newspapers put out the unlikely story that the Princess and her two private secretaries, Mr Hugh Jefferies and Mr Humphrey Bolle, were in fact Guy's students, that the Dowager Countess of Blakeley was the mother of a student, and that Lady Margaret Bland, lady in waiting, was the sister of another student However that may be, the Princess was invited to present the cup, and though she was denied that pleasure since the match was drawn, she and her attendants much enjoyed their visit to Richmond They were told that senior consultants are not always noted for their deference to students or for their gentleness to examination candidates , yet what could have been more graceful, the Princess remarked, than the way in which they surrendered their tea to the guests ? Lady Margaret also commented warmly on the courteous gesture of a distinguished surgeon in the committee box who took his pipe out of his pocket, eyed it ruefully, and then considerately put it back again Some may feel that the Dowager Countess having reached her allotted span, should forgo some of the more lighthearted activities that graced her younger days But that gallant lady is not bound by convention, and as the mother of three doctors, a dentist, and a medical student, all of the same hospital, she was determined not to miss this important occasion Indeed, we may join with the official of the United Hospitals Rugby Football Club in saying that her presence contributed much to the success of the afternoon

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Scotland's Lead

INTEGRATION is a beguiling word and we tend perhaps o mistake the repeated utterance of it for its achievement. Since the late war the need for integrating the hospital and general medical services has been voiced again and again, but despite some useful gestures—notably, prompting hospitals to offer part-time appointments to general practitioners—the process has not advanced far. Scotland has now given a new lead. The Department of Health together with the Joint Consultants Committee and the General Medical Services Subcommittee has evolved a plan by which young doctors may divide their training period between hospital and general practice and those who have completed training may continue as part time principals in general practice, spending the rest of their time in a hospital appointment. The training period, lasting two years is to start after the preregistration year or on completion of National Service the trainee will work half-time in hospital as senior house-officer or registrar, and half-time in general practice under the guidance of an experienced doctor.

The merits of this scheme are clear. The clinician who passes his early postgraduate years solely in hospitals equips himself fully for neither specialist nor general practice for a patient withdrawn into hospital from home and work and leisure may betray no more of the stresses which have brought him there than does a tissue section of a biochemical process. Furthermore whereas hitherto many who have found no permanent career in hospital have turned to general practice untrained, and often in the spirit of disgruntled outcasts, under the new scheme such practitioners will approach this alternative work prepared—and perhaps less reluctant. Nor will the scheme be valuable only to the trainees. At present the world of hospital practice is divided from the world of general practice by a lack of links in everyday activities and the trainees going to and fro cannot but bring the two together, to the refreshment of each. Finally, the scheme may mark the start of more coherent care of patients the prevalent disparity in treatment between hospital and general practice is surely due not only to differing resources but also to lack of mutual understanding.

This plan will call for good will between the two branches of the service, and suitable hospital posts are expected at first to be few. But small beginnings are not to be despised.

A New Serotype of Esch Coli

Two recent papers report the identification of *Escherichia coli* type O 128 B 12. TAYLOR and CHARTER[1] of the Salmonella Reference Laboratory at Colindale, describe how this serotype was first isolated from babies ill in Coventry during July, 1953, and ROGERS and his colleagues[2] give an account of the epidemic that this organism caused at the Birmingham Children's Hospital three months later.

A laboratory at a children's hospital has access to material isolated from circumscribed epidemics of infantile gastro-enteritis among a highly susceptible community but such a laboratory rarely has the means to identify all the antigens in a hitherto undescribed *Esch coli* serotype. The reference laboratory, on the other hand may handle specimens from similar epidemics from widely separated areas, and it is therefore in a position not only to make a careful analysis of the organisms but also to suggest when epidemics may be related. The reference laboratory is also in communication with similar laboratories in other countries, and a new serotype can thus be characterised within the internationally accepted classification. The serological classification of *Esch coli* depends on the identification of the somatic, surface and flagella antigens, and it is known that a particular somatic antigen may be associated with more than one type of surface or flagella antigen. Though the detailed serological analysis is not essential in routine investigations it is certainly essential to progress in this particular field. The extremely careful and detailed investigations[1] into the antigenic composition of *Esch coli* type O 128 showed that an unusual combination of antigens was present and it is worth noting that the Coventry and Birmingham strains were the only ones which had the surface (B) as well as the slime antigens they also had the same flagella (H) antigen, which could suggest that these were related outbreaks.

These accounts of *Esch coli* type O 128 lend weight to our recent remark[3] about the valuable help that the reference laboratories give to the hospital bacteriologists in this country we also noted how a similar liaison in the United States had led to the identification of another of the serotypes of *Esch coli* (O 127 B 8)[4,5] which are now considered to cause epidemic infantile gastro-enteritis. It is interesting to compare the methods by which control was established in the epidemics due to *Esch coli* type O 128, in Birmingham and type O 127 in America. The Birmingham workers, who were dealing with an epidemic which attacked babies already ill, closed their affected wards and only readmitted babies after those wards had been emptied and fumigated. It would be hard to prove that closing the wards prevented a more serious or prolonged epidemic in Birmingham, but the epidemic was certainly relatively mild. although the specific serotype was found amongst the babies in two wards. TODD and HALL[6] were the first to show that when babies became excretors of the specific serological types of *Esch coli*, chemoprophylaxis reduced the incidence of gastro-enteritis. When it is not expedient to close a ward or unit, this form of chemotherapy can be valuable, as STULBERG and his colleagues[4] showed. They had to deal with an epidemic amongst babies who were well but premature they continued to admit other premature babies to the unit and they relied on neomycin prophylaxis to limit the epidemic, although sometimes therapy had to be continued for very long periods because of the liability to bacteriological relapse.

Both American and British workers screened their new admissions for the presence of the new pathogenic sero-

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Warrington Infy Sr H O
U S A Cambridge, Mass Residencies

CASUALTY
Hackney E 9 H O
Whipps Cross, E 11 Sr H O
Colchester Essex County Sr H O
Southend Gen Temp Reg
Swindon Hosp Group Sr H O 's
Worcester Royal Infy Jr H M O

CHEST AND TUBERCULOSIS
Brompton S W 3 H O 's
London Chest E 2 H O s
Bristol Ham Green Sr H O
Broxburn, West Lothian Bangour Gen Reg or Jr H M O
Chesterfield Walton San Reg
Chester Barrowmore Sr H O
Edgware Chest Clinic & Gen Hosp Reg
Ipswich St Helen's H O
Manchester R H B Reg
Newcastle Gen Sr H O
Newcastle upon Tyne Walker Gate Sr H O
Scotland Northern R H B Jr H M O
Skipton The Hosp Grassington Sr H O or Jr H M O

DERMATOLOGY
Derby Derbyshire Royal Infy & Derbyshire Child's Reg

EAR NOSE AND THROAT
Birmingham R H B Reg
Blackpool Victoria Sr H O
Brighton & Lewes H M C Sr H O
Derby Derbyshire Royal Infy Sr H O
Liverpool United Hosps Temp Reg
Manchester R H B Reg
Portsmouth Group H M C Sr H O
Reading Royal Berks H O

GERIATRICS
Bristol Clin Area Sr H M O
East Anglian R H B Reg
Leeds R H B Cons

MEDICINE
Mile End E 1 H O
Royal Free W C 1 Jr H M O
St Stephen's S W 10 Pre reg H O
Bath Royal United H O
Birmingham United Hosps Sr Reg
Bristol United Hosps & South Western R H B Reg
Cardiff United Hosps Reg
Croydon Group H M C Locum Sr H M O
Cuckfield Sussex Pre reg H O
Darlington Dist H M C Jr H M O
Dorchester Dorset County Pre reg H O
Gainsborough John Coupland Jr H M O
Huddersfield St Luke's Jr H M O & Sr H O
Isle of Thanet H M C H O
Leeds R H B Pre-reg H O 's
Manchester Crumpsall Reg
Manchester R H B Reg
Middlesbrough Poole Hosp Nunthorpe Jr H M O or Sr H O
Plymouth South Devon & East Cornwall Sr H O
Portsmouth Group H M C Pre reg H O
Scotland Northern R H B Jr H M O
South West Met R H B Locum P t Cons or Sr H M O
Taplow Canadian Red Cross Mem H O
Torquay Torbay Sr H O
Tredegar Mon St James H O
Welsh R H B Reg
Ibadan Nigeria Univ College Hosp Sr H M O s
Northern Ireland Hosps Auth Locum Cons or Sr H M O

NEUROLOGY
National Hosps for Nervous Diseases Sr Reg Reg & Sr H O
Leeds R H B Pre reg H O

NEUROSURGERY
Whittington N 19 Reg
Leeds United Hosps Sr H O
Romford Oldchurch P t Locum Cons

OBSTETRICS AND GYNÆCOLOGY
East End Maternity E 1 H O
Hosp for Women W 1 Sr H O
Marie Curie N W 3 H O
Nelson S W 20 Reg
Bedford Gen Sr H O
Birmingham R H B Reg
Chichester Group H M C Reg
Doncaster H M C Sr H O or Pre reg H O
Doncaster Western Reg
Edgware Gen H O s
Huddersfield Royal Infy Pre reg H O
Ipswich & East Suffolk Pre reg H O
Leeds R H B Pre reg H O 's
Peterborough Mem H O
Portsmouth Group H M C Pre reg H O
Reading Combined Hosps H O
Romford Oldchurch Sr H O
Sunderland Royal Infy H O
Swansea Sr H O
Taplow Canadian Red Cross Mem Locum Reg
Ibadan, Nigeria University College Hosp Regs
Northern Ireland Hosps Auth Locum Cons or Sr H,M O 's

OPHTHALMOLOGY
Brighton Sussex Eye H O
Leeds R H B Sr H M O 's
Manchester United Hosps Sr H M O
Newcastle upon Tyne H M C Sr H O
Sheffield United Hosps Reg
Welsh R H B Reg

ORTHOPÆDICS
Ashford, Middx H O
Bath St Martin's, H O
Bebington Clatterbridge Jr H M O
Birmingham R H B Reg
Brighton Gen H O
Chertsey St Peter's Sr H O or Pre reg H O
Manchester R H B P t Cons
Medway & Gravesend H M C Locum Reg
Northampton Gen H O
Portsmouth Group H M C Pre reg H O
Romford Oldchurch H O
Scotland Eastern R H B Sr Reg
Southampton Royal South Hants Sr H O
South East Met R H B P t Cons
South East Met R H B Reg
South West Met R H B P t Locum Cons or Sr H M O
Stoke on-Trent North Staffs Royal Infy Sr H O
Swansea Sr H O

PÆDIATRICS
Hosp for Sick Child, W C 1 Sr H O s
St Stephen's S W 10 H O
Birmingham R H B Cons
East Anglian R H B Reg
Manchester R H B Cons
Portsmouth Group H M C Sr H O

PATHOLOGY
Royal Free Hosp Group Sr H O & H O
St Bartholomew's E C 1, & North East Met R H B Sr Reg
Bath St Martin's Sr H O
Birmingham R H B Reg
Edgware Gen Sr H O
Manchester West Manchester H M C Sr H O
Sheffield City Gen Sr H O
Tasmania Launceston Gen Path

PSYCHIATRY
Birmingham R H B Reg
East Anglian R H B Reg
Glasgow North Eastern Mental Hosps B O M Sr H O
Leeds R H B Sr H M O
Liverpool United Hosps, R H B & University P t Cons & Lecturer
Manchester R H B Cons
Romford Group H M C Temp Asst Psych
Sheffield R H B Sr Reg
South West Met R H B Sr H M O
Welsh R H B Sr Reg
West Malling Leybourne Grange Colony for Mental Defectives Jr H M O
Willerby E Yorks De la Pole Jr H M O

RADIOLOGY
National Hosps for Nervous Diseases Reg
Northern Ireland Hosps Auth Locum Cons or Sr H M O

RADIOTHERAPY
Middlesex, W 1 & North West Met R H B P t Cons

RHEUMATOLOGY
St Stephen's, S W 10 H O
Sheffield United Hosps /R H B Reg
Taplow Canadian Red Cross Mem Sr H O

SURGERY
Colindale N W 9 Reg
Dreadnought Seamen's S E 10 Pre reg H O
Hornsey Central N 8 Sr H O
Hosp for Sick Child, W C 1 Sr H O s
Nelson, S W 20 H O
New End N W 3 Pre reg H O
South London Hosp for Women S W 4 Locum H O
St Leonard's, N 1 H O
Wanstead E 11 H O
Barrow in Furness North Lonsdale H O
Bath Royal United H O
Bedford Gen Locum H O
Bedford Gen Pre reg H O
Birmingham Accident H O
Birmingham Solihull Sr H O
Blackpool Victoria Sr H O
Brighton Royal Sussex County H.O 's
Bury & Rossendale H M C Pre reg H O
Cardiff Royal Hamadryad Gen & Seamen's Sr H O
Carshalton Queen Mary's Hosp for Child H O
Carshalton Queen Mary's Hosp for Child Reg
Chelmsford & Essex Pre reg H O
Chesterfield Royal H O
Chichester St Richard's Regs
Cuckfield, Sussex Pre reg H O
Dorking Gen Sr H O
East Anglian R H B Sr Reg
Edgware Gen H O 's
Grantham & Kesteven Gen Reg
Haslemere & Dist H O or Locum
Hastings Royal East Sussex Pre reg H O 's
Hounslow Middx Reg
Huddersfield Royal Infy H O
Isle of Thanet H M C H O
Leeds R H B Pre reg H O 's
Leicester Gen Reg
Llanelly Jr H M O
Louth County Infy H O
Louth County Infy Sr H O
Maidenhead Reg
Manchester Christie Hosp & Holt Radium Inst Sr H O
Manchester West Manchester H M C Pre reg H O s
Newport, I W St Mary's H O
Northampton Gen H O
North Gloucestershire Clin Area Reg
Nottingham Child's Reg
Nottingham City H O
Nottingham Gen Pre reg H O 's
Plymouth S Devon & E Cornwall Gen Pre reg H O
Portsmouth Group H M C Pre reg H O 's
Scotland Eastern R H B Sr Reg
Sheffield City Gen H O
South East Met R H B Reg
Stockton & Thornaby H O
Swansea H O
Walsall Manor & Gen Hosps Locum H O s
Welsh R H B Regs
Worksop Victoria Reg

THORACIC SURGERY
Leeds R H B Pre reg H O
Welsh R H B Reg

TROPICAL DISEASES
University College Hosp, W C 1 Reg

GENERAL PRACTICE
Beckenham Kent Urban List Approx 2170

PUBLIC APPOINTMENTS
Barbados Gen Hosp M O 's
Birmingham City Education Committee School M O
Govt of Aden Asst Health Adviser
H M Oversea Service, Western Region Nigeria Specialist Obstetricians & Specialist Otolaryngologist

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(Further particulars of above vacancies available on request to Advertisement Manager)

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t with epithelial cells derived from the wound edges and the an appendages lying in the base of the wound, these cells row underneath the superficial clot and cover the wound ithin four days They then lie on a saucer, and are gradally lifted and brought level with the normal skin surface y a blister of exudate containing glycogen and protein, which ecomes invaded, between the sixth and tenth day after he injury, by round cells, capillaries, and reticulin fibres ew connective tissue is now forming and though the activity f the epithelial cells is still manifest at this stage in the formition of "pseudo" rete pegs epidermal regeneration is about o vane, for very shortly these pegs become separated from he surface and contained in small pearls by the developing onnective tissue The pegs are eliminated after three to six weeks by the connective tissue and the deep epithelium at the se of the wound becomes straight, but at no time does either epithelium or dermis in the donor area regain its original morphology Wounds deep enough to cause loss of dermis behave differently in that classical granulations must form and grow up from the base of the wound before epithelium can regenerate, it therefore seems that the dermis is in some way responsible for the initial invasiveness of epidermal cell in the earlier stages of wound healing just as it ultimately controls and limits it In conformity with the process in the main incision, Gillman et al. find that epithelium invades the track of a skin suture, thus accounting for the punctate scars which remain after removal of skin stitches. these can be avoided by closing skin wounds with adhesive tape, a method which they[2] and Williamson[3] recommend.

Q FEVER

Q (query) fever remains a suitable name for a disease whose natural history is still confused and obscure There can be no doubt that many human infections are derived from direct contact with cattle, sheep, or goats, alive or dead. *Rickettsia burneti* has been isolated from all three species it may be present in their milk or, in enormous numbers, in the products of conception. Infection of man by man is rare but laboratory infection not uncommon So far the likeness to brucellosis in epidemiological habit is close Not every human infection can however be traced with certainty to an animal source Some epidemics among soldiers during the Italian campaign were attributed in retrospect to sleeping in cow byres On the analogy of other rickettsial infections, it has been suspected that the original reservoir of *R burneti* might be in some arthropod. Infected ticks have been found in Australia, Germany, and England but their connection with human infection is not apparent In California (where the disease seems remarkably common) serological evidence of past infection was found, not only in 20% of those engaged in dairying, but in 1% of those who had no personal contact with animals and who drank no raw milk.

In this country blood from 95 out of 4456 donors gave a positive complement-fixation test for *R burneti*, and sporadic infections make up a small but fairly constant proportion of the aggregate of "atypical pneumonia". Many of these cannot be traced in any way at all to the larger domestic animals, while others occur in places where animals are known to be infected but where clear demonstration of the channel of infection is so far wanting A recent small epidemic in Cardiganshire exemplifies this[4] 15 people in three near by villages were infected within a few weeks No common factor was found in food, drink, or personal environment It was the lambing season (and the uterine discharges from an infected animal tend to be heavily charged with *R burneti*) but not all the patients were actively concerned with lambing Of the sheep with which some of the patients had been in contact 3 5% gave some serological evidence of infection but the rickettsia could not be detected in the ewes' milk. A pertinacious inquiry ended with the problem so far unsolved that the investigators suggest some unrecognised source of infection, common to man and animals. Those who see no future in the epidemiological investigation of infectious disease should accept the challenge Ticks are not the only arthropods which plague us and our beasts another rickettsial disease scrub typhus is spread by trombiculid mites Not much attention has been paid to infection in the smaller animals kept as pets. It was suggested long ago that the epidemics in Italy were due to the inhalation of dust containing particles of infected cow dung Knowing that *R prowazeki* will survive for many months in dried louse faeces, this was a most reasonable guess[5] Farm buildings are dusty places and even in this mechanical and tarmacadamed age animal faeces must make up an appreciable part of the road dust inhaled by the countryman every fine day and by his urban visitors at weekends

HIDDEN BENEFITS

Today we are all citizens and taxpayers of the Welfare State Many people feel that these two rôles give them the right to play a third—that of a critic—and they readily offer their views on the administration and scope of the social services

The commonest complaints are that the Welfare State has tried to do too much too quickly, that it has sapped the moral fibre of the nation, and that it has imposed an excessive burden on the middle classes But Prof R M. Titmuss[6] thinks that these objections arise mainly from lack of clearness about the meaning of the term "social service" Such uncertainty is, indeed, excusable, for during the past fifty years the term has been extended from provision for such limited communal needs as poor relief and sanitation to include the universities and public museums Nor has the Treasury, Professor Titmuss admits, made things easier The welfare services which it recognises as social services seem to be chosen haphazard, and its classification has been influenced by administrative convenience rather than similarity of purpose Thus family allowances count as a social service but remission of taxes for children does not, compensation to doctors for the goodwill of their practices counts as a social service but superannuation under an occupational pension scheme does not These two examples of apparently illogical classification are also examples of two large groups of concealed social services which Professor Titmuss describes as fiscal welfare and occupational welfare.

These two often unrecognised groups of social services now cost a lot of money—more perhaps than is generally recognised Thus a father with two children under 15, if he has an income of £2000 a year will receive over the life of the family a "bounty" of £1455 if he has an income of £400 a "bounty" of only £422 Similarly occupational pension schemes cost the Exchequer [7] £100 million a year, which is more than the present Exchequer cost of National Insurance pensions Professor Titmuss holds that, though these fiscal and occupational reliefs have sound and admirable aims—to strengthen the family or to promote good relations in industry—they distort our social services because, by offering greater benefits to the highly paid than to the less well paid, they are "enlarging and consolidating the area of social inequality". The alternative view, of course, is that these tax reliefs do not in fact do enough, in a period of inflation, to mitigate the egalitarian effect of taxes which rise so rapidly with income that (in the words of the Financial Secretary to the Treasury[7]) it has become hard to remunerate adequately men in any walk of life who carry great responsibilities Professor Titmuss's use of the word "bounty" is no doubt technically correct, but to the ordinary taxpayer it sounds a little odd as applied to permission to retain, for socially useful purposes, a little more of one's own money

AFTER MENINGITIS

We have suggested[8] that those who treat meningitis in childern have a duty to follow their patient's progress for many years The early results of treatment may seem better than they really are, for "mental defect is notoriously elusive in early childhood and epilepsy commonly matures silently between the primary insults and the onset of seizures"[9] Desmit,[10] writing from the Hague reports 114 cases treated between 1949 and 1954 The minimum follow-up period was rather short—six months 4 children (2 of whom died) were excluded from the survey Of the remaining 110, 8 died and and 16 were left with gross defects. Thus the least possible failure rate in this series was 22% The figure might well increase if the children were followed for a longer time Desmit points out that convulsions and prolonged coma were common in those with permanent damage, and he suggests that the illness in these children was encephalitic as well as menin-

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[6] Social Division of Welfare Rathbone lecture by R M. Titmuss Liverpool University Press. 1956 Pp 23 2s 6d

[7] See *Lancet* Feb 18 p 296

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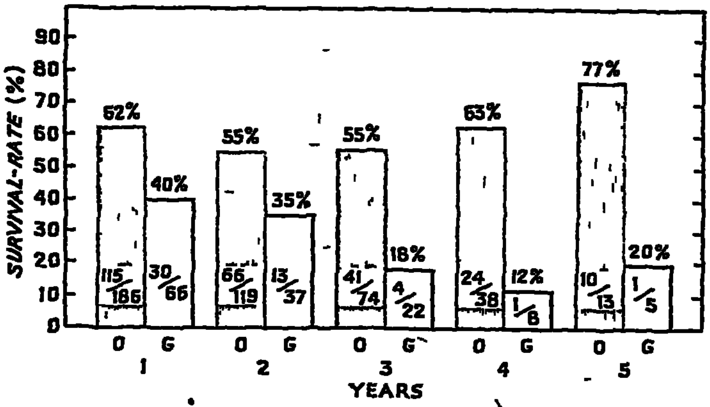

Fig 3—Influence of glandular involvement on survival-rate O = no glandular involvement. G = glandular metastases found

similar to that for patients with squamous cell tumours (43% and 46% respectively)

Influence of Glandular Involvement

The dominant influence of mediastinal-node involvement on prognosis has been stressed by many workers, Bignall and Moon (1955) state that the five year survival-rate of patients without glandular involvement was as high as 48%, whereas in those with glandular involvement the rate was only 11% The proportion of patients found at operation to have glands containing metastases depends largely on the thoroughness of the search for them (H C Nohl, personal communication) In only a few cases in this series was the hilum of the resected lung carefully dissected, nor were sections of all glands examined routinely, yet histological evidence of glandular metastases was found in 70 (27%) cases

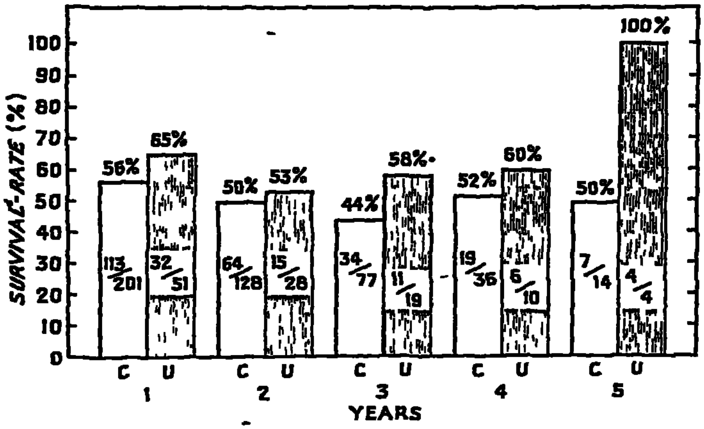

Fig 4—Influence of anatomical type of tumour on survival rate C = circumscribed lesions U = uncircumscribed lesions

Fig 3 compares cases in which no glandular metastases were found with those in which glandular involvement was proved histologically The survival rate after two years was very considerably lower in the latter group (35% as against 54%), and it fell off even more one year later (18% as against 55%) Since only 30% of the patients with glandular involvement eventually died because of local metastases, the finding of malignant glands in a resected specimen probably indicates that the disease is already widespread

Circumscribed and Uncircumscribed Tumours

Both Raeburn and Spencer (1953) and Walter and Pryce (1955) have emphasised that the majority of bronchial carcinomas originate at th periphery There is, however, a clinical entity often described as a "peripheral" carcinoma, the lesion is peculiar in that the greater part of the shadow cast on a radiograph is due to tumour tissue, and that it is far more commonly associated with pulmonary osteo arthropathy than are more centrally placed tumours (Semple and McCluskie 1955) In order to avoid confusion the term "circumscribed," originally used by Rabin and Neuhof (1934), has been applied to these characteristic round lesions They form th greater part (76%) of the present series

There was no significant difference between the proportions of the three cell types in the two groups, but glandular involvement was a littl commoner in the uncircumscribed tumours (31% as against 24%) Fig 4 shows that the "uncircumscribed" tumours had a slightly better prognosis (53%, as against 50%, survived for more than two years) This difference is interesting although probably not significant

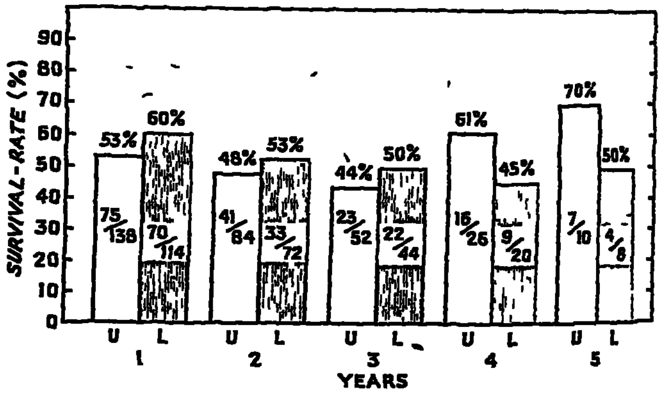

Fig 5—Influence of site on survival rate U = upper-lobe tumours L = lower-lobe tumours

Influence of Site of Tumour

The 264 tumours in this series were evenly distributed throughout the lungs, and there was no difference between the prognosis on the two sides, nor between the upper and the lower lobe (fig 5) In the cases analysed by Bignall and Moon (1955) tumours situated in the left lower lobe were associated with the lowest survival rate, but the majority of the lesions in this series were of the circumscribed type, in which the factor of proximity of the tumour to vital structures influencing operability, and so prognosis, did not come into play

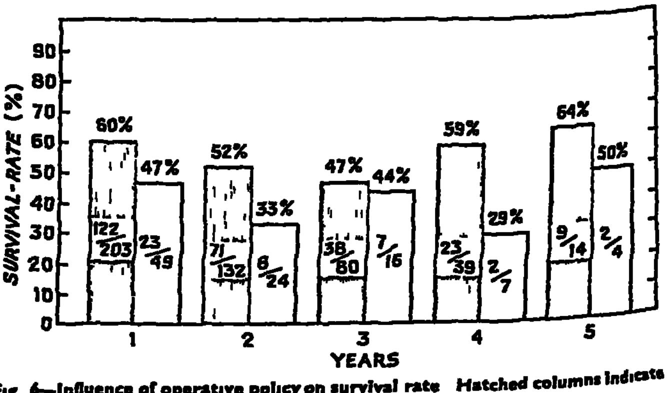

Fig 6—Influence of operative policy on survival rate Hatched columns indicate "policy" resections

Relative to the usage of antibiotics, superinfection this type is extremely rare. But when it occurs it is ten dramatic and disastrous, and constant vigilance therefore required whenever oral antibiotics are used ad particularly when an attempt is being made to erilise the gut. Several authors have remarked that atients look and feel quite well in the early stages of a apidly fatal diarrhoea.[22] In staphylococcal enterocolitis is probable that they remain well until the blood iochemistry becomes upset and possibly also staphylococcal toxin has accumulated to produce toxaemia.[22, 23] At this stage the patient becomes profoundly ill and may die within a matter of hours. The clinical course has been aptly compared with that of cholera. Being so much quicker, bacteriological examination of a slide is preferable to culture of the patient's stools and may more accurately reflect the bowel flora present. Usually one organism predominates. Those most often found are monilia, staphylococci, proteus, and eudomonas.

TREATMENT OF SUPERINFECTION

In staphylococcal cases early recognition is imperative, other organisms are not so rapidly fatal. In a number of reported cases symptoms have quickly resolved on stopping the drug,[3, 26, 27] which is clearly the first essential. When the blood biochemistry has become deranged, urgent and strenuous efforts are required to restore it to normal. The chief needs are for water, sodium, chloride, and potassium—in that order—and intravenous therapy is almost invariably necessary. Depending on the result of bacteriological examination of a smear of the patient's stool specific chemotherapy should be started as soon as possible. With the introduction of new drugs during the past year or two the prospects of success have improved considerably.

CHEMOTHERAPY OF SUPERINFECTION

Proteus.—This organism may be found in up to 0% of normal stools and is usually regarded as nnocuous. It may not be innocuous when it becomes the predominant organism in the bowel.[28] It is notoriously resistant to antibiotics. Some strains are sensitive to oral streptomycin 0.5 g q.i.d. or to neomycin 1.0 g q.i.d.

Pseudomonas pyocyaneus.—Least often guilty of the inister quartet, this organism is usually susceptible to polymyxin B, a bactericidal antibiotic effective against gram negative bacilli. Though originally nephrotoxic and still liable to produce malaise, fever, skin rashes, and pain when given intramuscularly, polymyxin produces no such side-effects when given orally, for it is very poorly absorbed.[29] It may be given as aerosporin 500,000 units every six hours.

Monilia.—*Candida albicans* may be found in 10–20% of normal stools and, after broad spectrum antibiotics in up to 60% of patients, though it rarely does any apparent harm.[30] While it is unlikely that these drugs heighten the virulence of monilia,[4, 31, 32] there have been any reports of both alimentary and generalised oniliasis following the use of broad-spectrum antiiotics. Hitherto this has been an exceedingly difficult condition to treat, but there are now promising reports of the use of diamidines,[33, 34] *p* hydroxybenzoic acid and its esters[31] and fatty acids.[35] Recently a new antifungal antibiotic 'Nystatin' has become available. This is derived from *Streptomyces noursei*, and in vitro it is very effective against fungi and yeasts especially in the dividing phase. It appears to be of considerable value for the treatment[36] or prevention[37] of intestinal moniliasis. Though only a small proportion is absorbed it is said to improve some cases of moniliasis of the skin and genito-urinary tract.[38] Oral dosage is 500,000 units thrice daily or twice this if necessary.

Staphylococcus.—Strains resistant to some or all of the usual antibiotics are found much more often in hospital than among the general public.[39] Staphylococcal enterocolitis, now the most serious of all forms of superinfection, is therefore essentially confined to hospital patients. It usually develops after three to five days of chemotherapy, when the normal bacterial population has been reduced to a minimum and the field is left clear for resistant organisms. Debility is a contributory factor. The best available drug for its treatment is erythromycin, which suppresses staphylococci but permits the return of *Escherichia coli*.[18, 27] The antibacterial spectrum of erythromycin is very similar to that of penicillin but it also affects some rickettsiæ and larger viruses. It is important to reserve it for the treatment of penicillin-resistant organisms or penicillin-sensitised patients. Its indiscriminate use would soon lead to the emergence of erythromycin insensitive staphylococci as resistance to it can develop with great rapidity.[40] It is issued in acid-resistant tablets of 100 mg each. The dose for an infant is 100 mg, for a child 200 mg, and for an adult 300 mg six-hourly. If necessary higher doses may be given as it is tolerated quite well and seldom gives rise to more than minor gastro-intestinal upset.

An alternative is to use neomycin which is a bactericidal antibiotic effective against gram-positive, gram-negative, and acid fast bacilli. It does not show cross-resistance with other antibiotics. Its parenteral use is strictly limited by its toxicity for the kidney and for the ear, but doses of under 0.5 g per day are regarded as safe for short periods.[8] Orally, only about 3% is absorbed and toxic effects of any sort rarely if ever occur.[41, 42] Its advantages are that at the present time it is effective against staphylococci (including those endemic in hospitals) and many strains of proteus and *Pseudomonas pyocyanea*. Resistance to it develops slowly.[43] It is particularly suitable for preoperative preparation of the bowel because it is effective in about twenty-four hours and sterility is maintained for two or three days after operation without further dosage. In a recent paper Rowlands and Scorer[42] found that 1.0 g orally every four hours for six doses sterilised the stools of nearly 30% of their patients. When preceded by 4 × 1 g doses at hourly intervals the proportion rose to 45%. Waisbren[43] also considers neomycin alone satisfactory, but Poth[41] found that on neomycin alone the stools of 10% of patients grew resistant *Aerobacter aerogenes*. He therefore gave 1.5 g of phthalyl sulphathiazole in addition to 1.0 g of neomycin four-hourly for forty eight hours before operation and he regarded this combination as the best available. Unfortunately strains of staphylococci resistant even to neomycin have appeared in America so the problem cannot yet be considered solved.[44]

SUMMARY

Symptoms affecting one or more parts of the alimentary tract often follow administration of antibiotics by mouth. Most are mild and transitory but still troublesome

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TABLE II—SURVIVAL OF PATIENTS TWO AND FIVE YEARS AFTER OPERATION, ACCORDING TO PRESENCE OR ABSENCE OF GLANDULAR INVOLVEMENT AT OPERATION

Group	Glands involved		Glands uninvolved	
	2 yr (%)	5 yr (%)	2 yr (%)	5 yr (%)
Bignall and Moon (1955)				
Pneumonectomy	25	16	64	49
Lobectomy	40	25	57	47
Present series				
Lobectomy	35	20	55	77

squamous carcinoma, and possibly bronchogenic spread took place at the time of operation

Discussion

The results of lobectomy in this series are as good as, if not far better than, those reported for pneumonectomy, even without considering the obvious advantages of a lower operative mortality and slighter loss of pulmonary function

It may be argued that the patients were selected when the tumour was early and localised, and before glands were involved, and that accordingly excellent results might be expected Indeed, glandular metastases were found in only 27% of cases, compared with 58% in the series of Bignall and Moon (1955) These workers point out, however, that comparison of the results of lobectomy and pneumonectomy on the basis of the presence or absence of glandular metastases fails to show any difference which would favour the more extensive operation—a conclusion that is borne out by the figures in this series (table II)

It was felt, therefore, that the survival figures for the pneumonectomies done by the same surgeons over the same period as the lobectomies should be collected, in order to establish the total survival for all resections If this was reasonably close to the survival after pneumonectomy in other series, then there would be good ground for favouring " policy lobectomy "

The ratio of pneumonectomy to lobectomy was found to be 4 1 There was wide variation between the results of pneumonectomy among the various surgeons, but there was close similarity between the lobectomy figures The reason for this discrepancy is not far to seek, the indications for lobectomy vary little, whereas there may be considerable difference of opinion as to what patients are suitable for pneumonectomy and how determined an effort should be made to remove the carcinoma The survival-rates for the conservative surgeons will necessarily be better than those of their more radical colleagues

Fig 8 shows the results of this investigation In all, 859 operations were considered The method of analysis has been different in the three series, but, in order to make the figures as nearly comparable as possible, the operative mortality has been extracted from Sellors's (1955) figures, and the figures of Bignall and Moon (1955) have been reanalysed by almost the same method as was used in the present series (A J Moon, personal communication) The only remaining difference in the analyses is that in the two series with which the present one is compared all the survivors at a given period were included whether or not they died later In the present series only those still alive at the time of analysis were considered It is apparent that there is a close similarity between the three series in the four year and five year periods, when the great majority of the patients who were going to die of their carcinoma had done so, but earlier than this the different method of analysis had caused a considerable discrepancy

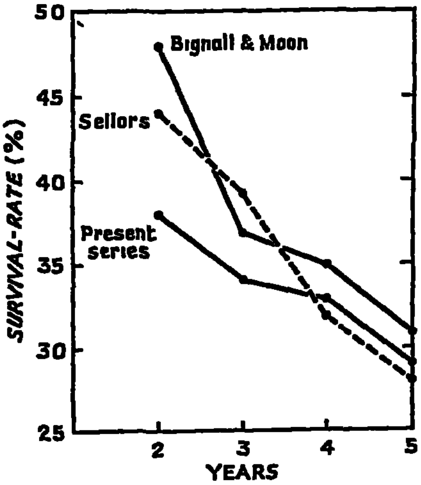

Fig 8—Survival rates after all resections by surgeons contributing to present series, compared with analyses by Bignall and Moon (1955) and Sellors (1955)

The influence of glandular metastases on the prognosis in bronchial carcinoma cannot be overstressed The question arises Can a radical lobectomy be performed? Several reports have described the lymphatic drainage of the lung, and Borrie (1952) traced the lymphatic pathways of individual lobes as far as the bronchopulmonary glands, but until these pathways have been traced still further to the mediastinal glands the planning of a radical lobectomy will not be feasible Recently Nohl (personal communication) has found that the drainage of individual lobes is consistent Extension of this work may show that it is as irrational to recommend pneumonectomy for an upper lobe tumour as it would be to remove the entire colon for carcinoma of the sigmoid

Boyd et al (1954) have already described a form of " radical lobectomy," but the operation cannot become established until lymphatic spread has been further investigated and until more information is available about the submucous spread in the bronchus proximal to the carcinoma

The present series appears to justify continuation of the policy of " lobectomy where possible " in the treatment of bronchial carcinoma It is hoped that when more is known about local spread of the disease the present figure of 10% of deaths from local metastases may be reduced

Summary

The results of 264 lobectomies for bronchial carcinoma were investigated

The two year survival rate was 50% and the five year survival-rate 61%

Patients with adenocarcinoma had the best prognosis and there was no difference between the prognosis for patients with undifferentiated and with squamous cell carcinoma

The presence or absence of glandular involvement had a close bearing on prognosis

Uncircumscribed tumours were associated with a slightly better prognosis than circumscribed tumours

Patients who underwent lobectomy for palliation did not do as well as those in whom the operation was carried out as a policy

The site of the tumour was unrelated to prognosis

Of the 119 deaths, 47% were due to general metastases, 23% to local metastases, 10% to the operation, and 16% to causes other than carcinoma

90% of the patients who died of metastases did so within two years of operation

There is probably a place for " lobectomy where possible " in the treatment of bronchial carcinoma

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Since unrestricted visits is the first essential for the patient a mental hospital, let *all* our mental hospitals throw open ide their doors—and keep them open —H G WOODLEY 'dzell, Angus)

accinia versus Poliomyelitis —Relative to Dr MacIver's cond communication (March 17), I would say that in urban eas in the United States smallpox vaccination takes place lmost universally before the child is a year old In some ral areas this vaccination will not be given until the child nters school, but I would not hazard a guess at the percentges concerned Many children are re vaccinated on going o school, and in the Service almost 100% of children as well s parents are vaccinated every three years Unfortunately oliomyelitis still occurs among our personnel It is to be hoped hat Dr MacIver's observation is correct, for it would be just ne more good argument for vaccination against smallpox— disease we can control —Colonel CHARLES H MORHOUSE, D (Third Air Force, Ruislip, Middlesex)

Production of Codeine —Dr Williams (March 17) shows a lamentable lack of knowledge of the pharmacology of acetanilide and related compounds, and appears to be unaware of the excellent work that has been done in this field by Brodie and others (B B Brodie, J Axelrod, *J Pharmacol* 1948, 94, 22, 29, F B Flinn, B B Brodie, *Ibid*, p 76 B B Brodie, J Axelrod, *Ibid*, 1949, 97, 58) Acetanilide is a dangerous drug because the body de acetylates part of it into aniline It is not generally considered, however, that it causes agranulocytosis Similarly, phenacetin is partially de acetylated into another, though less dangerous, amine, *p* phenetidine The active non toxic metabolite of acetanilide and of phenacetin is *n* acetyl-*p* aminophenol, which is 'Panadol'

To convert *n* acetyl *p* aminophenol into acetanilide the body would have to de hydroxylate it—a process that is unknown for phenols which are metabolised in the reverse direction by further oxidation, conjugated with glucuronic and sulphuric acids, or excreted unchanged

More than two million doses of *n* acetyl *p* aminophenol have already been given to humans, and there have been no authenticated reports of toxic effects All the available evidence suggests that panadol is a safe analgesic and one that is unusually free from side effects, which is the main reason for using it —L M SPALTON, B PHARM, director, Bayer Products Ltd (Kingston on Thames)

Medicine and the Law

Death due to Penicillin

AN anaphylactic reaction to penicillin caused the death, on Feb 3, of a man of 34 who the day before had undergone *tonsillectomy* at the Radcliffe Infirmary, Oxford[1] At the inquest the patient's doctor said that last October he had attributed symptoms in this man to hypersensitivity to penicillin. A dermatologist had concluded that a rash which had developed was due to a throat infection After the operation penicillin was ordered (nothing then being known of the hypersensitivity) A rash developed, and the treatment was changed A staff nurse noted this in the change book but did not remove the patient's name from the penicillin list On Feb 3 another nurse, about to inject penicillin, was told by the patient that he was hypersensitive She relied on the list

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[1] *Times* March 9 1956

Obituary

Sir MORTON SMART

Sir Morton Smart, G C V O, D S O, manipulative surgeon to King George VI and consultant in physical medicine to the Royal Air Force, died on March 16 at the age of 78 He was born in Scotland, the third son of John Smart, R S A, and graduated M.B from the University of Edinburgh in 1902 During the South African war, he had seen active service and in the 1914 18 war he again served as a combatant, this time as a *commander in the* R N V R, *and* was in charge *of a gun*boat flotilla at the Dardanelles This background of Service experience sharpened his interest in the problems of reablement He was' especially concerned with the application of his specialty to the problems of the casualties of war and industry and in 1940 he addressed a committee of the House of Commons on Physical Medicine in War time

Dr WILLOUGHBY-LYLE

We hear with regret of the death on March 13 of Dr Herbert Willoughby-Lyle An indomitable little man, full of energy and activity, he lived to the age of 85 And he lived to the full He was a famous physiology coach in his youth, a first class ophthalmologist in his prime, a vivid medical teacher, and for over 20 years dean of King's (whose medical school he completed by his own exertions) His association with the school began as a student and ended as dean emeritus it stretched from 1887 to 1931 and amply qualified him to turn historian His book, *King's and Some King's Men*, appeared in 1935 and he published an addendum five years ago He was a highly individual and lovable character, who will not be forgotten by his school or by the thousands he served Two of his family, Mr T Keith Lyle and Dr Eric Lyle, are members of the medical profession

News

The trials with an oral attenuated live virus poliomyelitis vaccine, now being carried out in Northern Ireland under the direction of Prof. G W A. Dick, are being extended to include medical students and children whose parents have agreed to their receiving the vaccine Only those volunteers with no antibody to one or other types of virus will be given the vaccine

On Feb 25 the degree of M D of the University of Cambridge was conferred on Robert Marshall, D.N Phear and Arnold Pines the degree of M B on J A Eddington and J F M Newman, and the degrees of M B B CHIR on J F Garner

The Royal Society of Tropical Medicine and Hygiene has awarded the Manson medal for 1956 to Brigadier J A Sinton, V C F R S

CORRIGENDA *Prevention of Hay fever* — Piriton maleate mentioned in Dr Stathers letter (March 10) is *chlorpheniramine* maleate

Chest Radiography in Pneumoconiosis —In our leading article last week the last sentence in the second paragraph should have begun, "When allowance is *made for* Durham miners going to the coalface ten years *later* than their Welsh colleagues '

Births, Marriages, and Deaths

BIRTHS

WESLEY JAMES —On March 10 at Southmead Hospital Bristol, to Jacqueline (formerly David) wife of Dr Oliver Wesley-James, a son

Vacancies

ACADEMIC AND EDUCATIONAL

Inst of Cancer Research S W 3 Clin Research Path

Oxford University Nuffield Dept of Orthopædic Surgery Graduate Asst A.

St Andrew's University Refresher Course for G P s 18th–29th June

Inst of Laryngology & Otology, & Royal National T N & E Hosp W C 1 Course for Cons Otologists 1st, 2nd & 3rd May

St Andrew's University Courses of Instruction for D P H & D P D Oct 1956/June 1957

Tuberculosis Educational Inst (Deeside San Aberdeenshire) Clinical Course 18th, 19th & 20th April

Edinburgh University Regius Prof of Clin Surgery

Glasgow Royal Infy McIntyre Clin Research Scholarship

Bristol University Asst Lecturers (Grade III) or Demonstrators in Physiology

University of London Readership in Clin Path

Singapore University of Malaya Sr Lectureship in Orth Surg

National Assoc for Prevention of T B Edinburgh Post-grad. Fellowship

St Andrew's University Queen's College Dundee Asst in Path

ADMINISTRATIVE

Newcastle R H B Deputy Sr Admin M O

ANÆSTHETICS

Lambeth, S E 11 Locum Reg

St George's S W 1 Reg

Hackney Group H M.C Sr H O

Hosp for Sick Child. W C 1 Reg

North Middlesex N 18 H O

Royal National T.N & E W Reg

University College Hosp, W C 1 P t Cons

Chesterfield Royal Reg

Dublin, St Laurence's Asst Anæs

Dudley Stourbridge & Dist Sr H O

Manchester Crumpsall Sr H O

Manchester South Manchester H.M C Sr H O

Manchester R.H B Cons

Newcastle R.H.B Reg

Nottingham Gen Reg

Sheffield R.H B Cons

Sheffield United Hosps Reg

Taplow Canadian Red Cross Mem Sr H O

U S A Cambridge Mass Residencies

TABLE II—HEPATIC FUNCTION BEFORE AND AFTER OPERATION IN PORTAL HYPERTENSION (ALL CASES)

—	Follow-up (yr) 1	Follow-up (yr) 3	Follow-up (yr) 5
Plasma proteins (g per 100 ml)			
Albumin	3·40 ± 0·58 3·81 ± 0·71 *(26)* P<0·05	3·57 ± 0·78 3·87 ± 0·50 *(15)* P<0·4	4·06 ± 0·54 3·81 ± 0·65 *(7)* P<0·6
Globulin	2·95 ± 0·83 3·21 ± 0·92 *(26)* P<0·1	2·65 ± 0·40 2·91 ± 0·75 *(15)* P<0·1	2·70 ± 0·97 3·30 ± 0·61 *(7)* P<0·2
Total	6·33 ± 1·00 7·06 ± 0·85 *(26)* P<0·01	6·21 ± 1·15 6·80 ± 0·86 *(15)* P<0·2	6·78 ± 1·30 7·14 ± 0·62 *(7)* P<0·5
Serum bilirubin (mg per 100 ml)	0·83 (0·1–1·4) 1·18 (0·2–3·5) *(26)*	0·91 (0·1–1·5) 0·81 (0·1–1·3) *(16)*	0·73 (0·3–1·1) 0·55 (0·1–2·1) *(8)*
Alkaline phosphatase (units per 100 ml)	12·4 (3–66) 11·5 (3–45) *(25)*	15·2 (3–66) 13·2 (3–33) *(14)*	11·6 (3–14) 11·4 (7–27) *(6)*

Values given are means ± S.D. or range, upper values preoperative, lower values postoperative. Number of cases in italic numerals in parentheses.

P values for difference between mean results at *x* years and before operation calculated by "Student's" *t* test.

cirrhotic liver was not followed by any greater immediate deterioration in hepatic function than that after other operations of comparable severity in patients with cirrhosis and (2) there was no significant difference between the results of hepatic function tests before and at 1–2 years after operation in patients who survived. The follow-up of these patients has now been extended and the findings essentially confirm our previous report.

The results of hepatic function tests immediately before operation have been compared with those at intervals of approximately 12 (11–17), 36 (33–40), and 60 (50–70) months after operation (table II). The tests and the analytical methods have already been described (Macpherson et al. 1954). For each test the mean postoperative values are compared with the corresponding mean preoperative values. When the scatter in the values is small it has been expressed as a standard deviation, when large, as in the values for alkaline phosphatase and serum-bilirubin, as a range.

The analysis (table II) shows that there is a significant difference between the results of the tests of hepatic function before and at the stated intervals after operation in 2 instances only (the plasma albumin and total protein levels at 1 year). The changes in all other tests were not significant, where they have been calculated, or obviously insignificant when only ranges are given. Thus operations for portal hypertension have not had permanent or progressive adverse effects on hepatic function in patients who survive them for up to 5 years.

In table III results are analysed according to whether the operation was splenectomy alone or a portal-systemic anastomosis. Apart from the rise in the plasma-albumin level at 3 years after splenectomy alone, none of the changes is significant. It may be noted that in the patients submitted to splenectomy alone the mean preoperative values for albumin and total protein were lower than in those submitted to portal-systemic anastomosis. However, the difference was significant only for albumin (P<0·01 and P<0·1 respectively). The corresponding values for globulin were higher, but not significantly so (P<0·7). Other values did not differ appreciably. These differences are probably attributable to the fact that the less severe operation was deliberately performed in some patients who were considered very poor surgical risks. After operation the difference between the two groups became smaller. It may be concluded that deviation of portal blood from the cirrhotic liver, whether partly by splenorenal (8 cases) or entirely by portacaval (1 case) anastomosis, did not cause any significant deterioration of hepatic function over a period of 3 years after operation.

One further analysis of the results was carried out. Other workers who have reported the progress under medical treatment of patients with cirrhosis (Post and Patek 1942, Ricketts et al. 1950, Douglass and Snell 1950) have observed a correlation between the level of the plasma albumin when the patient was first seen and the prognosis. In the present series no significant correlation was found between the survival time after operation and the preoperative values for albumin, globulin, and total protein (r = +0·20, +0·08, and −0·26 respectively).

Peripheral-blood Picture

The short-term effects of operation on the peripheral blood picture in 58 cases of portal hypertension have already been described (Macpherson and Innes 1953

TABLE III—HEPATIC FUNCTION BEFORE AND AFTER OPERATION IN PORTAL HYPERTENSION: ANALYSIS BY OPERATION

—	Splenectomy Follow-up (yr) 1	Splenectomy Follow-up (yr) 3	Portal-systemic anastomosis Follow-up (yr) 1	Portal-systemic anastomosis Follow-up (yr) 3
Plasma proteins (g per 100 ml)				
Albumin	3·06 ± 0·52 3·50 ± 0·74 *(14)* P<0·1	3·08 ± 0·53 3·82 ± 0·56 *(9)* P<0·01	3·81 ± 0·40 4·00 ± 0·56 *(9)* P<0·5	4·12 ± [illegible] 4·13 ± 0·31 *(7)* P<0·3
Globulin	3·14 ± 0·93 3·44 ± 0·92 *(14)* P<0·5	3·04 ± 0·71 3·23 ± 0·88 *(9)* P<0·7	2·80 ± 0·69 3·02 ± 0·83 *(9)* P<0·3	[illegible] 2·41 ± 0·50 *(7)* P<0·1
Total	6·17 ± 1·01 7·04 ± 1·00 *(14)* P<0·2	6·16 ± 1·46 7·06 ± 1·28 *(9)* P<0·3	6·50 ± 1·03 7·01 ± 0·55 *(9)* P<0·3	6·15 ± 0·10 6·57 ± 1·13 *(6)* P<0·4
Serum bilirubin (mg per 100 ml)	0·72 (0·1–1·3) 1·16 (0·2–1·3) *(10)*	0·79 (0·1–1·3) 0·56 (0·2–1·3) *(10)*	0·85 (0·1–1·4) 1·10 (0·5–2·0) *(5)*	1·22 (0·3–1·4) 0·68 (0·2–1·1) *(6)*
Alkaline phosphatase (units per 100 ml)	13·5 (3–66) 17·2 (3–45) *(14)*	18·7 (3–66) 18·1 (3–31) *(9)*	11·9 (5–15) 9·5 (5–10) *(5)*	9·0 (5–17) 9·8 (4–15) *(5)*

Values given are means ± S.D. or range, upper values preoperative, lower values postoperative. Number of cases in italic numerals in parentheses.

P values for difference between mean results at *x* years and before operation calculated by "Student's" *t* test.

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Printing of The Lancet

Now that work is being resumed in the London printing houses, the Proprietors of THE LANCET wish to thank subscribers for their forbearance while the journal could be issued only in token form As soon as possible it will be restored to its normal appearance and size, and the Proprietors will announce arrangements to be made in compensation for the deficiencies of recent weeks

Quality of Marriage

THE Royal Commission on Marriage and Divorce were asked to have in mind "the need to promote healthy and happy married life and to safeguard the interests and well-being of children" The most constructive and original of their recommendations[1] suggest new ways of protecting children and of preventing and repairing broken marriages

They are concerned at the sharp increase in the number of divorces during the last 20 years—27,471 in England and Wales in 1954 compared with 4735 in 1937—but they do not believe that marriage will be saved by making divorce more difficult Indeed they are evenly divided on whether the final breakdown of a marriage should not be recognised as grounds for divorce Of the nineteen members, nine recommend that when a husband and wife have lived apart for 7 years either spouse should be able to obtain a dissolution of the marriage provided the other spouse does not object Four of these members are prepared to waive the second spouse's consent if the separation can be shown to be due to his (or her) unreasonable conduct This method would make it unnecessary for people to commit a matrimonial offence in order to get a divorce, and would obviate the (often untrue) assumption that one spouse is more to blame than the other

Turning to a problem raised by an advance in medical technique, the commission hold that a wife who accepts artificial insemination by a donor without the consent of her husband is doing him a grave injury which should be recognised as a ground for divorce On the other hand they propose that a husband and wife who agree to artificial insemination, with the semen either of the husband or of a donor, should no longer be able to seek a decree of nullity Another new ground for divorce which has their unanimous support is detention in an institution for 5 years of a spouse who is a mental defective with dangerous or violent propensities They also recommend that, irrespective of the voluntary or other status of the patient, care and treatment in any institution recognised for the treatment of mental illness shall be acceptable as grounds for divorce, and that continuity of treatment shall be held to be maintained so long as the patient's name is retained in the hospital's current records If the patient discharges himself or is discharged but is readmitted to hospital within 28 days, continuity of treatment will also be held to be preserved Subject to these relaxations, they agree that the length of the period of care and treatment should remain at 5 years

Throughout their report the commission point out that their recommendations should be complemented by improved facilities for education, guidance, and conciliation Stepping frankly outside their terms of reference, they propose the development of a carefully graded system of education to fit young people for "marriage and family life," and they ask the Government to set up a body to review the marriage law and arrangements for premarital education and training Present facilities for marriage conciliation they temperately describe as "limited" Proposals to provide legal advice as well as legal aid have not yet been implemented, though 1s spent on advice might well later save £1 on aid The commission believe that this gap should be made good as soon as possible They are anxious that attempts at conciliation should continue to the last possible moment, and fourteen members think that a trial period of conciliation of up to a month should be allowed in cases of desertion and adultery without destroying the grounds for divorce where the trial fails

Every year some 20,000 children under 16 are affected by the divorce of their parents To ensure that this problem is brought home to the parents the commission suggest that a decree should not be made absolute till the court is satisfied about the arrangements made for the children's future This procedure would make clear that the interests of the children are as important as the divorce This constructive proposal illustrates the commission's conviction that, though divorce ends individual marriages, it can yet be one of the buttresses of marriage

Prophylactic Isoniazid

THE successful use of isoniazid in established tuberculosis and the low toxicity of the drug, have prompted the suggestion that it be used prophylactically If isoniazid given at the time of the initial infection prevents the development of tuberculosis, then the drug might be administered to uninfected persons exposed for short periods to a considerable risk of infection To be successful, however, a prophylactic should not only have a low toxicity but it should also either kill all the infecting bacilli or allow the development of a degree of immunity at least as great as that produced by B C G vaccination and it is as yet doubtful whether isoniazid does either of these things

FEREBEE and PALMER[1] have recently reported an experiment designed to test the preventive action of isoniazid in experimental tuberculosis About 1200 guineapigs were given isoniazid, and then infected intraperitoneally with about 5 million virulent tubercle bacilli Treatment with isoniazid was then continued for ten weeks The mortality among the group given 5 mg or more of isoniazid per kg body-weight was the same as in the uninfected control group The treatment of some animals was then stopped for four weeks, after which they were challenged for the second time with the same number and strain of tubercle bacilli To this second infection they showed a degree of immunity similar to that achieved by B C G vaccination of normal animals FEREBEE and PALMER did not investigate or discuss the mechanism responsible for immunity

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[1] Royal Commission on Marriage and Divorce Report 1951–55 Cmd 9678 H M S O 1956 Pp 405 11s 6d The chairman of the commission was Lord Morton and the medical members were Sir Russell Brain P R C P and Dr May Baird

[1] Ferebee S H Palmer, C E *Amer Rev Tuberc* 1956, 73, 1

3. The survival rate after portal systemic venous anastomosis is not significantly better than that in the control series. In its present state the series treated by portal systemic anastomosis is unfavourably weighted by two factors: (1) the use in 12 of the first 14 cases of the Blakemore Lord tube, which has been found to be so commonly followed by constriction or obliteration of the anastomosis that it has been discarded; and (2) a high postoperative mortality during the first 3-4 years of the period under review, when patients who would not now be considered justifiable risks (for example, because of fluid retention and gross ascites) were submitted to operation. Over the whole period there have been 12 deaths in the immediate post-operation period—a mortality-rate of 18%—but in the 4 years ended December, 1955, 36 operations were performed with only 3 deaths (8%). These considerations give us some reason to expect that a report on a larger number of cases in a few years' time will show an improvement on the present figures.

Cause of Death

20 patients died during the period of observation. The principal causes of death (table VII) were hepatic failure, hæmorrhage, and the effect of complications of operation. Usually there was more than one cause, hæmorrhage or operation precipitating the onset of hepatic failure in a patient with a severely damaged liver. 2 patients suffered from tuberculosis after operation and both recovered—a man aged 47 years from pulmonary tuberculosis 1 year after operation, and a girl aged 13 years from miliary tuberculosis 4 years after operation.

TABLE VI—COMPARISONS OF RESULTS OF TREATMENT

Period (yr.)	No. of patients exposed	Survivors	No. of patients exposed	Survivors	P*	P†
	MAYO CLINIC: ALL CASES OF CIRRHOSIS		PRESENT SERIES: ALL CASES TREATED SURGICALLY			
1	371	215 (57·5%)	64	50 (78·1%)	<0·01	<0·01
3	371	158 (42·2%)	54	37 (68·5%)	<0·05	
5	104	34 (32·5%)	30	12 (40·0%)	<0·5	
7	56	11 (19·6%)	11	2 (18·2%)	<0·9	
	MAYO CLINIC: ALL CASES OF CIRRHOSIS WITH HÆMORRHAGE		PRESENT SERIES: ALL CASES WITH HÆMORRHAGE BEFORE OPERATION			
1	67	36 (53·7%)	44	32 (72·7%)	<0·05	<0·[illegible]
3	67	31 (46·3%)	35	18 (51·4%)	<0·7	
5	36	11 (30·6%)	24	10 (41·7%)	<0·5	
7	14	3 (21·4%)	10	2 (20·0%)	<1·0	
	MAYO CLINIC: ALL CASES OF CIRRHOSIS WITH HÆMORRHAGE		PRESENT SERIES: CASES WITH HÆMORRHAGE TREATED BY PORTAL SYSTEMIC VENOUS ANASTOMOSIS			
1	67	36 (53·7%)	22	13 (59·1%)	<0·7	<0·7
3	67	31 (46·3%)	20	11 (55·0%)	<0·5	
5	36	11 (30·6%)	14	6 (42·9%)	<0·5	
7	14	3 (21·4%)	7	2 (28·6%)	<0·8	
	PRESENT SERIES: ALL CASES TREATED BY PORTAL SYSTEMIC ANASTOMOSIS		PRESENT SERIES: ALL CASES TREATED BY SPLENECTOMY ALONE			
1	26	16 (61·5%)	27	26 (96·3%)	<0·01	<0·05
3	24	13 (54·2%)	23	14 (60·9%)	<0·5	
5	15	6 (40·0%)	9	4 (44·4%)	<0·9	
7	7	2 (28·6%)	2	0	<0·9	
	PRESENT SERIES: CASES WITH HÆMORRHAGE BEFORE OPERATION (a) PORTAL SYSTEMIC ANASTOMOSIS		(b) SPLENECTOMY ALONE			
1	22	13 (59·1%)	16	15 (93·75%)	<0·02	<0·2
3	20	11 (55·0%)	14	6 (42·9%)	<0·5	
5	14	6 (42·9%)	8	3 (37·5%)	<0·8	
7	7	2 (28·6%)	2	0	<0·9	

P* = Probability of difference in numbers surviving in each exposure period being due to chance alone: calculated from χ^2 distribution (Fisher 1950).

P† = Probability of difference in numbers surviving in whole series being due to chance alone.

TABLE VII—CAUSES OF DEATH (20 CASES)

Causes	No. of cases
Hepatic failure:	
Primary, due to progress of disease	4
Following operation	8
Precipitated by hæmorrhage from varices	13
Complications of operation:	
Mesenteric thrombosis	2
Leakage at œsophagogastric anastomosis	1
Hæmorrhage at the site of operation	1

Intercurrent infection, except as a complication of operation, was not the cause of death in any instance.

Conclusions

The limitations of our analysis must be acknowledged. The number of cases is not large, and in the majority the period of observation has been relatively short. The heterogeneity of the group we believe to be balanced by the series which we have accepted as a control; and so far as we can ascertain, the only important variable in treatment has been the application of major definitive surgery in the cases we have reported. Finally, the statistical method is necessarily concerned with an impersonal analysis of the whole problem of portal hypertension as it has been presented. The individual patient seldom conforms to the mean of a series. Nevertheless, statistical analysis of the results of treatment in a changing pathological condition can provide guidance in particular cases, because it takes account of the failures as well as the successes, of the lapse of time since the treatment was undertaken, and of the natural history of the disease.

The following tentative conclusions have been drawn from our data:

1. Gastro-œsophageal bleeding is more likely after operation for portal hypertension associated with hepatic disease when it has been a presenting feature of the condition. Splenectomy alone is not the elective operation when there has been hæmatemesis or if œsophageal varices can be demonstrated, but is a satisfactory procedure when splenomegaly and hypersplenism are the presenting features. A portal systemic anastomosis which remains patent does appear to provide some additional protection against recurrence of bleeding; but further evidence from a larger series and a longer period of observation is required, because the onset of bleeding may be long delayed after such an anastomosis has been occluded by thrombosis. Limited œsophagogastrectomy appears to be a satisfactory method of treating recurrent bleeding after other operations.

2. Hepatic function was maintained in patients who survived 5 or more years after operations which sometimes involved deviation of all portal blood from the liver by portacaval anastomosis. In most instances, these were patients whose hepatic function was not greatly impaired before operation. When there is ascites or other evidence of severe hepatic dysfunction, operation should be postponed. If the indications for operation are urgent, the smallest procedure appropriate to the circumstances should be performed.

3. The leucopenia and thrombocytopenia which are characteristic of portal hypertension can be corrected immediately by splenectomy, and follow-up for 5 or more years shows that the improvement is maintained. Sometimes the power of resistance to infection has been noticeably increased after splenectomy. The anæmia usually responds rapidly to large doses of iron and to reduction in the frequency and severity of alimentary bleeding.

4. Statistical comparison of a series of patients treated medically with a series treated by operation in addition shows that the survival rate is slightly, but for the most part not significantly, better in the patients submitted

namely, that the pathogenesis of both clinical signs and changes depends largely on the nature and extent of the tigen antibody clash within the theca

TRIBUTE TO SIR THOMAS FAIRBANK

In a special issue of the *Journal of Bone and Joint Surgery,*[1] tive both in contents and in size, British orthopædic rgeons offer their affectionate tribute to Sir Thomas Fairbank his eightieth birthday For more than half a century he s enriched their branch of surgery, not only through his aching and publications, but also by his human qualities of ndness, understanding, and readiness to help selflessly and thout ostentation

This volume is a worthy tribute The subjects range from a storical review of British orthopædic surgery, a field in which homas Fairbank has already taken a permanent place, to rare seases of the skeleton, a subject in which he is today the orld's greatest authority St J D Buxton and Julian ylor have undertaken what must have been a labour of love, biographical appreciation of Thomas Fairbank the man, the rgeon, and the soldier, and Sir Reginald Watson Jones troduces the volume with the quotation "I will never be an d man, to me old age is always fifteen years older than am"

Sir **Russell Brain** has been re elected president of the oyal College of Physicians of London for the coming year

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[1] *J Bone Jt Surg* February (1956 38B 1 436) Published by E & S Livingstone, 16 Teviot Place Edinburgh, 1 £2, bound copies £2 5s

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In the Mental Hospital*

WORK THERAPY

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There is general agreement about the need to keep ven chronic regressed patients occupied where possible, ut, like so many other aspects of mental-hospital life, he different approaches to occupation have, as yet, een little studied We are still applying methods largely ccording to personal conviction, without a thorough nderstanding of what we are doing

The occupation offered to patients is, broadly speaking, f two kinds they may spend some part of their time n handicrafts in the occupational-therapy department, or hey may spend more regular hours on productive work f a patient is too ill to perform any but very simple asks, occupational therapy as given in most mental ospitals may help If his interest can be obtained in ome simple or familiar work, and particularly if the ccupational therapist can enter into a supportive relaionship with him, even the most elementary occupation nay be therapeutic it may bring out and direct controctively a variety of emotions which have been denied utlet, and it may do something to offset the restrictions f the mental hospital régime As now usually practised, owever, occupational therapy cannot claim the rehabiliative effect of productive group work, which is capable f leading to better contact with reality, to behaviour nore in accordance with social standards, and to the oundations of self esteem

In a simple form productive work has long been offered in most, if not all, mental hospitals, where patients help in the kitchen, laundry, or farm In some more progressive hospitals these essential services have been reorganised to offer patients a wider range of occupations From this in turn have developed experiments in the creation of workshops within the hospital, where patients are employed under near-factory conditions Because this more positive use of group work as a form of therapy is still largely empirical, our experience at the Social Rehabilitation Unit at Belmont Hospital may be worth describing in the present series of articles

A SLOW START

For some years we had great difficulty in persuading our patients with character disorders and poor employment records to show any interest or enthusiasm in the workshops They resisted the idea of work no matter how necessary this might seem to the staff Even when we pointed out that the work was valuable for the whole unit, we did not arouse enough interest and support to make the workshops function well Moreover the patients resented the absence of any money incentive

We had started off with the rather vague idea that the workshops should have some relation to future work and training for a job With this end in view we sought advice from the Ministry of Labour, who were most helpful At that time, soon after the late war, the building trades were short of trainees and we were advised to establish three working groups under the supervision of a trained bricklayer plasterer, and carpenter To this we added the occupations of hairdressing, gardening, and tailoring We avoided handicrafts for the men and chose something more related to ordinary work But, though a certain amount of useful building was done and the other workshops had their willing workers, the patients as a whole continued to grumble about the work programme, and we ourselves were diverting a great deal of energy into developing other community methods of treatment At that time we tended to think of the occupations as a preparation for training in those particular trades In retrospect, however, it seems clear that we never really expected that they would be of much use in helping the patient to choose a trade or as early training for it

During the last three or four years conditions have changed despite these difficulties We have become increasingly aware that patients will not take an active part in work therapy unless they are interested and identify themselves with the workshops We came to realise that the work would become meaningful to the patients only when the tasks met some of their fundamental needs

Because we were housed in a neglected bomb-damaged building, there was a real need to redecorate the rooms to make our home more cheerful The rooms contained many broken-down pieces of furniture which urgently needed attention if we were to have any pride in our surroundings, let alone any comfort Again, many of the patients were destitute and received only *7s 6d* a week pocket-money from the National Assistance Board so they needed new clothes or at least repair of those they had Also, their monotonous diet could be varied by growing more vegetables By forming a home group, we shifted the emphasis from prevocational training to work to meet the more urgent needs of the community Now we have five groups—furniture repair, painting and decorating, gardening, tailoring, and home groups—all engaged on tasks relevant to the needs of the community, and the patients' attitude to work has changed In observing the social processes within the groups we have been helped by weekly workshop discussions, which were suggested by the patients themselves These are attended by the patients, the social therapists who work with them alterations of urinary excretion of electrolytes during the first three days' treatment Of these 10 patients 3 gave no significant renal response to acetazolamide and showed neither a diuresis nor a loss of weight In the remaining 7 patients the cumulative increments of urine flow were 1 1–6 4 litres The increase in daily volume of urine appeared to be closely related to the increase in urinary excretion of sodium which was 64–624 m eq by the third day

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* A group of articles chiefly concerned with the value of active occupation and work for mental patients and the means whereby it is best provided

The increase in urinary excretion of sodium and potassium was in most cases about the same as the increase in excretion of bicarbonate, which averaged 119 m eq after twenty-four hours and 159 m eq after seventy-two hours Only cases 9 and 10 showed a satisfactory diuresis and clinical response to acetazolamide, and in both these patients the increase in urinary excretion of sodium was accompanied by approximately equal increments in the urinary excretion of both bicarbonate and chloride

Comparison of Effects of Mersalyl and Acetazolamide

Fig 2 shows details of the daily volume of urine and urinary excretion of electrolytes in 15 patients with congestive heart failure, each of whom had three to ten days' treatment with acetazolamide and with mersalyl alternately Acetazolamide 0 25–1 00 g was given either daily or on alternate days and mersalyl 2 ml on alternate days in most cases, but in some on successive days, each injection being preceded by an oral dose of ammonium chloride 2–4 g A representative example of the dosage schemes used is shown in fig 3 The data in fig 2 are the averages of all the days on which each drug was administered and thus represent the net effect of the diminishing response to acetazolamide, as already described

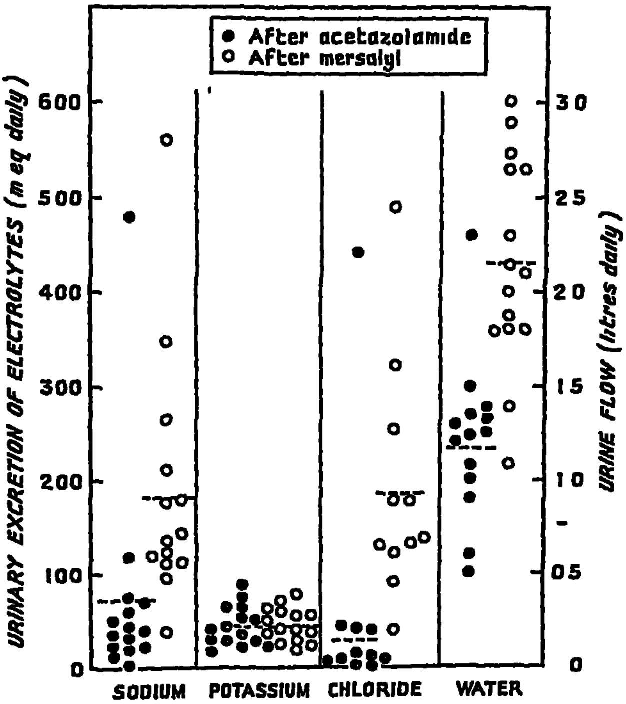

Fig 2—Average daily urinary excretion of water and electrolytes by 15 patients treated with acetazolamide and mersalyl horizontal lines represent mean values for all patients

In the group as a whole the diuresis effected by mersalyl was considerably greater than that caused by acetazolamide the average daily volume of urine of the 15 patients was 1 2 litres during treatment with acetazolamide and 2 2 litres during treatment with mersalyl The average daily urinary excretion of sodium was 182 m eq under treatment with mersalyl but only 73 m eq under treatment with acetazolamide The average daily urinary excretion of potassium caused by each diuretic was 44 m eq (fig 2) The dependence of the diuretic effect of both drugs on increased urinary excretion of sodium is illustrated by the results in 2 patients with hypertensive heart failure (fig 4) whose daily intake of fluid was strictly limited to 1 5 litres each

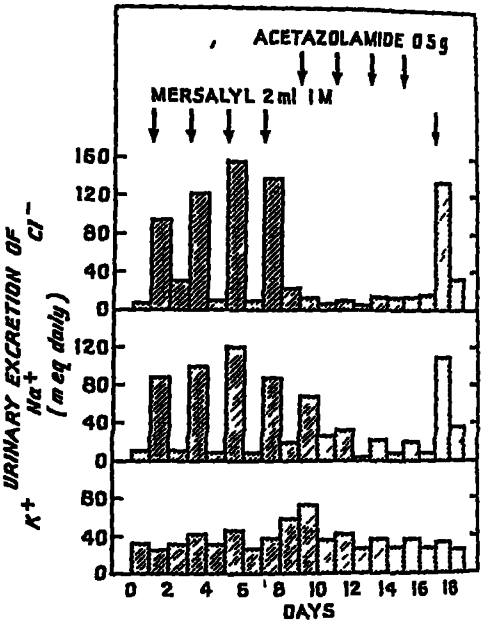

Fig 3—Comparison of effects of acetazolamide and mersalyl on urinary excretion of electrolytes in a representative patient.

Judged by loss of weight and by the decrease of oedema and venous pressure, the therapeutic effect of acetazolamide was inferior to that of mersalyl in 12 of the 15 patients 5 patients gave no response whatever to acetazolamide, 1 of these was also almost wholly resistant to mercurial diuretics 2 patients who had a large diuresis and a good therapeutic effect from acetazolamide also had an exceptionally good result from mersalyl

Fig 3 illustrates a representative example of the changes in electrolyte excretion brought about by

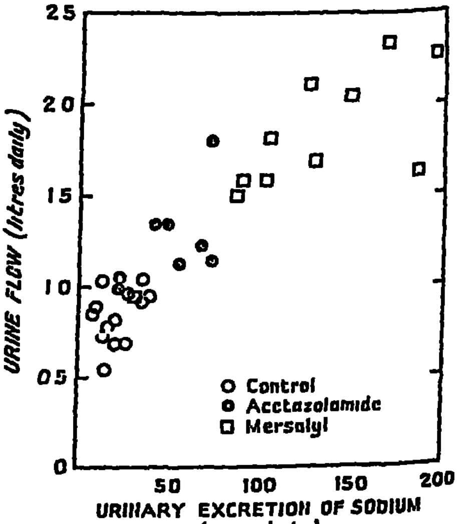

Fig 4—Urine flow and urinary excretion of sodium in 2 hypertensive patients with heart failure during control period (no treatment) and under treatment with acetazolamide and mersalyl

Special Articles

LLULOSE ACETATE FILMS AS A SUBSTITUTE FOR GLASS SLIDES IN HISTOLOGY

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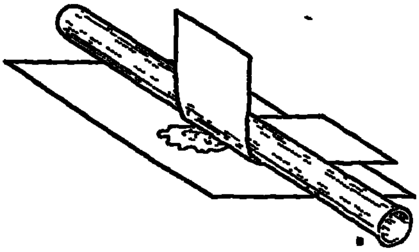
M D
om the Department of Pathology, University of Ottawa, Canada

ALTHOUGH plastic materials are commonly employed
r mounting large pathological specimens, they do not
em to have been adopted in histopathology The
ea of using cellulose acetate film as a substitute for
ass slides was borrowed from photography and radio-
gy, where the cost and bulk of glass plates caused their
andonment a long time ago The lightness and
mpactness of plastic are properties which commended
as a mount for microscopic sections, especially where
ts of slides were to be used for teaching Furthermore,
astic slides could be mailed in ordinary paper envelopes



g 1—Covering section mounted on a film slide with a strip of Scotch tape, using a test-tube as a roller

ccordingly an attempt was made to discover whether
ides made from strips of cellulose acetate are accept-
ble for histopathological preparations—strips of Scotch
ape being used instead of cover slips

rocedure

The photosensitive emulsion is removed from ordinary
-ray films by soaking them in hot water The film is
hen cut into strips 5 cm wide and placed in a 50%
olution of concentrated hydrochloric acid for two to
ve hours to remove the residue of the gelatin base
fter this the strips are washed well in tap water, dried,
nd cut into 6 5 cm lengths

The tissue sections are floated in a waterbath in the
sual way and picked up on the film slides Adhesives
gg albumen or gelatin solutions) are not necessary,
ecause capillary tension is sufficient to hold the section
the slide The film slides are allowed to dry and
laced in the spool of a universal ' Kodak ' film develop-
ng tank, where they undergo deparaffinisation, washing,
taining, dehydration, and clearing in the normal way
or deparaffinisation and clearing a variety of agents,
ncluding toluol, xylol, and benzene, give equally good
esults After staining and clearing, a piece of Scotch
ape (transparent adhesive plastic) 3/4 in wide is
mmersed in a clearing agent until the adhesive material
ecomes swollen and rolled over the film slide bearing
he mounted tissue section this is done with a test
tube, exerting even pressure (fig 1) The covered film slide is allowed to dry for a short while, wiped with a cloth, dipped into the clearing agent to remove the excess adhesive, and then trimmed

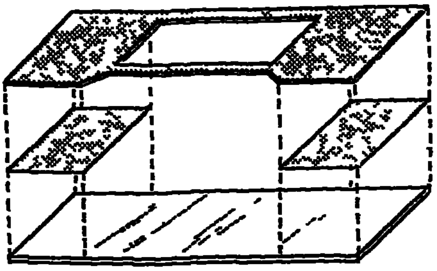


Fig 2— Exploded view of the viewing frame

Because the film slides are neither flat nor rigid, a frame was made to hold them while they were being examined under the microscope An "exploded" view of the frame is shown in fig 2

Two small rectangular pieces of uncleaned X ray film were glued to opposite ends of a glass slide leaving a space between them 5 cm long (the width of the film slide) Over this was glued a piece of strong, thin cardboard the same size as the glass slide, with a window 22 mm × 40 mm cut out of its centre When viewing, the film slide is pushed into the slot between the cardboard and the glass slide

Results

Under the microscope, tissue sections prepared in this way had the same appearance as sections on glass slides Scotch-tape covers were also found to be satisfactory when used with glass slides, and no difficulty arose when sections thus covered were examined with the oil-immersion objective The cellulose-acetate films were not affected by any of the reagents and stains in common use The material had sometimes been scratched during the removal of the emulsion, but the scratches were not usually seen when the sections were in sharp focus

Slides prepared in this fashion and kept in an ordinary slide box at room-temperature for four years have shown very little change The very slight clouding of the Scotch-tape adhesive does not interfere appreciably with examination of the sections The tissue shows no drying nor is there fading of the stain ; the Scotch-tape covers remained flat on both glass and film slides The microphotograph in fig 3 was taken when the preparation was two years old, and it has shown no change since then

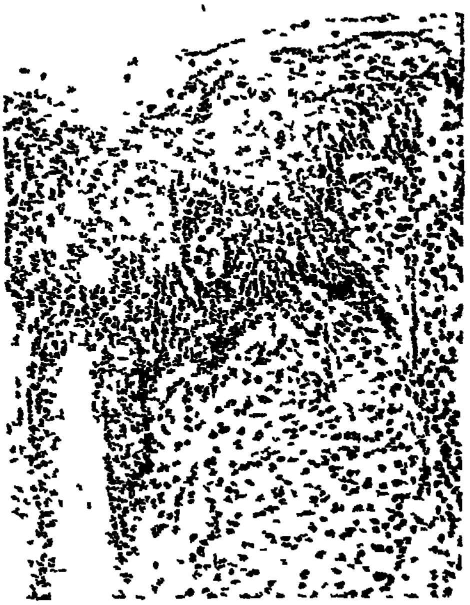


Fig 3—Chronic cervicitis Cellulose acetate film with Scotch tape cover (Hematoxylin and eosin × 485)

The main disadvantages of the use of these materials are the tendency of the film slides to curl slightly which, however, can be overcome by using the simple viewing frame described) and the slight clouding of the Scotch-tape adhesive Perhaps, if there were a need for it, an adhesive could be devised which would remain clear

The advantages include cheapness, ease of storage, and particularly convenience of transport, since they are light and unlike glass, need no protective packing

HÆMATEMESIS

CONTROLLED BY ADRENALINE AND STYPVEN

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"The effort to distinguish those patients who would recover without timely operation from those who would die without it has not been unsuccessful and still proceeds" (Aird 1949)

Any discussion on the treatment of gastroduodenal hæmorrhage still tends to resolve itself into arguments for and against surgical intervention Meulengracht (1935) was primarily responsible for the slow acceptance of surgical treatment, and he accomplished it with a single sentence "I consider a mortality of 1 or 2 per cent on dietary medical management makes the question (of operation) unreal to me and relieves me of the responsibility of having to decide in an individual case whether operation is advisable or not" (Aird 1949) It is very tempting to follow such a guiding principle, which says in effect "do nothing apart from performing a few simple rites, never make a decision, and salve your conscience with the knowledge that you will have achieved the best possible results" With this stroke, Meulengracht left his rivals, Gordon-Taylor and Finsterer, crying like voices in the wilderness What chance had a gospel of decision and selective action against an appeal such as this!

As so often happens, the truth lies somewhere between the diametrically opposed views, and it is now recognised that there is "an irreducible minimum of 10 per cent of sufferers from serious hæmorrhage who are condemned to death by the refusal of operation or by delay in advising it" (Aird 1949)

The crux of the problem is how to identify at an early stage the patient with "surgical" hæmatemesis, who is "bleeding from an artery of anatomical size fixed in scar tissue at the base of a chronic ulcer" (Ogilvie 1955) This cannot always be done with certainty, but the selection of patients for operation has been simplified by a slight bending of the facts to provide a clear-cut criterion for surgery, based on a logical conception of the underlying pathology Working on an 80% probability, the indications for operation are repeated or continued bleeding during medical treatment, middle age, a history of previous hæmorrhage, and pain preceding hæmorrhage Of these indications the first is naturally the most important, but, unfortunately, equally copious and repeated bleeding can result in the early stages from an acute lesion, and an acute lesion can be the real source of bleeding, though a chronic lesion is present as well

It is a pity to ablate the greater portion of an otherwise healthy stomach because of an acute transient lesion, or to operate on a quiescent chronic lesion at a time when the patient is least suited to undergo operation It is even more humiliating when the lesion comes to lie on the wrong side of the gastric resection and is demonstrated subsequently at necropsy These unhappy possibilities are covered by a bald though inaccurate statement that the bleeding from an acute lesion is never severe enough to be alarming If emergency surgery is undertaken in every case of serious and repeated bleeding, it means that a larger proportion of cases will be exposed to a risk by no means negligible in patients of this age and in this condition Surgery would be better confined to those patients who can be saved only by operation

TABLE I—NO OF PATIENTS ADMITTED AND MORTALITY RATE

Year	No of patients admitted	No of deaths and mortality rate
1950	68	8 (*12 1%*)
1951	79	10 (*12 6%*)
1952	79	9 (*11 4%*)
1953	93	9 (*9 7%*)
1954	92	6 (*7 6%*)

This leaves the discussion evenly balanced, the physician may lose a patient who could have been saved by surgery, and the surgeon may lose one by early operation who would have recovered spontaneously

Review of Past Experience

This review covers a period of five years (1950-54) during which time all cases of hæmatemesis were regarded as medical problems, and only those patients needing surgical treatment were referred to us by the physician

Table I shows the number of patients admitted to the Law Hospital with frank hæmatemesis and it also shows the total mortality-rate Like Tanner (1950), I feel that the total mortality-rate is a true index of therapeutic success, which depends on the closest liaison between physician and surgeon

Table II includes only those patients who had simple gastroduodenal lesions which failed to respond to medical treatment The figures quoted are *statistically* insufficient, but they provide a basis for discussion

TABLE II—PATIENTS TRANSFERRED TO SURGICAL WARD AND THE RESULTS OF OPERATION

Year	No of patients transferred to surgical wards	No of patients with chronic ulcers	No of patients with acute lesions	No of emergency operations	No of delayed elective operations	No of postoperative deaths	No of non-operative deaths	Total no of deaths
1950	3	2	1	3	0	1	0	1
1951	1	1	0	1	0	0	0	0
1952	8	7	1	8	0	4	0	4
1953	16	11	5	2	7	0	2	2
1954	11	7	4	2	5	0	0	0

These tables cover a period from routine medical treatment (1950 and 1951), through a period of this treatment combined with emergency gastrectomy (1952) to the present method, started in 1953 and finally established in 1954

Table I shows that there was no significant change in the over-all mortality-rate until 1954, and table II shows that nearly the same number of patients died in 1952 as in previous years, but that a higher proportion did so in my surgical wards

By the beginning of 1953 I became convinced that emergency gastrectomy was not the solution in the late stages of hæmorrhage A mortality rate of 50% in these cases compared with under 2% for 276 elective gastrectomies was disquieting No patient presented an insuperable technical difficulty and all had been prepared, and treated postoperatively, on recognised lines In the late stages of hæmorrhage, adequate restoration of blood volume with control of the bleeding by operation was not always successful, and it occurred to me that if I could devise some means of controlling the bleeding till a full physiological stabilisation could be attained, the results of operation would be more favourable In other words, I could choose the time and conditions for attack

Adrenaline and Stypven

The most feasible solution appeared to be a powerful styptic which could be given safely by mouth I had seen Russell's viper venom ('Stypven') used some years previously by my colleague, Dr J Bryant, in perfect safety, but with equivocal results It struck me that the reasons for its uncertain action were its inability to produce an occlusive clot in the presence of active bleeding and the unlikelihood of its entering the duo

Letters to the Editor

Tuberculosis Then and Now —Your annotation (Feb 11) s already been admirably answered by Dr Macdonald eb 25)

Most of your criticism seems to be based on comparison th the present state of other specialties Is it true that there no place for a comprehensive neurological service or a skin rvice or a heart service? Why should these ideas appear congruous except from the standpoint of our grandparents? In this city of 508,000 inhabitants, the notified deaths in 55 from three respiratory diseases were as follows bronchitis 3 pulmonary carcinoma 270, respiratory tuberculosis 67 f the 385 deaths from chronic bronchitis, the majority were the 65–75 age group (132 men and 52 women), and it would ot be unfair to assume that the men had on an average been nable to work for 10 years before they died Surely this is a ocial problem of some magnitude

Since 1948 we have been trying to run a comprehensive ealth service Why quibble at a comprehensive chest service? –A R BUCKLEY, M.R C P (Leeds Chest Clinic)

"Infectious Roseola"—In reply to Dr Keizer (Jan 21), the iagnosis of dengue fever was considered but thought unlikely for he following reasons no initial rash and no secondary rise of emperature on appearance of rash, no bradycardia, joint ains not a feature, rash unlike in appearance and initial istribution, usually no desquamation, no *Aedes ægypti* in he locality —F R FLETCHER, M.R C P (Folkestone)

Inguinal Herniorrhaphy —In this correspondence I have een disappointed to find *no* reference to the work of W J ytle (*Brit J Surg* 1945, 32, 441) May I suggest to Mr Doran that, in case of simple oblique inguinal hernia, after xcising and ligaturing the sac without disturbing the spermatic cord unnecessarily, he gets his anæsthetist to make the patient cough I think he will find that the upper fibres of the arch of the internal oblique muscle do in fact exert a partial shutter action —OWEN WILSON, F R C S E (Bangor)

Sulphonamides and Hypoglycæmia —A few days after reading your leader (Jan 28) I came across the following case

A girl, aged 6 years with mild infection of the upper respiratory tract was given sulphadiazine 0 5 g four times daily Her mother reported afterwards that for two nights running while taking the drug the girl woke up with palpitation, cold sweat, and a feeling of hunger After she had eaten some food the symptoms slowly subsided She had never before had such attacks

The description of the attacks is obviously consistent with hypoglycæmia —E SILBIGER, M D (Beersheba, Israel)

Patent Ductus Arteriosus —With reference to your leading article (March 10) we would like to draw attention to our recent paper on Patent Ductus Arteriosus with Pulmonary Hypertension (*Thorax* 1955, 10, 338) In this we reviewed 9 severely disabled children, aged 1–6 years, with symptoms of this syndrome dating from birth or very early infancy All were subjected to ligation or division of the ductus, and, with 1 exception, in which there was reversal of blood flow through the ductus, all were much improved thereafter 6 of the children were re catheterised at various intervals after thoracotomy and were found to have normal pulmonary arterial pressures and peripheral pulmonary vascular resistances

We concluded that the pulmonary hypertension was secondary to patency of the ductus with increased pulmonary blood flow Therefore, provided reversal of blood flow through the ductus is not present, it would appear that early operative treatment in these cases is essential to prevent irreversible changes in the pulmonary vessels —IAN M ANDERSON, M.R C P, H M T COLES, M.R C.P (Westminster Hospital, London, S W 1)

News

Sir James Paterson Ross and Prof W Melville Arnott have been appointed Sims Commonwealth travelling professors for 1957

Prof Carl Semb of Oslo will give a Moynihan lecture at the Royal College of Surgeons of England on Friday, April 20 at 4 P M on Partial Resection of the Kidney

Dr G S W Organe Dr B R M Johnson and Dr A I P Brown have been elected to the board of the Faculty of Anaesthetists of the Royal College of Surgeons of England

Under the Therapeutic Substances (Control of Sale and Supply) Regulations, 1956, which come into force on March 31, bacitracin, and tetracycline and viomycin and their salts are brought within the scope of the Penicillin Act, 1947, under which they may be supplied only on prescription

Mr L N Pyrah has been elected to a personal professorship of urological surgery in the University of Leeds Prof Digby Chamberlain professor of surgery in the university, has been elected to the the chair of clinical surgery

Dr F Avery Jones will give the Lumleian lectures on Tuesday and Thursday April 10 and 12 at 5 P M at the Royal College of Physicians of London Pall Mall East S W 1 on Clinical and Social Problems of Peptic Ulcer

The annual congress of the Ophthalmological Society of the United Kingdom will be held at 1, Wimpole Street London, W 1, on Thursday Friday and Saturday April 26 27 and 28, under the presidency of Mr O Gayer Morgan

Surgeon Captain H M Willoughby, R N V R has been appointed honorary physician to the Queen in succession to Surgeon Captain J B Oldham

The Association of Surgeons of Great Britain and Ireland is to hold its annual meeting at the Royal College of Surgeons of England, Lincoln s Inn Fields London W C 2, on April 19–21, under the presidency of Sir Clement Price Thomas

In Blackpool schools liquid milk has been replaced by milk tablets (*Times* March 16 see *Lancet*, Feb 25, p 302)

Dr J H Edwards has been appointed lecturer in social medicine in the University of Birmingham

The following have been admitted to the fellowship of the Faculty of Radiologists C V Cimmino T J Deeley, C J Don Philip Jacobs G A S Lloyd B F Vaughan, R W Wilkinson W C Woods

The Minister of Health s policy on comprehensive health centres is explained in a letter to London County Council The Minister is averse to the acquisition of sites long before they are needed and future centres should be considerably smaller than that at Woodberry Down Centres says the Minister should secure the closer association of the local health authority services with other services especially the general medical services and generally conditions for a centre will be suitable only in large new housing areas London County Council has agreed in principle to release sites reserved for comprehensive health centres except parts needed for local authority services

On Wednesday April 4, at 5 30 P M, Sir Henry Dale O M F R S will open the Wellcome Museum of Orthopædics at 234, Great Portland Street London W 1 The museum which is part of the Institute of Orthopædics will be open daily to students and other medical visitors The first exhibition on the pathology of bones and joints will be held from April 5 to 27

New fellows of the Royal Society include the following members of the medical profession Dr Hans Grüneberg reader in genetics University of London Dr C S Hallpike, director of the otological research unit of the Medical Research Council, Dr R G Macfarlane Radcliffe lecturer in hæmatology University of Oxford, and Dr W D M Paton professor of pharmacology Royal College of Surgeons of England The list also includes Mr Arthur Wormall D SC professor of chemistry and biochemistry St Bartholomew s Hospital Medical College

The annual general meeting of the Mental After Care Association will be held on Thursday April 19 at 3 P M, at Caxton Hall, Caxton Street S W 1 when Sir Russell Brain P R C P will speak

The British Psycho Analytical Society, to mark the centenary of Freud s birth is holding a series of six lectures on Psycho analysis and Contemporary Thought The lectures will be given at Friends House Euston Road London N W 1 at 8 30 P M on Tuesdays and Fridays beginning on April 13 The lecturers will include Dr D W Winnicott Dr Elliott Jaques, and Dr John Bowlby

Births, Marriages, and Deaths

DEATHS

MONTGOMERY —On March 22, at Bournemouth, Thomas Robson Montgomery, M D Lond M R C P senior physician Royal Victoria and Bournemouth Hospital and Christchurch Hospital

Vacancies

ACADEMIC AND EDUCATIONAL

Royal Free Hosp School of Med Florence Stoney Prize

Royal Free Hosp School of Med Annie McCall P G Fellowship in *Midwifery*

Royal College of Phys of London Lumleian Lectures Clin & Social Problems of Peptic Ulcer 10th & 12th April

New Zealand University of Otago Dunedin Virus Research Officer

Berkeley Fellowship Graduates in Med of Middlesex Hosp Med *School*

Glasgow Royal Infy McIntyre Clin Research Scholarship

ANÆSTHETICS

Hosp for Sick Child W C 1 Reg

Hosp for Sick Child W C 1 Sr H O

Prince of Wales s Gen, N 15 Sr H O.

University College Hosp, W C 1 Reg

Bristol Clin Area Sr Reg

Edinburgh Northern Group of Hosps *H O*

Leeds United Hosps Sr H O

Manchester R H B Cons

Sheffield United Hosps Reg

Sothampton Group of Hosps Reg

Taplow Canadian Red Cross Mem Sr H O

in patients who have a slow, persistent oozing from the lesion between attacks of hæmatemesis Nature attempts to combat blood loss by inducing hypotension, which continues so long as there is bleeding Any blood transfusion during this phase produces only a reluctant response from a circulatory system set in hypotension to combat blood-loss, over-loading of the circulation is likely to occur before there is an appreciable rise in blood-pressure The aged, with their less labile vascular tree, are the first to suffer Once oozing has been checked, even the oldest patient responds to transfusion in the normal way

Conclusion

This form of treatment has been in use for the past two and a half years, both in Dr Aitkenhead's wards and my own In no instance has the use of adrenaline and stypven given the slightest cause for anxiety even in the most desperately ill patient

Nearly all the patients transferred to my care have resisted routine medical treatment, but there have been no operative deaths This shows that the method is worthy of a more extended trial than I have been able to make, and it should give equally satisfactory results at the hands of all who wish to use it

In conclusion postoperative bleeding from a gastrojejunal suture line is the one condition least often controlled by adrenaline A bleeding point in the anterior wall of the anastomosis is often recessed between infolded layers of normal mucosa which form an effective barrier to the adrenaline and stypven

I have to thank Sir Heneage Ogilvie for his invaluable criticism and help in the preparation of this paper

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PARATYPHOID-C OSTEOMYELITIS OF THE TIBIA

GEORGE WHITE
M B Birm
SENIOR HOUSE OFFICER

M J MEYNELL
M D Sheff, B Sc, M R C P, D P H
CLINICAL PATHOLOGIST

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OSTEOMYELITIS is a rare complication of salmonella infections Even in typhoid fever, which gives rise to metastatic bone involvement more commonly than any other salmonella infection, the incidence of osteomyelitis has been reckoned to be as low as 0 82% (Winslow 1923) Paratyphoid B is the next in order in frequency, but bone involvement was found to arise in only 2 instances of 1038 cases reviewed by Webb Johnson (1917) Even more rare, judging from the number of reported cases, is osteomyelitis complicating infection with any of the other salmonellæ We have found only 28 reported cases of osteomyelitis due to salmonella other than *Salmonella typhi* or *Salm paratyphi B*, the organisms were *Salm cholera suis* (17) *Salm enteritidis* (5), *Salm typhimurium* (4), *Salm panama* (1), and *Salm oranienburg* (1) We have found no previous report of a case of paratyphoid C osteomyelitis

Case-report

The patient was a Jamaican, aged 40, who had lived in this country for a year and was employed as a metal pickler He had had yaws in childhood He had never, as far as he could remember had any abdominal pain, and careful questioning revealed no past disturbance of bowel habit He was first seen in the casualty department on Oct 25, 1955, when he complained of pain in his left ankle and lower leg which had caused him difficulty in walking and had kept him awake at night for the past six weeks There was no history of a blow or injury to the leg

Examination revealed a diffuse swelling over the lower anterior portion of the left tibia with superficial redness of the skin and severe tenderness to firm pressure over the bone Radiography showed thickening and widening of the distal quarter of the tibia with some central osteolytic areas, well marked periosteal elevation was present, particularly in the lower portions He was admitted to hospital for investigation under the care of Mr J C Fulford His pulse rate and temperature were normal, but, despite bed rest and immobilisation of the leg in plaster, the pain grew steadily worse On Nov 1 radiographic examination of the left tibia showed that the periosteal reaction had increased in extent and thickness Blood count red cells 4,500,000 per c mm, hæmoglobin 90% (13 4 g per 100 ml), white cells 4700 per c mm (polymorphs 70% eosinophils 4 5%, basophils 0 5% lymphocytes 18%, monocytes 7%) Erythrocyte sedimentation rate (Westergren) 42 mm in the first hour, Wassermann reaction negative, serum alkaline phosphatase 8 King Armstrong units

Operation —On Nov 4 the skin was incised and the periosteum was found to be much thickened This was incised and stripped from the bone, to which it was clearly adherent Drilling into the bone resulted in a gush of clear fluid, followed by about 5 ml of yellow pus The marrow cavity was explored, a gauze pack impregnated with yellow soft paraffin was inserted and the skin lightly sutured over the wound

Bacteriological examination —Gram staining of the pus showed no organisms Overnight culture on blood agar yielded a pure growth of gram negative bacilli Subculture on desoxycholate and McConkey's media produced a profuse growth of non lactose fermenting colonies The organism, which was motile, gave the biochemical reactions of a salmonella H and O suspensions of the patient's organism were agglutinated by standard *Salm paratyphi C* sera to a 1 250 dilution The patient's serum agglutinated standard suspensions of *Salm paratyphi C* O to a titre of 1 125 and of *Salm paratyphi C* H to a titre of 1 50 Dr Joan Taylor, of the Salmonella Reference Laboratory, reported "The organism has the following antigenic structure O = 6 7, H = C 1 5 The biochemical reactions confirm the organism to be *Salmonella paratyphi C*" Examination of the urine and fæces on three occasions revealed no pathogenic organism Blood culture on Nov 7 was sterile after incubation for three weeks

Treatment —The organism was found to be fully sensitive to chloramphenicol and accordingly the patient was given 500 mg six-hourly As a precautionary measure he was transferred to Little Bromwich Infectious Diseases Hospital on Nov 9 after removal of the pack from the wound He recovered completely, and the wound is well healed

Discussion

Compared with common pyogenic osteomyelitis (staphylococcal and streptococcal), that due to salmonella infection is usually less destructive and the bony lesions heal more quickly Paratyphoid bacilli are known to linger in the bone-marrow long after they have disappeared from the urine and fæces (Macdonald 1941) Reported cases suggest that as a rule the longer the interval between the acute intestinal infection and the onset of osteomyelitis, the milder is the clinical course of the osteomyelitis itself (Giraccai and Idriss 1952) It is commonly reported that activation of the clinically latent micro organisms can be produced by trauma or physical strain (Lever and Barber 1945), but no such history was obtained in this case Since the osteomyelitis is a late, and sometimes very late, complication of salmonella infection, its nature is unsuspected in most cases, as it was in the present one Only serological studies and, above all, bacteriological examination of pus from the lesion will establish the diagnosis

In the West Indies by far the commonest type of salmonella infection is paratyphoid C In 1952, 584 cases of paratyphoid were notified in Jamaica alone (World Health Organisation 1953) Many immigrants (35,000) have come to Great Britain from the West Indies, and the possibility of paratyphoid C infection should enter into the differential diagnosis of illness in such

LOBECTOMY FOR BRONCHIAL CARCINOMA

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SINCE 1933, when Graham first successfully resected a bronchial carcinoma (Graham and Singer 1933), the standard operation for this condition has been pneumonectomy Allison (1946), Brock (1948), and Brock and Whytehead (1955) combined pneumonectomy with more extensive dissection of the mediastinum in an effort to achieve truly radical removal of the neoplasm

Pneumonectomy still carries a high mortality Moreover, removal of so much pulmonary tissue necessarily limits the patient's activities, and renders him increasingly liable to become a respiratory cripple On the other hand, lobectomy has been regarded as quite inadequate, and only one paper specifically on this operation has appeared in the English language since 1949 in 1950 Effler described the results in 5 cases

Nevertheless lobectomy has been widely practised, for most reports on the treatment of bronchial carcinoma refer to some patients treated by this operation Sellors (1955) includes 86 cases, there were 74 in the series analysed by Bignall and Moon (1955), Churchill et al (1950) refer to 57, Boyd et al (1954) to 32, and Therkelsen (1952) to 12 All these workers note that the results of the operation are good, but this they attribute to careful selection of the patients they recommend the procedure only for those with small peripheral tumours, for the aged, and for those with a low respiratory reserve

Material

This account of lobectomy for bronchial carcinoma is based on the work of the following surgeons (the number of cases contributed by each is shown in parentheses) K Mullard (35), G Cruikshank (32), C A Jackson (32), M Bates (26), A M Macarthur (20), R Abbey Smith (14), E F Chin (11), M M Brown (11), K Harrison (10), I M Hill (8), B P Moore (8), L Bromley (6), H R S Harley (2), and myself (49) The 1st case was operated on more than six years ago, and the last in May, 1954 In all, 264 patients were subjected to lobectomy All the facts on which this analysis is based were collected by the surgeons concerned

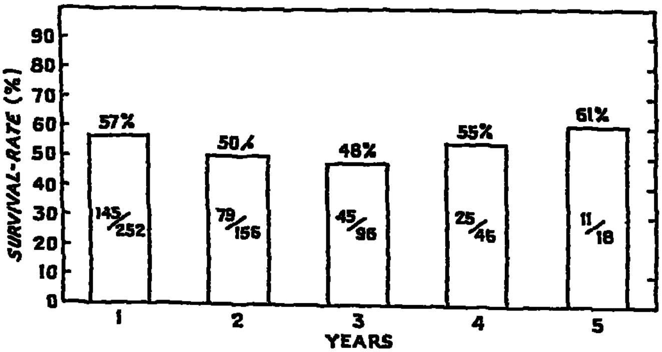

Fig 1—Survival in whole series "Actual" and "possible" survivals are shown inside columns

19 (7%) of the patients were women The distribution of the patients by age groups was as follows

31–40	*41–50*	*51–60*	*61–70*	*71+*
10 (4%)	55 (21%)	117 (43%)	77 (30%)	5 (2%)

Method of Analysis

Survival-rates have been recorded as follows

$$\frac{\text{Actual survival}}{\text{Possible survival}} \times 100$$

The "*possible survival*" consists of the total number of patients operated on in each year, less those who died as a direct result of the operation but including those who died later from causes other than carcinoma of the bronchus

The "*actual survival*" consists of those patients operated on in the twelve month period concerned who were still alive at the time of analysis

The figures have been recorded on a cumulative basis

Results

Fig 1 shows the survival rates for the whole series Of the 264 patients, 12 died at or soon after operation, and of the remaining 252, 145 (57%) have survived for a year or more Of the 156 operated on two or more years ago 79 (50%) survive, of 96 operated on three or more years ago 45 (48%) survive, of 46 operated on four or more years ago, 25 (55%) survive, and of 18 operated on five or more years ago 11 (61%) survive

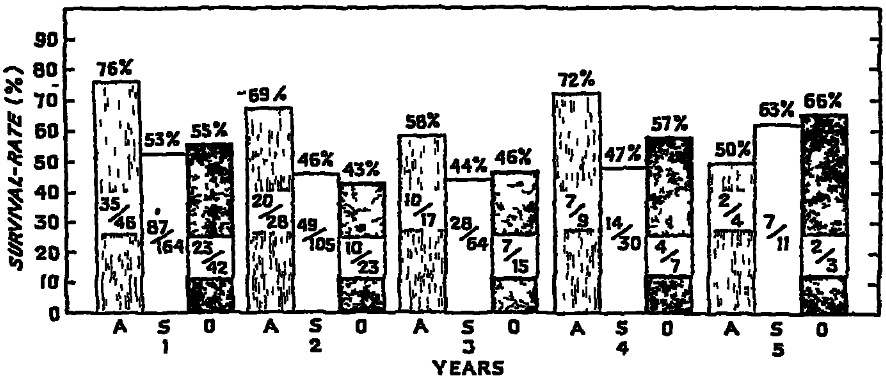

Fig 2—Influence of cell type on survival rate A = adenocarcinoma S = squamous carcinoma. O = undifferentiated carcinoma.

Influence of Cell Type on Results

Although many pathologists were involved in this investigation, there was a wide measure of agreement as to the histological classification of the tumours Three types were recognised adenocarcinoma, squamous carcinoma, and undifferentiated carcinoma Tumours sometimes described as "polygonal cell" and as "transitional cell" carcinomas have been included in the "squamous" group, tumours described as "alveolar cell" and as "columnar cell" have been classified as "adenocarcinomas"

Of the 264 patients 172 (66%) had squamous carcinomas, 49 (18%) adenocarcinomas, and 43 (16%) undifferentiated tumours These proportions are almost identical with those reported by Walter and Pryce (1955) and show how little the cell type of bronchial carcinoma varies with its site

Fig 2 shows the results according to cell type. The patients with adenocarcinoma have the best survival rate (69% at two years), but those with undifferentiated tumours do not appear to have nearly as bad a prognosis when lobectomy has been possible as they do when the lesion is more extensive, their two-year survival-rate is very was obscured by mucus and consisted of greatly exaggerated folds, resembling cerebral convolutions (see figure) These changes were most distinct along the greater curve, where the stomach was up to 4 cm thick, and in this region the muscular coats were also hypertrophied A sharp line of demarcation separated the body of the stomach from the apparently unaffected antrum, and there was no ulceration or scarring of the duodenum

Microscopy—Giant hypertrophic gastritis Infiltration of all coats of stomach, but mainly of mucosa and submucosa, by plasma-cells, lymphocytes, and occasional eosinophils, polymorphs, and macrophages In the more severely affected areas there were occasional micro abscesses, and in these areas, too, fibrosis extended from the submucosa into the muscularis and serosa A small acute ulcer was present in the depths of a fold (a similar ulcer might well have led to hæmorrhage) The inflammation was not confined to the hypertrophied portion of the stomach but extended with diminished intensity towards the pylorus Here and in the adjacent duodenum there were many lymph follicles in the mucosa, some with prominent germinal centres The mucosa was grossly hypertrophic, but it was very well differentiated and there was no suggestion of carcinoma The larger folds seen macroscopically had a connective tissue core derived from the submucosa, while the small secondary folds consisted of mucosa only Mucus secreting cells not only covered the surface and lined the gastric pits, but also extended to the deepest parts of the gastric glands Zymogenic and parietal cells were present in reduced numbers A few glands penetrated the submucosa for a short distance, and some of these, as well as some glands in the deep layers of the mucosa, showed cystic dilatation. Pronounced inflammatory changes (reactive hyperplasia, sinus catarrh, and plasma cell infiltration) affected the greater and lesser curve lymph-nodes

Discussion

In this case the diagnosis was not suspected before or at operation, and it was only after histological examination of the stomach that carcinoma was finally excluded Brunn and Pearl (1926) observed that the diagnosis was usually in doubt until the stomach had been exposed at laparotomy, and, from a study of more recent case reports, this still applies despite improved techniques in radiology and gastroscopy

Maimon et al (1947), describing radiographic appearances, found that the stomach was diffusely involved in each of their six cases, but the greater curve was principally involved The mucosal folds were greatly thickened, indurated, and enlarged, producing an exaggerated saw tooth appearance, often with broad, deep, sharp notches, especially along the greater curve Softness of the rugæ was an almost constant finding, and, as had previously been noted by Spriggs (1943), the flexibility and maintained power of dilatation and contraction of the involved area, and the ability of the peristaltic waves to traverse it, were characteristic findings These observations were, however, largely retrospective In three of Maimon's (1947) cases carcinoma was diagnosed preoperatively, and in only one were the barium meal findings correctly ascribed to diffuse gastric polyposis

Gastroscopic examination, in Maimon's experience, was equally unrewarding and they concluded that, although their cases were strikingly similar, the differentiation of giant gastritis from malignant neoplasm was extremely difficult and at times impossible Thus in one of Schindler's (1939) patients carcinoma was wrongly diagnosed by gastroscopy, and in another an extragastric tumour could not be excluded

In treatment, severe and persistent blood loss, a rare complication exemplified in the present case justifies radical surgery but when there is no such urgency, medical treatment should first be tried Spriggs (1943) obtained relief of symptoms with objective signs of improvement by means of gastric ' self lavage " The patient drinks a pint of warm water containing a small teaspoonful of sodium bicarbonate an hour before meals, and lies down for twenty to thirty minutes first on the left side and then on the right

When operation is preferred, or " self lavage " has been unsuccessful, an extensive resection through healthy tissue, as for carcinoma, is unnecessary, because incomplete removal of the affected mucosa may be followed by spontaneous regression in the portion left behind (Grime and Whitehead 1951) In order to avoid total gastrectomy and its unpleasant sequelæ, however, it is essential to recognise giant hypertrophic gastritis before the stomach is excised

Summary

A man, aged 39, with giant hypertrophic gastritis presented with bleeding which failed to respond to conservative measures, and he was subjected to total gastrectomy

In this disorder severe hæmorrhage is exceptional and the lesion is usually mistaken for carcinoma

In treatment partial gastrectomy is preferable, but relief is sometimes obtained from gastric " self lavage "

I am grateful to Dr Donald Hunter and Mr J E Richardson for permission to publish this case and for their helpful advice and criticism, and to Dr R G F Parker for his report on the microscopical findings

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FEMORAL PERIARTERIAL SYMPATHECTOMY FOR DELAYED HEALING AFTER AMPUTATION

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SURGEON

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M B Edin
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FEMORAL periarterial sympathectomy, first described by Jaboulay in 1889 (Miles and Wilkie 1936), was brought into prominence by Leriche (Leriche and Heitz 1917, Leriche and Robineau 1927) whose original case reports suggested that it would be of value in vasomotor and trophic disturbances of the extremities Since its introduction it has been used for various conditions, including Raynaud's disease, diabetic and arteriosclerotic gangrene, chronic ulceration of the leg, frostbite, and causalgia

The results of the operation have varied, its effects are local and transitory and it has therefore fallen into disfavour

Black (1924) reported 10 cases of leprosy in which periarterial sympathectomy brought about healing of chronic ulcers and stumps after spontaneous amputation, but Bernheim (1925) reported only 4 successes in 9 cases of Raynaud's disease or thromboangiitis obliterans

Gask and Ross (1934) considered that it had a definite though limited value, and Kuntz (1946) suggested that some peripheral vasodilatation always followed the operation but that the results did not justify its continued use

Aird (1949) maintained that its only advantage was in reducing spasm after embolectomy Slessor (1953), discussing

TABLE I—DEATHS DURING AND AFTER OPERATION

Cause	No	% of all deaths	% of all cases
Operative	12	10	4
Other causes	19	16	7
General metastases	55	47	21
Local metastases	27	23	10
Unknown	6	4	2

Policy and Palliation Resections

Cases treated by lobectomy as a policy were compared with those in which the operation was dictated by expediency In the latter group fell those in which the surgeon felt that the operation of choice was pneumonectomy, but in which reasons, such as respiratory insufficiency or advanced age, justified lobectomy alone as a palliative procedure Such cases are usually recommended for lobectomy

These two groups are compared in fig 6 The 264 cases included only 49 in which the operation was considered to have been palliative As might be expected their survival rate was lower than that of cases where the operation was planned Nevertheless 33% survived for more than two years, compared with 52% of those in whom the operation was deliberate

Cause of Death

The cause of death was known with reasonable certainty in 113 of the 119 patients who died during or at any time after operation Table I shows how these deaths were distributed

The operative mortality was much lower than that in any of the series of pneumonectomy cases recently published, and a quarter of these deaths were of patients whose operation was regarded as palliative

Of the 19 deaths due to causes other than carcinoma, 4 were attributed to respiratory failure, it seems certain that had pneumonectomy been carried out on any of these patients, they would not have survived the operation The survival of this group must to some extent account for the lower mortality of lobectomy, since a large proportion of the patients who die after pneumonectomy do so as a result of respiratory failure There were 6 late deaths due to coronary thrombosis, and the other 9 patients succumbed to various other causes, including carcinoma of the bladder

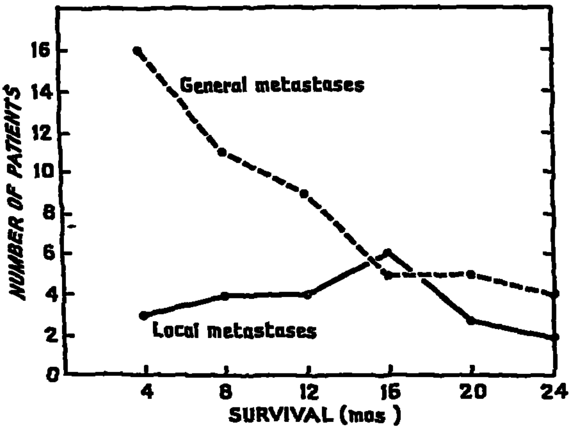

Fig 7—Time after operation at which patients died by four-month periods

Death due to Metastases

In assessing the place of lobectomy in the treatment of bronchial carcinoma it is essential to ascertain the proportion of cases in which local recurrences develop, since it may be argued that with the more limited operation this form of metastases must be more likely

In the present series the diagnosis of general metastases was based largely on clinical manifestations, and in only some of the cases was general spread confirmed at necropsy The clinical evidence of such metastases is, however, usually sufficiently strong for valid assumptions to be based upon it

The clinical evidence of local metastases is usually clearer, and it is certainly more obvious after lobectomy than after pneumonectomy, whereas after pneumonectomy a local metastasis is very unlikely to be radiographically apparent, after lobectomy the shadow cast by a local recurrence may be visible at an early stage and could seldom be missed if death were due to it

Finally in attempting to make the distinction between death from local metastases and death from general metastases, patients who were found to have secondary tumours in either lung were classed with the "local" group, whereas the 4 cases in which necropsy revealed both local and general metastases were classed with the "general" group, since each of these 4 patients died within six months of their operation

55 late deaths were attributed to general metastases, and 27 to local metastases Thus 47% of the 119 patients who died were almost certain to have done so whatever form of resection had been carried out In those whose death was due to general and to local metastases, glandular involvement was found as follows

	Glandular involvement	
	55 deaths from general metastases	*27 deaths from local metastases*
Present	21	9
Absent	34	18

There is little difference between the two groups

The fact that so many of the patients with *general metastases* died within such a short time after the operation is strong evidence that the secondaries were already present at the time Fig 7 shows the period after operation at which these patients died, compared with similar figures for those who succumbed to local metastases The figures show a close resemblance to those of Aylwin (1951), whose cases had been treated by pneumonectomy

Of the patients who died of general metastases, 36% did so within a year of operation, and 90% within two years Ochsner et al (1948) pointed out that if a patient survived for two years after a resection for carcinoma, he had a very good chance of living for five years, this fact is amply borne out by these figures, and for this reason the results of different methods of treating bronchial carcinoma should not be compared until at least two years after operation

Of the 119 patients who have died since their operation, 27 succumbed to *local metastases*—that is, 10% of the whole series The period of survival was different from that of the patients who had more widespread secondaries in that the deaths were more evenly spread over the first two years (fig 6), reaching a small peak at sixteen months Possibly if a more radical removal of the glands had been undertaken some of these patients might have survived, but nevertheless the smallness of the proportion who died from this cause, and its close correspondence to that in the series of pneumonectomies described by Aylwin (1951), suggest that there are no grounds for rejecting lobectomy on this count

Patients with pulmonary secondaries were a particularly interesting subgroup of those with local metastases In all there were 12 such cases, and, although no comparative figures are available, my impression is that this occurrence is rare after pneumonectomy Of the 12, 3 are still alive, 1 after removal of a secondary from the other lung In 6 cases there was recurrence on the same side as the original operation, and in 3 of these there were also secondaries on the other side, these cases are easily accounted for by retrograde lymphatic spread, or by the fact that tumour tissue was left behind in the residual lobe The other 6, where the recurrences were on the side opposite to that of the operation, are less easy to explain, in each of these cases the tumour was the local functioning of the vascular tree Gerard (1951) showed that an important feature of the pathogenesis of causalgia is an over-all decrease of sensory stimuli and a resultant neural imbalance Something of this nature may take place in vascular lesions, and local sympathectomy may act in a way similar to many sympathetic blocks by changing the balance of neural activity at various levels rather than by a more mechanical or local effect

Summary

In 2 cases of arteriosclerotic gangrene where healing had not followed mid thigh amputation, perifemoral sympathectomy was performed at a further operation, which led to healing

These cases are a reminder of the occasional usefulness of periarterial sympathectomy, an operation which is usually regarded as out of date

We are indebted to Dr S Sevitt and his laboratory staff for the pathological reports One of us (M R F) was in receipt of a full time grant from the Medical Research Council

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Preliminary Communication

THE FATE OF ^{32}P-LABELLED BACTERIAL LIPOPOLYSACCHARIDE IN LABORATORY ANIMALS

RAPID changes in the resistance of laboratory animals to experimental infections can be produced by the injection of the lipopolysaccharide fraction of endotoxins extracted from gram-negative bacteria [1–3] It has been suggested that these lipopolysaccharides contain the substrate for the bactericidal property of the serum [1, 3]

To study the nature of this reaction further we labelled lipopolysaccharide with radioactive phosphorus (^{32}P) as an integral part of the macromolecule and found that fresh serum from various animals can liberate phosphate from this material While attempting to define more precisely the rôle of these materials in modifying the level of non specific immunity, we also studied the fate in mice and guineapigs of the ^{32}P after intravenous injection of this lipopolysaccharide

MATERIALS AND METHODS

Preparation of Radioactive Lipopolysaccharide

Escherichia coli 2380 was grown on the minimal medium of Davis and Mingioli [4] containing 1% Difco casamino-acids and in which the phosphate had been replaced by 10 mC of ^{32}P per litre in the form of carrier-free sodium phosphate The 1% casamino acid contained sufficient extraneous inorganic phosphate to satisfy the growth requirements of the organism Radioactive lipopolysaccharide was extracted from the bacteria by the phenol/water method of Westphal et al [5] The final material was entirely nondialysable and had a counting rate of 2000–2500 per µg a minute

For the in vitro experiments a small 'Perspex' dialysing cell was used The mixture of 10 µg of radioactive lipopolysaccharide and serum dilution (1 2 ml) was separated from a physiological-saline solution (2 4 ml) by a 'Cellophane' dialysing membrane, and an outlet tube from each chamber permitted 0 1 ml samples to be withdrawn at intervals for assay of ^{32}P

In the in vivo experiments all the animals were injected intravenously, mice (weighing 20–22 g) into a tail vein and guineapigs (weighing about 350 g) into a saphenous vein Blood samples were removed directly from the heart, and various organs were homogenised Serum samples were placed directly on nickel planchettes, and blood or organ homogenates were absorbed by filter-paper discs stuck on the planchettes by shellac and dried by heating from above All the specimens were counted under a thin mica end-window Geiger counter for such a time that the probable error of counting did not exceed 5%

RESULTS

In vitro

Incubation at 37°C of radioactive lipopolysaccharide with sera from several common laboratory animals and with human sera rapidly liberated dialysable phosphate This activity appeared to be greatest in rats and mice and least in rabbits

Heating of the sera at 56°C for 30 minutes abolished this activity, hæmolytic complement did not appear to be necessary, since mouse serum, which contains none, was highly active The removal of divalent cations by ethylene diamine tetra acetic acid (E D T A) greatly reduced this activity The optimal pH was about 8 Although this phenomenon has the characteristics of a phosphatase reaction, there was no obvious correlation with the content of alkaline phosphatase in the sera measured by the King Armstrong method

In vivo

When 5–60 µg of lipopolysaccharide labelled with ^{32}P was injected intravenously into mice or 100 µg into guineapigs, a large proportion was rapidly removed from the blood about 40% disappeared within the first minute, and 60–75% was eliminated from the circulation in 8 minutes Thereafter the remaining 25–40% persisted in the blood during the next hour without very appreciable diminution The distribution of radioactivity in the body showed, as might be expected, that this material is taken up by the reticulo endothelial system This was confirmed by autoradiography At least half of the removed radioactive lipopolysaccharide appeared in the liver and spleen, and smaller amounts were detected in the lungs, adrenal glands, and kidneys The absence of radioactivity from brain tissue showed that this large molecule cannot cross the blood brain barrier The highest level of radioactivity attained by the reticulo endothelial system developed within 15 minutes of injection

The third of the originally injected radioactive lipopolysaccharide which is not removed by this macrophage activity did not appear in the circulating leucocytes but remained in the plasma in a non dialysable form and was only gradually eliminated Thus 17–22% still persisted after 6 hours, 10% after 24 hours, and 2% after 48 hours A constant level of radioactivity was maintained in the liver throughout this period of gradual elimination from the plasma During the same time, however, radioactive dialysable phosphate was detected in the urine, appearing as early as 15 minutes after injection, and continued until the radioactive lipopolysaccharide had virtually disappeared from the blood

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SURGICAL TREATMENT OF PORTAL HYPERTENSION

RESULTS IN 64 CASES

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THAT assessment of the benefit resulting from operations for portal hypertension presents a difficult problem is evident from the widely divergent views (Blakemore 951, Witts 1953) The reasons for this difficulty lie in he composite nature of the disorder when it is associated with hepatic disease Some of these reasons are illustrated by the following brief case records

Case 1 —An elderly man was seen for another condition 26 years after splenectomy elsewhere for hæmatemesis and ‘Banti's syndrome” Bleeding had recurred at intervals for [illegible] years after the operation, but he had remained symptom-free during the succeeding 21 years (Learmonth 1951)

The point illustrated by this case is that the bleeding vessels in the œsophagus or their feeders may undergo spontaneous obliteration

Case 2 —A woman, aged 27 years, experienced three episodes of hæmatemesis during the 6th year after a severe and prolonged attack of toxic hepatitis Splenectomy, left nephrectomy, and splenorenal anastomosis (end to end, using a ‘Vitallium’ tube) were performed in December, 1946 She married and lived a normal life for 7½ years There was mild melæna in October, 1952, and more severe bleeding which led to her death in August, 1954 Necropsy showed that the anastomosis had been occluded for a long time

Evidently there may be complete freedom from symptoms for many years after a technically imperfect operation

Case 3 —A girl, aged 8 years, underwent splenectomy at the hands of the late Sir David Wilkie in 1934. The liver was noted to be cirrhotic. In 1954 she was seen again because of hæmatemesis which, it was learned, had recurred frequently in the intervening 20 years.

Repeated hæmatemesis is apparently not incompatible with long survival even in patients known to have hepatic disease

These examples indicate the need for a long follow-up of many cases in order to assess accurately the value of surgical treatment in portal hypertension However, such is the interest of this condition that we believe it justifiable to review now the progress of 64 cases of intrahepatic portal obstruction treated in the professorial surgical unit of the Royal Infirmary of Edinburgh during the 8 years up to the end of 1953 68 operations were performed on these patients, as follows portacaval anastomosis, 7, splenectomy and splenorenal anastomosis, 19, splenectomy alone, 27, limited œsophagogastrectomy, 8, splenic arterial ligature, 4, other operations, 3

Criteria for Assessment

We have accepted four criteria for assessing the effectiveness of operations in portal hypertension (1) a substantial reduction after operation in the incidence and severity of bleeding from varices in the lower œsophagus and the fundus of the stomach, (2) no demonstrable adverse effect on metabolic functions, and in particular on hepatic function, (3) improvement in the blood picture, and (4) improved chances of survival

Incidence of Hæmorrhage

There is no conclusive evidence on this point, because the incidence, severity, and effect of hæmorrhage in chronic hepatic disease are unpredictable and control figures from medically treated patients are concerned with mortality only In about 40% of reported cases the hæmorrhage is terminal (Ratnoff and Patek 1942, Reynell 1951), and a further 30% die within a year of the first hæmatemesis These are, in general, cases with severe hepatic damage The remaining 30% form a group in which hepatic disease may not even be suspected till hæmatemesis occurs

TABLE I—INCIDENCE OF GASTRO ŒSOPHAGEAL BLEEDING AFTER OPERATION IN PORTAL HYPERTENSION DUE TO HEPATIC DISEASE

Operation	Cases with preoperative bleeding		Cases without previous bleeding	
	No	No with postop bleeding	No	No with postop bleeding
Portal-systemic venous anastomosis	22	10	4	0
Splenectomy	15*†§	11	12	2
Splenic arterial ligation	2*‡	2	2	1
Œsophagogastrectomy	8†‡§	0		
Other			3	0
Total	47	23	21	3

* † ‡, § = 4 patients common to two categories

The incidence of bleeding after operation in the present series is shown in table I, from which the following conclusions are drawn

1 Bleeding after operations for portal hypertension occurred much more frequently in patients who presented with hæmatemesis, irrespective of the operation performed

2 After splenectomy alone the incidence of bleeding was very high when hæmatemesis had been a presenting feature, and was low if alimentary hæmorrhage had not been detected before operation. Similar results have been recorded by Pemberton and Kiernan (1945) The reason for this difference appears to be that once the anatomical pattern of the collateral circulation has been established in portal hypertension, it does not change (Macpherson 1953)

3 *In only 1 of the 10 cases with bleeding after portal systemic venous anastomosis* was the anastomosis observed to be patent, in 5 it was seen at necropsy to have been occluded, in 4 its condition was not known, but as 3 of these were splenorenal anastomoses performed with a *vitallium* tube they probably did not remain patent In 1 of these 4 cases the bleeding was from an eroded artery in an acute gastric ulcer and was not attributable *to* the portal hypertension.

4 The recurrence of bleeding after operation was as *variable and unpredictable* as in the cases treated medically The earliest onset was in the immediate post operation period and the longest interval was 6 years

5 Splenic arterial ligature has proved ineffective in preventing further hæmatemesis, but there has been no recurrence of bleeding over periods of up to *2 years after limited* œsophagogastrectomy. Because the follow-up is so brief, this statement must be regarded as a progress report only.

Hepatic Function

In a report on hepatic function *after* operations for portal hypertension (Macpherson et al 1954) we showed that (*1*) diversion of the portal blood stream from the

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Systemic Associations and Treatment of Skin Diseases

KURT WIENER, M D, dermatologist, Mount Sinai Hospital, Milwaukee, Wisconsin London Henry Kimpton 1955 Pp 556 £6 6s

DR WIENER'S earlier book, published in 1947, was devoted to the skin manifestations of internal disorders *In this complementary volume he describes what is known of the internal derangements associated with dermatoses* He has done an enormous *amount* of work, and the text has no less than 2759 references from all over the world

The first few chapters are absorbing, but they are on diseases which *might* well be classified as internal or general rather than dermatological Interest flags as the dermatoses give a grudging yield of features of general interest The second half of the book, dealing with systemic treatments, is equally encyclopædic but the arrangement and selection of material is often uncritical The *final chapter* is about unorthodox treatments, which to the innocent inquirer *may seem* just as appropriate as many of the empirical remedies in the preceding chapters

Expensive, extensive, exhaustive, and exhausting

Peripheral Vascular Disease

A J BARNETT, M D, M R C P, assistant director, Alfred Hospital Clinical Research Unit, Melbourne, J R E FRASER, M D, M R A C P, sometime registrar of the unit Melbourne Melbourne University Press *London* Cambridge University Press 1956 Pp 210 *57s 6d*

THIS book is based on the monograph successfully submitted by Dr Barnett and Dr Fraser for the Stawell memorial prize essay for 1952 Its declared purpose is to present a "practical approach" to the problem of vascular disease of the extremities

A brief *survey* of the historical development of the *subject* introduces a review of vascular physiology An account of methods of diagnosis, particularly venous plethysmography, *and the pathology of common diseases* is *followed by a discussion of* clinical features and treatment The book does not set out to be an encyclopædia of vascular diseases and *the authors concentrate on the common lesions*, which they *present* with *a* good number of case histories There is much *to* recommend such an approach, but it is surprising that a "practical" book *should devote ten pages to the physics of* blood flow and only five lines to the clinical *aspects of* peripheral emboli Some lack *of* balance is also noticeable in the chapter on *treatment*, in which *surgery does not receive* enough attention

Despite these *reservations*, there is much to admire in this useful book

Die Überfunktion der Nebennieren

RUDOLF CHWALLA Vienna Maudrich *1955* Pp 330 £14 *2s*

THE large necropsy material of the distinguished Viennese pathologist, A Priesel, has been the basis of this monograph Its leading idea is the functional *entity* of the adrenal gland and the identical pathology of "hyperadrenalism," whether the cortex or the medulla or both are enlarged

Some diseases *and types of constitution* are said to be associated with *enlarged adrenals* the diseases include arteriosclerosis, hypertension, arteriolosclerotic contracted kidney, diabetes obesity, pulmonary emphysema, malignant growths (particularly carcinoma of the prostate), urinary bladder, and bronchus, and primary carcinoma of the liver *As for physique*, enlarged adrenals are found mainly among pyknic individuals

The hilar cells of the ovary (as androgen secreting elements) *and the rete ovarii* are discussed in detail Dr Chwalla notes the occurrence of eosinophil hyperplasia of the pituitary and eosinophil adenoma in conditions usually associated with *basophil hyperplasia*

Unfortunately there is no proper statistical analysis of the material nor does the writer say how the increase of cortical *or medullary* tissue was ascertained An intense yellow colour in the adrenal cortex was often taken to mean large amounts of lipids and hence hyperfunction, even without *enlargement* of the cortex In view of the rapid turnover of corticoids, this view will be accepted by few pathologists

Some of the arguments against the functional entity of the adrenals—for example, the hyperproduction of a single one of its *hormones, sometimes* with depression of another one, and the beneficial effects *of cortisone* in the adrenogenital syndrome —are not given sufficient prominence

One in Six

An Outline of the Cancer Problem I HIEGER, D SC, Royal Marsden Hospital, *London* London Allan Wingate 1955 Pp 80 12s *6d*

WRITTEN for the layman, this short book should acquaint him *with the* nature, scope, and *prospects of* cancer research at the present time Dr Hieger describes, with the authority of *an expert, the* extent and character of the problem, the ways of tackling it, statistical and *experimental*, and the current state of knowledge, and *he* indicates the possible or probable lines of advance The immense complexity *of the subject*, on the one hand, and the industry and ingenuity of those attacking it, on the other, are well illustrated Among the more *striking chapters* are those on cancer and ageing, cancer theories, *and* "lung cancer, smoking and smoke", and there *are instructive* photomicrographs, and a useful glossary It is all excellently done

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Cybernetics —The report of the tenth and last conference *held by the Josiah* Macy, jun, Foundation on this subject has been published under the editorship of Prof Heinz von Foerster (New York 1955 $2 75) It includes a contribution by Mr W Grey Walter, D SC, on activity of the brain

Chemical Physiology and Pathology of the Mind (*London* H K Lewis *1956* Pp 26 - 5s) —The inaugural *lecture which Prof H McIlwain delivered at the Institute of* Psychiatry last April has now been published *as a monograph* In it he describes the contributions of Maudsley, Mott, and *Mann to the study of mental diseases*

Studies on Fertility, 1955 (Oxford Blackwell Scientific Publications 1955 Pp 158 *25s*) —The seventh annual volume of the proceedings of the Society for the Study of Fertility is the second to appear in book form It contains a selection of the papers read at the annual conference of the society at Birmingham in 1955 and some reports on original work from research workers who are not members of the society

Les gamma-globulines et la médecine des enfants (Paris Masson 1955 Pp 298 Fr 2000) —In December, *1954, the Centre International de l'Enfance held* a seminar in *Paris* on this subject Prof A Tiselius (Uppsala) presided over the *meeting* and the *speakers from* this country included *Mr* R A *Kekwick*, D SC, *Dr Reginald Lightwood*, Dr F O *MacCallum*, and Dr J C McDonald *A report* of the seminar has now appeared under the editorship *of* Dr Raymond Gautier

St Clair Thomson's Diseases of the Nose and Throat (*6th* ed *London* Cassell 1955 Pp 967 90s) —This well established textbook has again been revised by Sir Victor Negus *Of* several new features, perhaps the most useful is a very clear description of block dissection of the neck The international nomenclature has been adopted in a pictorial description of the tracheobronchial tree, and there is a good description, well illustrated, *of* the transpalatal approach to the nasopharynx New hope is given in the treatment of spontaneous rupture *of the œsophagus*, thanks to a greater awareness of the *condition and improved* techniques in thoracic surgery We *are pleased to see that* the confusing term "nasopharyngeal polypus" is rejected as a synonym for nasopharyngeal fibroma but it seems a pity that the name should be retained at all, *especially as the more* widely accepted term 'antro choanal *polypus*' gives a much better idea of the origin and behaviour of these polypi The descriptions of laryngoceles and *of* varicose veins of the œsophagus are still inadequate for a *postgraduate* book of this size and the subject of laryngeal *paralysis* remains unnecessarily complicated and confusing This latter section, however, is improved by some useful drawings of *one* of the many operations now available for the relief of stridor in cases of bilateral *paralysis* Furthermore, these are minor criticisms of a book which is beautifully written and excellently produced, with an unusually fine index The extensive bibliography has been brought well up to date The *book* is sure to keep its position as the laryngologist's most widely used *source of reference*

TABLE IV—CIRRHOSIS WITH PORTAL HYPERTENSION: EFFECT OF SPLENECTOMY ALONE OR WITH OTHER OPERATIONS ON BLOOD PICTURE

—	Before operation	After operation		
		1 yr	3 yr	5 yr
Hb (%)	64.2 ± 24.7 *(34)*	93.8 ± 12.7 *(25)* $P<0.01$	94.1 ± 12.3 *(16)* $P<0.01$	102.4 ± 9.8 *(8)* $P<0.01$
Red cells (million per c.mm.)	3.78 ± 1.08 *(30)*	4.65 ± 0.54 *(25)* $P<0.01$	4.53 ± 0.64 *(10)* $P<0.01$	5.30 ± 0.93 *(5)* $P<0.01$
White cells (thousands per c.mm.)	4.45 ± 1.13 *(34)*	10.4 ± 4.5 *(25)* $P<0.01$	10.5 ± 3.1 *(16)* $P<0.01$	10.8 ± 1.7 *(7)* $P<0.01$
Platelets (thousands per c.mm.)	137 ± 42 *(25)*	356 ± 186 *(24)* $P<0.01$	333 ± 96 *(13)* $P<0.01$	327 ± 69 *(5)* $P<0.01$

Values expressed as means ± S.D. Number of cases in italic numerals in parentheses.
P values for difference between *x* years and before operation.

The findings demonstrated that the characteristic leucopenia and thrombocytopenia were corrected only if splenectomy was included in the operation. Relief of the portal venous congestion by portal systemic venous anastomosis and other measures such as splenic arterial ligation produced no such improvement. The results of a longer follow-up in 34 patients with intrahepatic portal obstruction who were submitted to splenectomy either alone or as part of a more extensive operation show that these changes in the blood picture persist, an over-all improvement in the peripheral-blood picture, with a significant rise in all values, having been maintained in patients surviving such operations for periods up to 5 years (table IV). Correction of a leucopenia averaging 4000 white blood cells per c.mm. to a sustained count of 10,000 per c.mm. would seem an important factor in increasing the ability to combat intercurrent infections. This feature has been specifically observed in 3 patients who were subject to recurrent infections of the respiratory tract. In general the number of circulating granulocytes has tended to increase in the immediate post-operation period and the number of lymphocytes to increase subsequently, so that a year or more after splenectomy the differential leucocyte-count is similar to that found before operation but the absolute figures are greater.

The improvement in the platelet-count may also have contributed to the survival of some of the patients. Spontaneous bleeding from sites other than the œsophagus is unusual in portal hypertension, even when the platelet-count is 50,000 per c.mm. or less; but it is reasonable to assume that such a thrombocytopenia renders bleeding from œsophageal varices an even more serious hazard. We consider that correction of the thrombocytopenia should be one of the aims of operation for portal hypertension.

The hæmatological records of 8 cases in which alimentary bleeding had not been detected before operation have been abstracted from the whole group (table V). The initial leucocyte and platelet counts were depressed in these cases, but the anæmia was much less prominent. Operations, which in each case included splenectomy, corrected the leucopenia and thrombocytopenia; and though the hæmoglobin level and the erythrocyte counts rose subsequently, the increase was naturally less striking than for the whole group shown in table IV.

These observations agree with previous reports by Davidson (1934) and by us (Macpherson and Innes 1953). The balance of evidence at present suggests that in patients with intrahepatic portal obstruction the enlarged spleen plays little, if any, part in depressing the formation of erythrocytes and hæmoglobin. The anæmia probably results from a combination of causes—loss of iron and protein by alimentary bleeding, low intake and poor absorption of iron (Davidson 1934), and possibly defective utilisation because of hepatic dysfunction (Macpherson 1953). The improvement after operation in this series should probably be ascribed to the administration of adequate doses of iron, and in many of the cases to a reduction in the frequency of alimentary bleeding.

Survival

Evaluation of a method of treating a disease or one of its complications must be based on the natural history of the disease. This axiom applies especially to conditions which are the result of many different causes and which may show very varied rates of progression. Hepatic cirrhosis is such a condition. Once it has become manifest the direction and rate of change depend on many factors—perhaps in particular upon the ætiology, the response to prolonged medical treatment, and the incidence of complications. Hence, to assess the value of surgery in the treatment of portal hypertension due to hepatic cirrhosis it is essential to compare statistically the results obtained in two large groups of cases which are as nearly as possible comparable clinically and in all features of treatment other than the operation in question. Two series treated almost entirely by medical measures have been reported within the past 15 years. For purposes of comparison with the results of operation in the treatment of portal hypertension the series reported by Ratnoff and Patek (1942) is not acceptable, because in 42 of the 106 patients who experienced hæmatemesis the bleeding was a terminal event. The cases analysed by Douglass and Snell (1950) are more suitable for two reasons: (1) most of the 67 cases they report had survived their first hæmatemesis long enough to be referred to the Mayo Clinic, and (2) the medical treatment was similar to that in the Edinburgh series. In table VI the results of medical treatment in all their cases of cirrhosis and in the cases complicated by hæmatemesis are compared statistically with the results in the present series after all forms of surgical treatment, and in particular after portal systemic venous anastomosis or splenectomy alone. Survival rates have been calculated from the time the patient presented in the control series, and from the time of operation in the cases treated surgically.

The following deductions are permissible from this analysis:

1 Survival rates of all cases treated surgically are significantly better than after medical treatment (*a*) for the whole period under review and (*b*) at 1 year and 3 years after operation.

2 The survival rate in cases with hæmorrhage as a presenting symptom is just significantly better after surgical treatment at 1 year, but is not significantly better than the control series at the other periods or over all.

TABLE V—INTRAHEPATIC PORTAL OBSTRUCTION WITHOUT DETECTABLE BLEEDING: EFFECT OF SPLENECTOMY ALONE OR WITH OTHER OPERATIONS ON BLOOD PICTURE

—	Before operation	1 yr after operation
Hb (%)	87.5 ± 8.1 *(8)*	98.2 ± 6.7 *(8)* $P<0.02$
Red cells (million per c.mm.)	4.45 ± 0.30 *(7)*	4.83 ± 0.50 *(7)* $P<0.02$
White cells (thousands per c.mm.)	3.98 ± 1.9 *(8)*	11.8 ± 5.0 *(8)* $P<0.01$
Platelets (thousands per c.mm.)	118 ± 95 *(6)*	406 ± 130 *(5)* $P<0.01$

Values expressed as means ± S.D. Number of cases in italic numerals in parentheses.
P values for difference between *x* years and before operation.

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o surgery. Individual case-records often appear to ndicate unequivocal improvement after operation. It s worth recalling however that Ratnoff and Patek 1942) observed that patients with cirrhosis who survived their first hæmatemesis for 1 year had more than a 50% chance of surviving 5 years. It is against this background that the survival-rate after operation must be measured. Statistical proof of the merits of surgical treatment in portal hypertension and hæmatemesis cannot be provided for another 10 years. Longer follow-up will exclude the possibility of a fortuitous remission of symptoms coinciding with the post-operation period and will take account of the effect of the better selection and preparation for operation which have been shown by experience to be desirable.

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ACETAZOLAMIDE (DIAMOX) IN THE TREATMENT OF CONGESTIVE HEART-FAILURE

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Previous clinical trials of the diuretic effect of the carbonic-anhydrase inhibitor acetazolamide ('Diamox') in heart-failure have given highly conflicting results (Belsky 1953, Friedberg et al. 1953, Counihan et al. 1954, Relman et al. 1954, Ruskin 1955, Schwartz et al. 1955).

We report here the clinical and biochemical effects of acetazolamide in the treatment and prevention of cardiac œdema in 30 patients.

Material and Methods

Of the 30 patients studied 18 had congestive heart-failure. In 15 of these we compared the diuretic effects of acetazolamide and of mersalyl. In addition 12 patients who had recovered from an attack of congestive heart-failure were treated with acetazolamide alone for continuous periods of three to sixteen months to prevent recurrence of œdema.

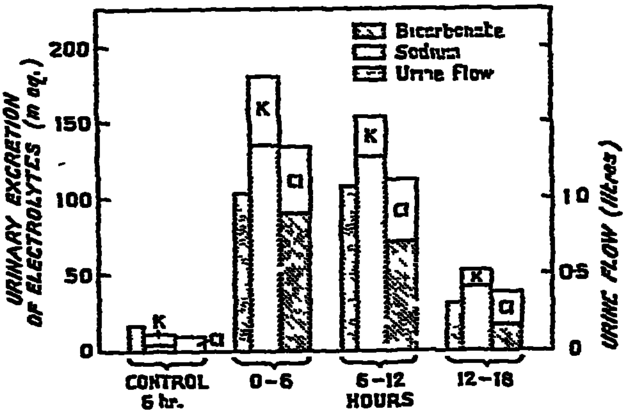

Fig. 1—Changes in urinary excretion of electrolytes and in urine flow produced by acetazolamide 0·2 g. two-hourly.

All the patients with heart-failure were treated in hospital. Their intake of water and salt was kept constant and they were weighed at the same time each day after micturition. Urine was collected under oil during the whole period of observation and was analysed for sodium and potassium by flame photometry and for chloride by electrometric titration (Sanderson 1952). The urinary level of bicarbonate was calculated by the Henderson-Hasselbalch equation after manometric estimation of the carbon dioxide (Van Slyke and Neill 1924) and measurement of the pH with a glass electrode.

Results

Changes in Urine Flow and Electrolyte Excretion Produced by Acetazolamide

Fig. 1 illustrates the changes in acid-base composition of the urine of a patient with congestive heart-failure during the first eighteen hours' acetazolamide therapy. The most striking alteration was a large increase in the excretion of bicarbonate accompanied by a raised rate of urine flow and by increased excretion of the "fixed" cations sodium and potassium. In this patient the urinary output of chloride was moderately increased, but in the great majority of patients acetazolamide caused no material alteration in the excretion of this ion. Each successive dose of acetazolamide had progressively less effect, and the composition of the urine reverted to normal after twenty-four hours in spite of repeated doses.

In 10 cases we obtained control measurements of urine flow and excretion of electrolytes for one or more days before beginning acetazolamide therapy. The accompanying table gives details of the cumulative

CUMULATIVE CHANGES IN URINARY ELECTROLYTE EXCRETION CAUSED BY ACETAZOLAMIDE

Case no.	Type of heart-disease	Daily dose acetazolamide (g.)	Water (litres)		Sodium (m.eq.)		Potassium (m.eq.)		Chloride (m.eq.)		Bicarbonate (m.eq.)	
			1st day	3rd day	1st day	3rd day	1st day	3rd day	1st day	3rd day	1st day	3rd day
1	M.S.	0·5*	−1·23		−27		−23		−32		Not measured	
2	C.P.	0·7	−0·06		−16		−6		−14		Negligible	
3	A.S.	0·4*	−0·13	−0·26	−35	−40	−2	−21	−9	−3	Negligible	
4	H.H.D.	0·5*	−0·58	−1·80	−26	−95	−3	−6	−13	−44	Not measured	
5	H.H.D., T.I.	0·5*	−0·60	−1·12	−90	−177	−7	−21	−4	−7	Not measured	
6	Const. peric.	0·25*	−0·57	−2·22	−33	−76	−34	−45	−1	−3	−36	−56
7	C.P.	1·2	−1·0	−1·25	−160	−232	−66	−158	−7	−18	−128	−155
8	C.P.	1·2	−1·58	−2·30	−81	−64	−67	−165	−14	−67	−168	−177
9	C.P.	0·6	−2·95	−4·37	−322	−612	−65	−148	−107	−394	−202	−237
10	C.P.	0·25*	−2·40	−6·45	−377	−624	−69	−174	−172	−361	−228	−323

M.S. = Mitral stenosis. C.P. = Cor pulmonale. A.S. = Aortic stenosis. Const. peric. = Constrictive pericarditis.
H.H.D. = Hypertensive heart-disease. T.I. = Tricuspid incompetence. * = Single daily dose.

twenty-four to thirty-six hours by bilateral cortical necrosis of the kidneys in about 70% of animals. It was concluded that a single intravenous injection of toxin produced a generalised Shwartzman reaction in cortisone-treated animals. **Spain** et al[18] investigated the response to subcutaneous injection of turpentine in albino mice. Cortisone suppressed all elements of the cellular inflammatory reaction, and diffuse tissue necrosis appeared at the site of chemically induced inflammation. **Shulman** et al[19] produced localised burns in the cheek pouch of the hamster. In normal animals dilated tortuous blood-vessels ("rosette formation") were seen and healing was complete in 80% of the animals after six days; but in cortisone treated animals the rosette formation was delayed, prolonged vasoconstriction was seen, infections were common, and little or no healing was seen after as long as thirteen days. **Zweifach** and his associates have described in recent years some investigations of the inflammatory reaction to microtrauma in transparent tissues, particularly the mesentery of the rat, and the rôle of hyaluronidase, adrenaline, adrenal cortical hormones, and other factors.[20–23] Microinjection of hyaluronidase produced sudden tiny ruptures in the capillary wall, in contrast to a gradual change in endothelial permeability after mechanical or chemical microinjury. According to **Zweifach**, the inflammatory response is a complex reaction which cannot be reproduced by a single biochemical agent, either histamine or leucotaxine.

Further striking results have come from the use of the transparent chamber for the rabbit's ear. This technique which was introduced by **Sandison**[24] in 1928, has lately been improved by **Allison** et al[25] to permit observations with higher magnification and the application of a controlled thermal microinjury by a heated platinum wire. The circulatory changes followed in this way conform closely to previous findings, but new facts have been added by the study of the cellular reaction. Within a few minutes of injury, leucocytes adhere to vessel walls, at first on one side only—the endothelial surface nearest to the injury. This response may be well advanced in vessels which show no alteration of their calibre or are even constricted. Adhesion to the wall also precedes the emigration of leucocytes, and their movement is at least in the first phase, a random one without evidence of chemotaxis. After a cell has passed through a vessel wall there is apparently a defect in the endothelium, for quite often one or more cells follow exactly the same route to the perivascular tissue. The movement of leucocytes is one of active motility but the diapedesis of erythrocytes, which often leads to extensive hæmorrhage, seems to be a purely passive phenomenon. The formation of a gelatinous precipitate near the site of injury, first reported by **Zweifach**,[23] has been confirmed by a different technique. The prevention of this precipitation and the inhibition of the localised Shwartzman phenomenon by heparin, and the decrease of fibrinogen which is observed during the generalised Shwartzman phenomenon, indicate the important rôle of fibrinogen in the inflammatory response. When large doses of cortisone are given to the experimental animals before the thermal injury, a profound change takes place in the inflammatory reaction. There is evidence that the circulatory effects, such as prolongation of the ischæmic phase, are of little importance and that the main action of cortisone is exerted during the earliest stages of inflammation, thus inhibiting and delaying the adherence of leucocytes to endothelial walls and therefore their emigration and accumulation in tissue spaces. The findings suggest that cortisone has a direct action on the endothelial cells and on leucocytes, protecting them in some way against the diffusible breakdown products of tissue or plasma components.

The American Medical Student

Dr **John Ellis** prefaces his account of the American medical student[26] by an account of "medical students everywhere." Most of them, he says, are, at the time of coming to their medical school, poorly educated—not so much perhaps because they have learnt so little of the "humanities" as because of the low standard of their early scientific education. They have difficulty in realising that, despite scientific advance, medicine is still full of mysteries, and they are astonished that therapy is so often of no avail. Many are convinced that they should try to acquire the whole content of medical knowledge, and they are attracted to teachers whose didactic dogmatism makes learning a passive process. Above all, they appreciate results: they like to see the patient get better. "Hence the attraction of curative medicine as opposed to preventive; the feeling that organic disease is the really important thing; the preference for the physical sign rather than the more difficult elucidated history." Lastly, the long and sheltered years of study make them apprehensive about taking responsibility; and to devise ways in which they can be trained to do so is becoming increasingly difficult.

Beyond these universally shared qualities, Dr **Ellis** reflects upon the characteristic traits which distinguish the American student. Unlike his British counterpart, who has to "decide on medicine" at 16 and then work intensively for stiff examinations in physics, chemistry, and biology, the American student can leave his decision until he is at least 18. He gets his premedical education in a more leisurely way at college; and, though this may be of a lower academic standard, he emerges from it not only more mature but also without those bad habits of learning which are so often acquired by British students in their struggle to memorise vast quantities of facts. These college years also help to prevent mistakes in the "preselection" of students, which Dr **Ellis** regards as always more important than the much more commonly discussed selection.

The high standard required in preliminary science by British universities tends to frighten away from medicine the boy who is unaware of any aptitude

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acetazolamide and shows the diminishing renal response to it in comparison with the sustained and more potent effect of mersalyl.

Prolonged "Prophylactic" Treatment of Heart-failure with Acetazolamide

12 patients who had had at least one previous attack of congestive heart-failure but were not œdematous when treatment was begun were treated with acetazolamide for continuous periods ranging from a few weeks to sixteen months. All other diuretics except 'Monotheamine' were withheld, but the amount of salt in the diet was restricted.

Of 9 patients with cor pulmonale 3 had a recurrence of heart-failure in the sixth, twelfth, and sixteenth weeks of acetazolamide therapy, the respective dosages being 500 mg. on alternate days, 250 mg. daily, and 250–750 mg. daily. When heart-failure had developed, acetazolamide was withdrawn and treatment with mersalyl was begun at once and produced a large diuresis in each case. In the remaining 6 patients with pulmonary heart-disease heart-failure did not develop during an average period of treatment of eight months.

In 2 of the 3 remaining cases severe congestive heart-failure developed in the fourth week of acetazolamide therapy; 1 of these 2 patients subsequently had a spontaneous diuresis as a result of rest in bed only, and the other had an excellent diuretic effect from mersalyl and rapidly became free from œdema.

Toxic Effects of Acetazolamide

No major toxic effects were observed. Almost all the patients who received 0·5 g. or more of acetazolamide daily became slightly drowsy and languid, and some complained of malaise, headache, and paræsthesiæ of the fingers, toes, lips, and nose. One patient developed a light-sensitive dermatitis after five days' acetazolamide therapy (0·5 g. daily). No symptoms or signs of potassium deficiency developed even in the patients treated for almost a year.

Discussion

The results agree with the opinion of Relman et al. (1954) that acetazolamide is of little value in severe congestive heart-failure due to hypertensive, ischæmic, or valvular disease. The diminishing effect of successive doses of acetazolamide has been previously described by Nadell (1953) and Friedberg et al. (1952) and was invariable in our patients; it appears to be the chief factor limiting the diuretic action of acetazolamide. The diuresis caused by acetazolamide depends almost entirely on the increased urinary excretion of bicarbonate, and the findings of Counihan et al. (1954) suggest that the diminishing renal response to acetazolamide is caused by reduction of the plasma-bicarbonate level by loss of bicarbonate in the urine. Once, therefore, maximal effect has been obtained from acetazolamide—i.e., when 150–250 m.eq. of bicarbonate has been excreted in the urine—an appropriate time must be allowed for the plasma-bicarbonate level to regain its normal value before acetazolamide will again act as a diuretic. We have found that several days are required for recovery from the effects of even a single dose of acetazolamide, and in the full cycle of treatment and recovery only about 2 litres of œdema fluid may be lost in most cases. This is a poor therapeutic result compared with the loss of several litres of œdema fluid which may follow a single injection of a mercurial diuretic. Resistance to the action of mercurial diuretics may also develop after repeated administration, but this is relatively infrequent compared with the invariable development of resistance to acetazolamide.

In a minority of patients acetazolamide causes increased urinary excretion of chloride ion as well as of bicarbonate. We observed this effect in only 3 of the 18 patients whose urinary excretion was studied in detail. In these 3 patients, 2 of whom had cor pulmonale, the increase of urine flow and of the urinary excretion of sodium was considerably greater than in the remainder, and they were the only patients on whom acetazolamide had a good therapeutic effect judged either on its own merits or in comparison with mersalyl. This finding is in agreement with the results of Schwartz et al. (1955), who deduced that the urinary excretion of chloride must have increased in their 8 patients with cor pulmonale who had a good diuresis as a result of acetazolamide therapy.

Of the 12 patients to whom we gave acetazolamide in the hope of preventing a recurrence of their previous congestive heart-failure 5 developed œdema and venous congestion while under treatment. In 6 cases with cor pulmonale heart-failure did not develop during treatment; but all of these patients concurrently restricted salt in their diet, and 4 had been free from congestive heart-failure for at least six months before treatment with acetazolamide was begun. It is therefore difficult to draw any positive conclusion about the prophylactic value of acetazolamide in these patients.

The longest interval between doses in this study was seventy-two hours and this is too short for full recovery of the plasma-bicarbonate level. It is therefore possible that a longer interval between doses might have been more effective in preventing œdema. It is highly unlikely, however, that single doses of acetazolamide at intervals of four or five days would be equally as effective as a mercurial diuretic given at similar intervals.

Summary

We describe the effects of treatment of 18 patients with congestive heart-failure with the carbonic anhydrase inhibitor acetazolamide ('Diamox').

In 3 patients acetazolamide produced a moderately good diuresis; in 10 the diuretic effect was small; and in 5 it was negligible.

The diuretic efficacy of acetazolamide was inferior to that of mersalyl in 12 of 15 patients in whom these two drugs were compared.

No serious toxic reactions were observed from acetazolamide.

In 5 of the 12 cases where acetazolamide was administered to prevent recurrence of heart-failure, œdema and venous congestion developed during treatment.

We are grateful to Prof. C. H. Stuart Harris and Dr. C. E. Davies for advice and encouragement, and Mr. A. F. Nicholls and Miss S. Exley for technical assistance. The acetazolamide was supplied by Messrs. Lederle.

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"... Only now are engineers beginning to think about machines that are competent to answer 'perhaps' as well as 'yes' or 'no' or belch out strings of numbers. If I were asked—as indeed I often am—what will be the prosthetic brains of the future I should not suggest anything like the instruments of the present day; rather I should envisage some sort of 'hunch generator' that would deal speculatively with events much as I think our brains do, but would begin life as metallic meduses and would acquire human wisdom without the shocks and disappointments that, in us, breed prejudice and despair. Whether, like the legendary Medusa, they would petrify their observers, will depend on the reflective cunning of our descendants."—W. GREY-WALTER, D.SC., in *Cybernetics*. New York: Josiah Macy, jun. Foundation. 1955, p. 31.

is obvious the high-grade feeble minded person often presents a complex social and medical problem The Mental Deficiency Acts require a twofold assessment there must be medical evidence of mental defect originating before the age of 18 years, and social evidence that broadly speaking, the person in question is under one of the social disadvantages enumerated in the Acts The social criterion of unfitness for independence of one group of this high-grade class—those "found neglected"—has lately been defined by a High Court judgment reported on p 378 Before this the view was taken that a defective could be detained as "found neglected," as it were, in anticipation of social failure, but it will now be necessary to show that failure has in fact occurred and that the person is physically suffering thereby

Most of those who have to administer the law will welcome this clarification, but though the cause of individual liberty is upheld, it includes the liberty to suffer In medical terms, the symptoms of the disorder must now be manifest before treatment may be ordered this ensures that only the sick will be treated but it appears to overlook the value of prevention However, if the public accept this judgment, doctors should not object to it The fact that high grade mental deficiency, like delinquency and many other social evils, is sometimes associated with disorders which can be treated by medical means, is no reason for accepting it as an exclusively medical responsibility Just as in mental illness the community is beginning to share with the doctor the responsibility for prevention and aftercare, so this judgment may lead to an increasing awareness of the social needs of high-grade mental defectives, many of whom could be dealt with in the community if society would accept them

Annotations

MITRAL STENOSIS AND PULMONARY HYPERTENSION

THE mechanism and significance of pulmonary hypertension in mitral stenosis is not fully understood At present, the evidence suggests that it arises in at least two ways Organic narrowing of pulmonary arterioles was described at necropsy as long ago as 1936 [1], and more recently it has been confirmed in a proportion of biopsy specimens,[2] pointing to a structural cause for the increased pulmonary resistance On the other hand, the pulmonary artery pressure has been shown to rise sharply in response to exercise in severe mitral stenosis [3,4], and Davies et al [5] found that it could be considerably reduced in certain cases by giving the ganglion blocking agent, hexamethonium Since in neither circumstance did the cardiac output vary significantly, these observations suggest the presence of a reversible vasoconstriction mediated through the autonomic nervous system Whether, as Wood [6] believes, such an increased vascular resistance is a protective phenomenon guarding the lung capillaries against the consequences of a high pressure is not yet decided Davies et al questioned this view after they had reduced the pulmonary arteriolar resistance without dire results in several patients, including 2 in whom an attack of pulmonary œdema rapidly cleared after hexamethonium

Scott et al [7] have recently confirmed that the pulmonary artery pressure may be reduced by ganglion blocking drugs Their 6 patients were given tetra ethylammonium chloride (T E A C), and the pressure fell in 3 They suggest that a good response to T E A C may predict a successful result from valvotomy, and this was confirmed in 2 patients who underwent surgery, though a good result was also obtained in a patient who had not responded to T E A C The experience of Baker, Brock and Campbell [8] suggests that organic vascular changes may be reversible, for in some of their patients the pulmonary artery pressure continued to fall for as long as two years after valvotomy If this is so, preoperative assessment with T E A C or hexamethonium, although of theoretical interest, would be of little practical value, and in any case many more observations are needed Aitchison, Cranston, and Priest [9] have recently reported a rise in pulmonary-artery pressure in patients with mitral stenosis to whom they gave hydrallazine hydrochloride ('Apresoline') Since this drug lowers systemic blood-pressure, such a result was at first surprising, but it is apparently due chiefly to the tachycardia it induces It is well known that a rise in heart rate, by lessening diastole, renders pulmonary œdema more likely when there is obstruction at the mitral orifice [10] Consequently Aitchison et al warn against giving hydrallazine to patients with mitral stenosis

THE UNVACCINATED NURSE

APART from one or two steadfast opponents of vaccination, no one will deny that recent successful vaccination is efficient protection against smallpox Unfortunately, the proof is too often made plain when those unprotected by vaccination come in contact with the disease, and fall ill By no means rarely those who are at particular risk—nurses, orderlies, or domestic staff—are among the victims A recent instance was the Brighton outbreak in 1950 13 nurses and hospital domestic servants had smallpox after contact with an R A F officer who was admitted to the hospital with unrecognised smallpox His clothing was sent to a laundry, and 6 people there were also infected 5 of the hospital staff and 2 of the laundry workers died In the ward concerned, 7 of the staff were unvaccinated, and out of a total of 113 nurses and maids in this infectious diseases hospital, 27 had never been vaccinated

During the war a number of soldiers abroad died of this preventable disease, and in many cases there was no visible evidence of successful vaccination to support the written record The need for prompt revaccination of those exposed to the risk of contact was illustrated when more than 30 of the staff and patients of a general hospital overseas contracted smallpox A known case of confluent smallpox had been admitted to this hospital and imperfectly isolated, and there was some delay in revaccinating the nurses and orderlies—with the inevitable sequel Fortunately, the disease among most of the contacts was well modified, for they had been vaccinated in infancy or on joining the Army, or both

Attention has been drawn recently to the vaccination state of hospital nurses in this country The Sheffield Regional Hospital Board [11] has noted that nearly three quarters of the nurses and other hospital staff in the denum before becoming inert. If I could produce a temporary ischæmia of the gastric or duodenal lesion with a relaxation of the pyloric sphincter, the necessary conditions for the effective use of stypven might be obtained.

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I recalled an incident that occurred several years previously. I had been called to deal with a case of severe and persistent hæmorrhage following gastro-enterostomy, in circumstances where neither blood nor anæsthetist were readily available. Gastric lavage produced no improvement and in desperation I injected 5 ml. of adrenaline hydrochloride (1 in 1000) down the Ryle's tube. The bleeding ceased, and to my intense relief there was no systemic reaction.

I felt that the important point was not that adrenaline had stopped the bleeding, but that it could be taken by mouth in a dosage that would have proved fatal given any other way. Stypven was similar to adrenaline in this respect; injected into the blood-stream it would be fatal, but it could be taken safely by mouth.

Dosage.—Initially a dose of 5 ml. of adrenaline and 1 ml. of stypven was given to patients who were not fit for operation. The dose was increased when I realised that both drugs could be given in complete safety, and that enough had to be given for the drugs to permeate the stomach contents and pass into the duodenum while still active. The optimum dose (which can be exceeded in perfect safety) was found to be 40 ml. of adrenaline and 5 ml. of stypven.

The use of adrenaline was at first purely theoretical, but once its safety was established beyond question, I persuaded Dr. Leitch to administer 10 ml. of adrenaline to 2 volunteers who had been referred for barium meal examination. The patients were chosen because the capacity, motility, and emptying times of their stomachs were known. Dr. Leitch reported that there was no alteration in the volume or motility of the stomach after adrenaline, but there was a complete absence of mucosal rugæ, the pylorus was fully patent, and the barium flowed rapidly into the duodenum.

The shrinkage of the gastric mucosa allows the stypven obviously easier access to the lesion, particularly a small acute erosion.

Technique

This treatment calls for the closest liaison between physician and surgeon, and I have to thank Dr. A. C. Aitkenhead for her wholehearted cooperation, and Mr. A. Tomney, who has evolved the most efficient way of using adrenaline and stypven.

Every patient admitted to the medical ward is permitted a single attack of frank hæmatemesis. If, however, he bleeds a second time while at rest in bed, a no. 10 stomach-tube is passed, usually intranasally, and the stomach is washed out with 1 pint of sterile water. 20 ml. of adrenaline hydrochloride (1 in 1000) is inserted down the tube, and the tube left in situ. After twenty minutes to half an hour, gastric lavage is repeated; a further 20 ml. of adrenaline is then injected, followed a few minutes later by 5 ml. of stypven, which is cleared from the tube by 5 ml. of sterile water.

The stomach tube is withdrawn and a slow intravenous transfusion of 2 to 4 pints of blood started. An enema is given the following morning to remove melæna, and the medical dietary regime is resumed. Dr. Aitkenhead prefers to retain the stomach-tube and aspirate at intervals to detect any fresh bleeding, but I feel that the patient is more comfortable without the tube. Any significant fresh bleeding is immediately shown by a return of pallor, sweating, a rise in pulse rate, and a fall in blood-pressure.

The most successful time to use adrenaline and stypven is immediately after bleeding has taken place. The patient is still hypotensive and, if the occluding clot is washed away, bleeding is not severe and can be controlled temporarily by adrenaline.

No amount of washing can remove large intragastric blood clots completely, and the initial dose of adrenaline occasionally acts as a mild emetic, causing the patient to vomit once and so clear his stomach. Should this not occur the interval between the first and second gastric lavages permits the greater portion of the fluid contents to pass through a patent pylorus, and the second lavage then clears what is left. The second dose of adrenaline again shrinks the gastric mucosa and permeates freely between the stomach wall and the retained blood clot. If bleeding has recurred, it is again arrested and the stypven, following the same route with little or no delay, is able to produce a stable occlusive clot over the bleeding point.

As soon as the patient recovers sufficiently, a barium meal examination is carried out. If a definite lesion is reported, he is treated by a delayed elective gastrectomy, and table II shows the low mortality-rate in 1953–54 following this form of treatment.

Treatment with adrenaline and stypven can be used in complete safety in any patient, irrespective of his age, general condition, and degree of exsanguination, and it gave such excellent results at first that I concluded that emergency gastrectomy was no longer necessary. But in 1953, 2 patients died from hæmorrhage after adrenaline and stypven, and necropsy showed that they had been bleeding from arteries of considerable size lying in the base of chronic ulcers.

Adrenaline and Stypven as "Preselectors"

It then occurred to me that these cases had been examples of "surgical" hæmatemesis, which I mentioned earlier in this paper, and that adrenaline and stypven had acted as "predictors" or "preselectors" of the patients who should have immediate operation.

If bleeding recurs within a period of seventy-two hours after the administration of adrenaline and stypven, it is proof that the patient has "surgical" hæmatemesis. It stands to reason that an occlusive blood clot in a large vessel whose walls are fixed in fibrous tissue will not withstand indefinitely the hammer-blows of a rising blood pressure, however tough the clot may be.

Should the repeated hæmorrhage be excessive and the patient collapse, adrenaline and stypven are used again but only as a preparation for operation. The drugs control the bleeding for a further period, during which time resuscitation can be achieved by rapid blood-transfusion without risk of a sudden disastrous hæmorrhage as the blood-pressure returns to normal. Adrenaline and stypven may be unnecessary in less severe degrees of bleeding. The patient should then respond satisfactorily to emergency gastrectomy: the 4 patients who had emergency gastrectomies in 1953 and 1954 were typical cases of "surgical" hæmatemesis (table II).

The knowledge that recurrent bleeding must be due to a chronic ulcer is useful if the resected portion of the stomach shows no lesion: the lesion must be in the gastric remnant, and can be looked for and dealt with accordingly.

Bleeding occasionally recurs on the fifth day after the administration of adrenaline and stypven in cases of non-surgical hæmatemesis. It seems that the underlying pathological process outlasts the period of effective control by the stypven clot. The hæmorrhage, however, is rarely severe and recovery is spontaneous.

Discussion

The advantage of this treatment is that it can be employed at the earliest possible moment in any case of hæmatemesis where a gastroduodenal lesion is suspected. It forestalls the rapid deterioration in the patient's condition caused by repeated hæmorrhage and incidentally saves a considerable amount of blood.

We found that all acute gastroduodenal lesions stopped bleeding immediately after the administration of adrenaline and stypven: adequate transfusion then ensured an uneventful recovery without further bleeding. A high proportion of chronic gastroduodenal lesions responded in the same way.

Since the adoption of the adrenaline and stypven technique, the effects of "over-transfusion" are no longer seen. The reason is that this condition only develops no financial recognition of the added responsibility of the N H S technician's work as part of a team concerned with the well being of patients The low salary at entrance is a reflection of the low educational standards which were accepted by the I M L T, but now that *these standards have been raised there are good reasons* for making the scales of junior technicians the same as those of the "scientific assistant" *grade of the Civil* Service, which would require a further increase of £80–100 a year up to the technician grade (holder of the A I M L T)

The most disappointing change in the new arrangements is the limitation of senior technicians in small laboratories to a maximum of £725 Their responsibility for other staff may be less, but their responsibility to the pathologist and to the patient is greater This limitation will increase the drift of energetic and ambitious young men to the large laboratories in the towns, leaving the equally important laboratories in country hospitals inadequately staffed, both in quantity and in quality On the other *hand, there is provision for promoting technicians who* are regularly engaged on individual work of special *difficulty*, responsibility, or *skill* as senior technician II (up to £800) *or* chief technician I (up to £900), independently of the general staffing of the laboratory If this provision can be used to upgrade technicians in sole charge of a laboratory or in charge of blood grouping and compatibility testing—who certainly undertake work of special responsibility—it may counteract to some extent the centripetal effect of the new grading

On the whole the new salary scales are reasonable, but they are not yet likely to attract many school-leavers, nor do the senior scales offer a good career in a country hospital It might be an advantage to unite the three grades senior technician I and II and chief technician I, into a single grade of supervisory technician, which would take nineteen years to climb, but which could be entered *with six or thirteen years' seniority by those appointed* to the grades now called senior technician II *or* chief technician I

ANOTHER FAMILIAL ENCEPHALITIS

WE remarked some time ago[1] on the difficulty of framing a rational classification of the different types of encephalitis in childhood Brewis[2] showed that less than a third of cases were sequels to recognised infections Classification in terms of causal agents is usually impossible, and Brewis suggested a useful symptomatic classification, but he found that nearly a quarter of his cases were too bizarre to fit into any group

A familial encephalitis *affecting 3 children of the same* parents was described by Miller and Gibbons[1, 2] in 1954 Harvey, *Haworth, and Lorber,*[4] *of Sheffield,* have *now* added a fresh syndrome to the familial group A father and 5 of his children were affected The father was mentally retarded, and he had kyphoscoliosis, choreo athetosis, and pes cavus His children fell ill in, as it were, familial epidemics characterised by fever and often by loss of consciousness After the acute illness, athetosis, hypotonia, and mental dullness remained as sequelæ The wave of acute illness recurred at least thrice After each attack *deterioration* was *evident* Very careful investigation by the Sheffield workers failed to reveal any signs of the known degenerative diseases of childhood, nor, indeed, did their special investigations reveal anything more than some non specific electro encephalographic changes

Harvey et al suggest that this syndrome may have a double ætiology the acute febrile episodes may have been attacks of viral encephalomyelitis striking down brains which were *genetically predisposed to fail* in a particular way

THE LIVER IN SARCOIDOSIS

SARCOIDOSIS is often suspected on clinical and radio*logical evidence* In the absence of a specific biochemical or bacteriological test, however, the diagnosis is finally reached by the *exclusion of other diseases,* especially tuberculosis and other varieties of granulomatosis Histological confirmation, although highly desirable, is usually lacking since it entails a *biopsy examination of* the lung or an affected and accessible lymph gland Aspiration biopsy of the liver *provides a much more* convenient method of obtaining material suitable both for microscopy and bacteriology

The first account of liver biopsy in sarcoidosis appeared in 1943[1] In the next ten years several small series were published dealing with 92 patients in 71 of whom sarcoid follicles were demonstrated in the liver Mather, Dawson and Hoyle[2] have lately recorded the most extensive and *detailed study of this kind yet published* It is based on 200 biopsies in 93 patients with the clinical and radiological diagnosis of *sarcoidosis,* in 32 with various forms *of* tuberculosis, and in 37 with miscellaneous diseases The results fully confirm the great diagnostic value of this procedure Typical lesions were found in 59 of the 93 cases of sarcoidosis The proportion with positive findings appeared to be independent of the clinical manifestations, of the tissues clinically affected or of the degree of tuberculin sensitivity A comparison of the lesions with those in tuberculosis showed that in the *absence of caseation the two are indistinguishable* Attempts to demonstrate acid-fast bacilli microscopically, by culture, or by guineapig inoculation were *also* equally unsuccessful Repeat biopsies on several patients revealed the remarkable persistence of the characteristic follicles in many cases, although sometimes clinical recovery was accompanied by complete resolution or hyaline scarring Repeat biopsies were also used to study the effect of treatment Only combined treatment with cortisone and streptomycin produced significant results in 3 out of 9 patients the lesions disappeared completely, and in the remaining 6 decrease in size or number was accompanied by fibrosis

The degree of hepatic involvement is noteworthy The estimated average number of lesions in the whole liver in the positive cases was 150,000 Despite this severe involvement there was little evidence of disturbed hepatic function Hyperglobulinæmia, when present, was more probably the result of the generalised disturbance of the reticulo endothelial-system than an indication of hepatic dysfunction Histologically, too, the liver parenchyma was normal apart from some fatty change in about 10% of cases Diffuse fibrosis, which so *often* affects the sarcoid lung was notably absent from the liver

A *comparison of the prevalence of* hepatic lesions in sarcoidosis and tuberculosis is of interest In miliary tuberculosis tuberculous lesions have been found in the liver in every one of the few cases investigated but in primary tuberculosis in only 16 out of 25 cases Thus the proportion of positive findings in sarcoidosis and primary tuberculosis is almost identical *If the two* diseases are entirely unrelated the similarity of *these figures* is remarkable Failure to demonstrate tubercle bacilli in sarcoid lesions *is the major objection to regarding* sarcoidosis as a manifestation of tuberculosis If, however, as Mather and his colleagues suggest,[2] sarcoidosis represents an exaggerated and long lasting reticulo endothelial reaction following primary tuberculosis, this criticism is largely met The chemical demonstration of specific bacterial residues in the lesions[3] would give strong supporting evidence

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[1] *Lancet* 1954 ii 374

[2] Brewis E G *Brit med J* 1954 i 1298

[3] Miller H G Gibbons J L *Ann intern Med* 1954 40 755

[4] Harvey C C Haworth J C Lorber J *Arch Dis Childh* 1955 30 338

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[1] Van Beek C Haex A J C *Acta med scand* 1943 113 125

[2] Mather G Dawson J Hoyle C *Quart J Med* 1955, 24 331

[3] Consden R Glynn L E *Lancet* 1955, i 943

people Owing to the relatively large number of women from that area who are employed in the catering trade, one should be alert for the carrier of *Salm paratyphi C*

Summary

A case of paratyphoid-C osteomyelitis of the tibia is described Surgical drainage and chloramphenicol therapy brought about complete recovery

Attention is drawn to the occurrence of paratyphoid-C infection in West Indians

We wish to thank Mr Fulford for permission to publish this case, and Dr Taylor for her help in identifying the organism, and Miss M N Ellis for secretarial assistance

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GIANT HYPERTROPHIC GASTRITIS

WITH HÆMORRHAGE REQUIRING EMERGENCY GASTRECTOMY

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GIANT hypertrophic gastritis, a rare chronic inflammatory disease of unknown origin, is of clinical interest because it is usually diagnosed as carcinoma Its pathological features, however, are distinctive and were first described by Menétrier (1888), who termed the lesion *polyadenome en nappe* Giant hypertrophic gastritis is to be distinguished from so called chronic hypertrophic gastritis, which is often a variant of normal (Palmer 1954), and also from the polypoid lesion sometimes found in the pylorus near a peptic ulcer or the stoma of a gastro-enterostomy (Spriggs 1943)

Menetrier (1888) found that the stomach in one of his cases was

> "bulky and markedly dilated When cut, the mucosa was greatly swollen and thickened, and thrown into enormous protruding folds, the appearance resembling that of cerebral convolutions These folds were as thick as a finger, sinuous and separated by deep crypts, lying on the whole parallel to the long axis of the stomach They were particularly thick on its posterior wall, where the craters were 2–3 cms deep The hypertrophy affected the greater part of the stomach, sparing the cardia to a distance of 3 cms, and terminating abruptly in a sharp edge 8 cms from the pyloric sphincter The mucosal surface was composed of innumerable mammillations, 3–4 mms wide and 4–5 mms high, which were surrounded by small craters It was reddish violet in colour, there were many scattered ecchymoses, and the whole affected surface was covered by a thick layer of viscous mucus which was difficult to detach In section, although the hypertrophy was mainly due to thickening of the mucosa, the submucous and muscular layers and the peritoneum were also seen to be involved"

On palpation the exposed stomach has a peculiarly boggy texture, which has been likened to that of a varicocele (Bourne and Wood 1948), a bunch of fish worms (Maimon et al 1947), or, more aptly, a placenta (Strauss et al 1928), and the neighbouring lymph-glands are sometimes enlarged

The symptoms of giant gastritis are unremarkable Mild or severe dyspepsia may have been present for a few weeks or many years, while anorexia and weight loss may help to suggest the presence of carcinoma In one patient (Grime and Whitehead 1951), a firm well defined mass, which moved on respiration, emerged from beneath the left costal margin, but in all other cases nothing has been felt in the abdomen Swelling of the ankles, an unusual finding in this disorder, has been attributed to a fall in the plasma-protein level Anæmia is common, but acute bleeding has been described in only six patients (Brunn and Pearl 1926, Strauss et al 1928, Buckstein 1940, Spriggs 1943 Maimon et al 1947, Kilbourne 1953) None of these required urgent operation, but in the patient described here gastrectomy was performed for uncontrollable hæmorrhage

Case-record

A labourer, aged 39, who was admitted on Jan 12, 1955, for four years had complained of epigastric discomfort and fullness after meals, loss of appetite, flatulence, and constipation, and these symptoms were unrelieved by diet, alkaline powders, or aperients He had lost about seven pounds in weight Four weeks before admission he became tired and pale, and on one occasion he fainted at stool Twenty years and thirteen years previously he had had epigastric pain, which persisted for six months on each occasion, and while on war service in Egypt he had been ill with dysentery for three weeks His consumption of alcohol was moderate (two pints of beer on occasional weekends), and he smoked 10–15 cigarettes a day There was nothing relevant in his family history

On examination he was well nourished, anxious, and pale, and there was no œdema His pulse rate was 90 per minute and blood pressure 130/70 mm Hg No abnormal tenderness or mass was found in the abdomen His hæmoglobin was 38% and plasma proteins 6 7 g per 100 ml (albumin 4 3 g and globulin 2 4 g)

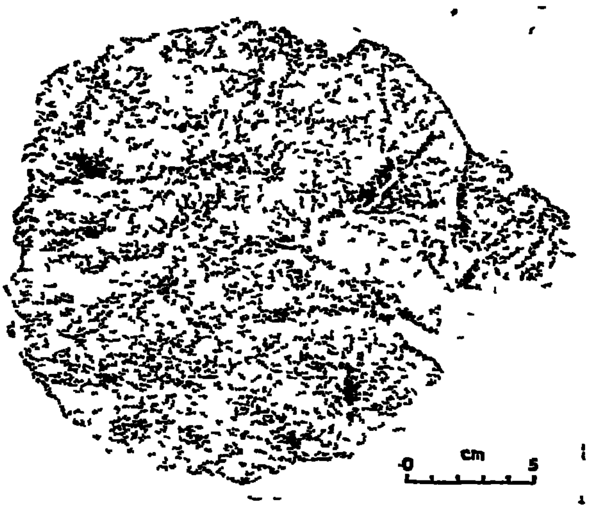
Treatment and Progress—The patient's condition improved with medical treatment and blood transfusion ($3^{1}/_{2}$ pints), and was discharged on Feb 10, four consecutive stools (Feb 8–10) containing no occult blood A barium meal examination on Feb 10 was negative

He returned on March 18, having vomited about 2 pints of blood that morning He was again pale and was moderately shocked, his pulse rate was 110 per minute and blood-pressure 90/50 mm Hg Blood was transfused, 2 pints in twenty four hours, but on March 22 his condition had not improved and a further 3 pints was given Three days later pallor was as great as on admission, and recovery with medical treatment now seemed unlikely More blood was given, and at 8 30 P M on March 25 he underwent laparotomy by Mr J E Richardson

Laparotomy and Subsequent Progress—The stomach was enlarged, and its proximal two thirds diffusely thickened, especially along the greater curve There were no palpable lymph glands Total gastrectomy and œsophagojejunostomy (Roux en Y type) were performed The patient's recovery was delayed owing to antibiotic induced staphylococcal enteritis, but he was eventually discharged in good condition Four months later he was symptom free and had almost regained his normal weight

Pathological Examination

The removed stomach showed, as was later realised, all the features of giant hypertrophic gastritis On palpation it was heavy and boggy, like a placenta, its mucosal surface



Mucosal surface of stomach

settle down to the grind for their diplomas and memberships and the like We attract a high proportion of good exam candidates (this department holds at the moment the top students of three successive years) and it *irritates* such a man to see his less gifted classmates, by mere application and tagging on to the right ski-lift of time and jobs, acquiring an ever more glittering array of letters after their names

He can, it is true, take the D C P or the D PATH of the University of London But the D C P, excellent in itself, has become too easy for those who take the Postgraduate School course and too hard for those who don't, and has ended up almost entirely a colonial preserve And I have yet to meet anyone who bothered to take the D PATH

Above that level, most people take an M D But before I come to that, let me examine the main alternatives The most important, because most often attempted, is the M R C P Now it happens that in the eyes of the Minister of Health (to whom all consultants must be Physicians, Surgeons, or Obstetricians) we count as coming under the College of Physicians, and it is therefore very reasonable of us to attempt to become members of that College But now that good anæsthetists and good theatre sisters and good transfusion services have taken most of the adventure out of surgery, and physicians have rediscovered the pleasures of research, glamour and hordes of candidates have returned to Pall Mall, and the palings that guard it have been pitched correspondingly higher

The failings of the M R C P exam as a qualification for physicians don't concern me here they are probably not very serious And even so far as the pathologist is *concerned it's not very unreasonable to ask him to* write a stiff paper in physiology and physician's medicine, and even stand his viva in them, for all medicine—all human biology come to that—is grist to his mill (he ought to be able to, and often could, make a fair stab at most of the F R C S and M R C O G papers too) But the clinical exam is another matter The ability to spot a shaded chest resonance or a glossopharyngeal paralysis or a flattened T in lead V436, or to winkle the crucial history out of a hysteric—these are not of the least importance to anyone but the practising consultant physician they are his special skill, his party trick (It would be as irrelevant to ask the physician to sort *out a really sticky* reticulosis under the microscope, or to isolate an abnormal hæmoglobin, or phage-type a few staphylococci these are *our* party tricks, but the pathologists who are graciously permitted to act as examiners for the M R C P are not tempted to introduce them to that exam)

It is true that one can be let in by the back door on submission of published work There are snags about that though There is the back door atmosphere, the *uncomfortable* implication *that one had funked the* honest examination By the time one has written enough papers *to* qualify, an M R C P is not as much use as it might have been earlier And it *is* possible to find one's submission rejected, and that is a worse blow in one's orgulous forties than in one's resilient youth (though, of course, it can be managed so that hardly anyone knows about it)

If the R C P is to be accepted as our *College*, it ought to contain more pathologists And the only proper way to this is the institution of an M R C P (PATH) But that seems improbable There is of course the M R C P (PATH) of Edinburgh but the unnatural keenness of competition among physicians has given to the Edinburgh Membership in medicine, merely because it is ever so slightly easier than the London one, an undeserved stigma as a soft option, and the reasonable and respectable pathological Membership has suffered in consequence

One comes back to the M D, and, as I said earlier most people take it But the M D is a most nebulous and unsatisfactory degree Every university is a law *to itself in the standard* it expects In at least one it can be had for little more than the asking by anyone on the teaching staff In most a thesis has to be of a remarkably low standard before it is rejected altogether Some universities demand a thesis alone, some an exam alone, some either, some both Contrast the M R C P , or even, nearer home, the M B the latter is the stiffest baccalaureate going in any university, its standard is even, and a mere pass in it is equivalent to good honours in most subjects, while the M D is in many universities the cheapest doctorate (academically cheapest, not in cash) And because nearly all M D s are tied to the M B one cannot pick and choose if the university of one's qualification offers a poor M D , one can only be content with it

It is not surprising that there is a movement towards medical PH D S One has there at least a fairly even *standard, and thesis regulations which on the whole* work well But the letters have an odd unmedical look after one's name, and except for academic appointments they probably still frighten more than attract the jungly fringes *that* still control most selection committees And there are other snags

What's to be done ? If we must have an exam, I hanker still after a London M.R C P (PATH)—with the same written paper and (within limits) viva as the physicians, but a more appropriate practical exam Failing that, a Cambridge M D or a Scottish M D at commendation level, thrown open to all comers and with free use of external examiners Or perhaps, as a last resort, a Fellowship of the Pathological Society (preferably, for ostentation, the Royal Pathological Society) with a thesis, a stiff practical exam in one elective subject, and a stiffer written *paper in medicine* as a whole This last and least likely I especially like to contemplate, for it must go without saying that all such established pillars of the society as myself would automatically (and cheaply) become Foundation Fellows

Cloud Cuckoo ? Manifestly None of these is likely to happen Yet, after all, does it matter ? For in truth, Barbara, we do not *do* so badly as we are What purpose in the last analysis, do all these exams serve ? Vain glory, and the profit of the examining bodies (who might else have to find it in even more questionable ways)—granted, but what else ? A coarse sieve for the early rejection of hopeless aspirants and a rough guide for appointment to jobs, and perhaps a stimulus to work at a critical stage of one's career—who would honestly claim more for them ? But though some *pathologists would have been better* discarded early, and some selection boards make mistakes, and some of us don't work as hard as we ought—though all these things happen, I know of no evidence that they happen more often among us than in more carefully organised trades, or that *the* adoption of a rigid exam structure would make the least difference

We have of course two things in our favour that perhaps apply rather less in other subjects *One is our* papers, of which we write more *than most people No one* worth his salt can sit daily in a pathology laboratory watching the continual pageant of the so called routine without feeling the urge to tell the world about some of it, and a pathologist who doesn't write a paper or two as often as he can can nearly always be written off And once one has committed oneself to print a few times, one is exposed for good or ill to the judgment of the discerning eye better than by all the testimonials and *degrees and certificates in the world* sympathectomy and palliative operations for occlusive arterial disease, does not mention the operation. Most workers, however, do not deny that temporary local vasodilatation follows the operation.

We report 2 cases in which femoral periarterial sympathectomy was undertaken to encourage healing in amputation stumps following arteriosclerotic gangrene.

Case-reports

Case 1.—A man, aged 76, attended the casualty department on Aug. 8, 1950, with a week's history of inflamed toes. There were sloughing ulcers on the adjoining sides of the right 4th and 5th toes and redness and swelling of the dorsum of the foot. The foot was cold, and no pulsation was felt in the dorsalis pedis, posterior tibial, or popliteal vessels. The patient was anxious not to be admitted and he was treated as an outpatient; but on Aug. 21, there was wet gangrene of the adjoining sides of the affected toes and he was admitted to hospital. His skin was otherwise healthy. Blood-pressure 210/100 mm. Hg.

Investigations.—His hæmoglobin-level was 12·6 g. per 100 ml. and white-blood-cell count 7800 per c.mm. (polymorphs 75%). Blood-urea 35 mg. per 100 ml. Urine normal.

Medical Treatment and Local Amputation.—Tolazoline hydrochloride ('Priscol') 75 mg. daily was given by mouth, and penicillin was given systemically. The inflammation subsided and the gangrenous area dried. The patient refused amputation of the leg, and local amputation was performed on Sept. 1, when it was noted that bleeding was poor. He was discharged from the ward on the 12th day after operation with no sign of healing but no gangrene.

He was readmitted three months later on Dec. 4 with spreading gangrene of the forefoot. His hæmoglobin level was then 10·1 g. per 100 ml. and this urine contained protein.

Amputation was agreed to, and was performed at mid-thigh level on Dec. 13, with penicillin and chloramphenicol cover. The wound showed no sign of healing nor of inflammatory reaction, and on Dec. 29 (the 16th postoperative day) a small area of dry gangrene appeared and this spread during the next week.

Periarterial sympathectomy was performed and the wound edges were excised and resutured on Jan. 16, 1951 (the 34th day after amputation).

Progress.—Some erythema appeared at one end of the wound on about the 6th postoperative day, but the wound had healed uneventfully by the 22nd day. The stump remained soundly healed during a 4-month follow-up and was still healed when he was admitted to another hospital 10 months later with gangrene of the other foot.

Case 2.—A man, aged 70, attended the casualty department on Feb. 20, 1955, having fallen a few days previously.

On examination there was infective gangrene of the 4th and 5th toes of the right foot, extending along the outer side of the foot to the lower leg, which was almost completely encircled by a large ulcer. Pulsation was felt in both femoral and popliteal arteries. His general condition was exceedingly poor; he was dehydrated and undernourished.

Investigations.—Radiography showed patchy calcification of the dorsalis pedis artery at the level of the tarsus. His hæmoglobin level was 14·1 g. per 100 ml. and white-blood-cell count 23,350 per c.mm. (polymorphs 87·5%).

Medical Treatment and Amputation.—The patient was admitted to hospital and given systemic penicillin and chloramphenicol and intravenous saline, plasma, and blood. On Feb. 23, a mid-thigh amputation was performed. Postoperatively his general condition improved slowly. His urine contained pus cells, red blood-cells, and occasional hyaline and granular casts, but no sugar. The stump showed no sign of healing; it was dry initially but it became moist and œdematous by the 8th postoperative day; on the 15th day, a small hæmatoma developed which increased in size and was evacuated on the 20th day. By the 30th day there was still no sign of healing. His hæmoglobin level fell from 15·0 g. per 100 ml. on Feb. 23 to 12·6 g. per 100 ml.

Periarterial Sympathectomy.—The patient was transfused with 800 ml. of blood and periarterial sympathectomy was performed on March 29 (34 days after amputation). At operation $^{3}/_{4}$ in. of the common femoral artery was stripped of its adventitia. The wound edges were excised and resutured.

Progress.—A small area of necrosis developed at the side of the stump wound with some inflammation which was maximal on about the 10th day but which improved thereafter; healing was complete by the 22nd day. Skin-temperature recordings preoperatively and on the 17th day after operation showed no significant change. After his discharge from hospital an area over the stump $^{1}/_{2}$ in. long broke down, but it healed slowly over a period of 5 weeks.

Discussion

The problem presented by these 2 patients is not uncommon. Lehman and Figueira (1953), in a review of 75 cases of arteriosclerotic gangrene treated by amputation, found delayed healing in 25 and necrosis in 15. Necrosis might be treated by reamputation at a higher level, but one is loth to take that step when mid-thigh amputation has already been done and healing may still not occur.

An alternative is to improve the local circulation sufficiently to ensure that the wound heals after simple excision and suture. In the 1st case oral tolazoline was given early without appreciable effect, thus confirming Lynn's (1950) observation in cases of occlusive vascular disease of an increased blood-flow after intravenous tolazoline, but no significant improvement after oral therapy. Lumbar sympathectomy has a more widespread and lasting effect, but this is no minor operation for the frail, elderly patient. Periarterial sympathectomy was tolerated well by both patients, and although healing was not entirely uneventful the results were very different from those of the initial amputations and it was not necessary to shorten the stump. In each case it was considered that simple excision and suture would certainly have failed.

The rationale of this operation has been the subject of considerable discussion.

The femoral artery receives its main sympathetic-nerve supply from the posterior division of the femoral nerve in a bundle which reaches the artery at the point where the profunda branch is given off. It derives a few filaments from the iliac plexus and, in the adductor canal, from the saphenous nerve and the nerve to vastus medialis (Mitchell 1953).

It is reasonable to suppose that perifemoral neurectomy will lead to dilatation of proximal vessels without necessarily affecting more peripheral vessels. The clinical effect is known to be transitory; Lambert Rogers (1931), studying the effect of this operation on chronic leg ulcers, found that healing proceeded for 5 weeks, and if the skin was healed by that time it was likely to remain so, but an ulcer still present tended to increase in size. Apparently therefore perifemoral sympathectomy will be most useful when an increased blood-supply is required in the more proximal part of the limb and when healing is likely to occur within 5 weeks of the operation. The 2 present cases satisfy both these criteria, and it can be hoped that, although the vasodilatation has subsided, the blood-supply will remain sufficient for the demands of a stump that is never likely to be submitted to the pressure of a prosthesis.

After sympathectomy there is no clear correlation between evidence of increased blood-supply and the clinical result. Indeed, in some patients with vascular insufficiency incised tissues may bleed freely yet not heal. It appears that the insufficiency is caused not only by narrowing of the blood-vessels but also by loss of their normal intermittent action and capacity to react. Experience of sympathectomy for vascular disorders has emphasised the effects of interfering with efferent nervous pathways, but the insufficiency may be caused partly by absence of normal afferent stimuli; thus sympathectomy may act not only by reducing vascular tone but also by interfering with the afferent side of the reflex arcs which control vascular function, thereby provoking a new pattern of stimulation which can alter this way, 70% survived and then underwent an anastomotic procedure to reduce the portal hypertension He favours hypotensive spinal anæsthesia during anastomotic surgery

Portal Hypertension

Dr A L DE ALMEIDA (Brazil) combined percutaneous splenoportal venography with intrasplenic manometry in assessing 97 patients with portal hypertension and in healthy subjects Of the radiographic findings in portal hypertension, he stressed the tortuosity and dilatation of the portal vein, the presence of collateral channels, and the acuteness of the angle of the portal vein with the vertebral column His measurements of the intrasplenic pressure have proved of practical importance in the diagnosis and management of portal hypertension

Bilirubin

Dr J L BOLLMAN (U S A) used the technique of reverse phase chromatography, evolved by Billing, Cole, and Lathe in England, for the identification of different bilirubins in hepatectomised dogs As would be expected, he identified indirect bilirubin in the serum In addition however, he discovered a new pigment which passes into the urine It reacts slowly in the van den Bergh reaction, although more quickly than indirect bilirubin and it is soluble in chloroform It is probably similar to pigment 1, which has been described in Great Britain

Cirrhosis with Ascites

Dr J CAROLI (France) divided his ascitic cirrhotic patients into asthenic and sthenic groups In both groups the majority of patients were alcoholics Most of the asthenic patients were female, and usually they were jaundiced, anorexic, and depressed and had lost much weight They responded badly to all forms of treatment, including diet and paracentesis abdominis The sthenic group lost their ascites in three to four weeks with multiple small paracenteses of 2-3 litres three times weekly, while receiving a 350 mg low sodium diet containing 3000 calories

Secretin Test

Dr D A DREILING (U S A) reported the results of the secretin test in 1500 patients with pancreatic and biliary tract disease *The result is abnormal in the presence of tumours* of the head and body of the pancreas Tumours of the tail of the pancreas and encroaching contiguous tumours do not affect the test It is of no practical value in the diagnosis of acute pancreatitis, because it cannot be undertaken in the acutely ill patients and it returns to normal quickly in convalescence A false positive secretin test may be obtained when the indwelling duodenal tube is displaced, so the site of this should be checked by fluoroscopy False negative secretin tests are obtained when ulcerating growths permit diversion of pancreatic secretion into sites other than the duodenum

Classification of Hepatic Cirrhosis

A special subcommittee, under the chairmanship of Dr SHEILA SHERLOCK, recommended that hepatic cirrhosis should be defined anatomically and clinically Essential anatomical features are as follows (*a*) involvement of every part of the liver, but not necessarily every lobule , (*b*) cellular necrosis at some stage of the disease , (*c*) nodular parenchymal regeneration , (*d*) diffuse fibrosis (*e*) disorganisation of the lobular architecture with connective-tissue bands uniting centrolobular zones with the portal tracts Clinically the disease is chronic and may be accompanied by liver cell failure and/or portal hypertension

The classification of cirrhosis should be morphological, ætiological, and functional Three morphological types suggested were portal, postnecrotic, and biliary , the biliary type was subdivided according to the presence or absence of obstruction of the extrahepatic biliary tract The accepted ætiological factors are malnutrition, ethyl alcohol, viral hepatitis extrahepatic biliary tract obstruction, cardiac failure, hæmochromatosis, and rarely congenital syphilis

The functional classification should include liver cell failure and portal hypertension, if either or both are present and also assessment of the activity of the disease, which indicates whether it is progressing, regressing, or stationary

It was recommended that the following terms b abolished because they are useless or confusing pseud cirrhosis, monolobular and perilobular cirrhosis, atroph and hypertrophic cirrhosis, capsular cirrhosis, fatty cirrhosis, bronzed diabetes, pigmentary cirrhosis, para cirrhosis, neoplastic cirrhosis, hypersplenomegalic cirrhosis, cirrhosis of the Banti and of the Fanconi syndrome, Hanot's cirrhosis, tuberculous cirrhosis, malarial cirrho toxic cirrhosis, alcoholic cirrhosis, and posthepatitic cirrhosis The committee excluded the last two terms not because it disagreed that ethyl alcohol and viral hepatitis are ætiological factors, but to maintain the argument that cirrhosis should be first classified morphologically, and then ætiological and functional description be added

It was urged that all physicians should test this method of classification, to determine its practicability and possible pitfalls

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Medicine and the Law

"Found Neglected"

THE applicant was brought up in a poor law institution She was educated at ordinary schools and later employed in the institution but did not give satisfaction Once she was 17, there was no power to detain her at the institution and it was feared she might leave Therefore in June, 1948, she was removed to a mental institution under a "place of safety" order On Dec 9, 1948, magistrate made an order under the Mental Deficiency Acts 1913 to 1927 that she be detained in a mental institution on the ground that as a feeble minded person "found neglected" she was subject to the Acts There was evidence before the magistrate that she was a border line high grade mental defective After training she was allowed to live with her half-brother on licence The applicant applied for a writ of habeas corpus on the ground that she had not been "found neglected" and therefore there was no power to make the detention order The Court inquired whether there was evidence on which the magistrate could hold that the applicant was "found neglected," and the medical superintendent and the Board of Control argued that a mental defective who did not receive the special care and education which would be received in a mental institution was neglected within the meaning of the Act of 1913 and that, therefore, although the applicant was living in the poor-law institution she was "found neglected" in June, 1948 The Court reserved their judgment

Mr JUSTICE HILBERY, reading the first judgment said that the Act of 1913 did not authorise the detention of all mental defectives however circumstanced applied to persons who in addition to being defective were found neglected, abandoned, without visible means of support, or cruelly treated The words "found neglected" meant found through neglect in some degree of distress , "neglected" connoted physical suffering from a lack of essentials through want of reasonable care, and the words could only apply to a condition which was in existence, not a future condition which it was apprehended would or might come about the Mental Deficiency Act 1927, Parliament had dealt with the situation of a mental defective whose need was training which could not be provided in his home, and the local authority could not act because a defective needed care and training, but only if the parent or guardian of the defective had made a representation to the authority There was no evidence before the magistrate who made the order that the applicant was a mental defective "found neglected" and, therefore, The radioactive lipopolysaccharide removed by the reticulo endothelial cells appeared to be firmly held by them Thus only by the second day did the radioactivity of the liver begin to decrease, and a third of the original amount was still present at the end of a week One of the interesting features of the mechanism of early rapid clearance is that a constant proportion of widely varying sublethal doses of radioactive lipopolysaccharide was removed after intravenous injection That this finding does not necessarily indicate the presence of two differing substances in our material is shown by the fact that radioactive lipopolysaccharide, re extracted from the blood of guineapigs 30 minutes after injection, is treated in the same proportionate manner as the original preparation when injected into further animals

The intravenous administration of large doses of lipopolysaccharide depresses the ability of the reticulo endothelial system to remove a second injection of radioactive lipopolysaccharide 30 minutes later In some experiments the activity of the reticulo endothelial system appeared to have fallen as low as 25% of the normal This effect did not appear to depend solely on the bulk of material injected, because it required 1 mg of crude bacterial cell walls to produce the same degree of depression as 0 1 mg of purified lipopolysaccharide Furthermore, even 20 mg of trypan-blue could not depress the reticulo-endothelial system so much in half an hour

Finally, the initial clearance of radioactive lipopolysaccharide from the blood-stream by the reticulo-endothelial system is even greater in animals which had received 1–50 µg of lipopolysaccharide 48 hours previously If, however, very large doses of lipopolysaccharide were given and the animal survived, the activity of the reticulo endothelial system tended to remain subnormal after 2 days

DISCUSSION

A possibility which must be excluded is that the ^{32}P liberated from radioactive lipopolysaccharide in both the in-vitro and the in-vivo experiments was present as an impurity in the material Two findings are against this interpretation different batches of radioactive lipopolysaccharide have behaved similarly, and radioactive lipopolysaccharide re-extracted from the blood of a guineapig behaved identically with the initial material

The fate of lipopolysaccharide appears to involve two mechanisms in the animal body

(1) The reticulo endothelial system has been associated with resistance to the effects of endotoxins, for susceptibility is greatly increased after " blockading " with such substances as 'Thorotrast,' trypan blue, and colloidal iron [6,7] Further Biozzi et al [8] have shown that the ability of this system to phagocytose carbon particles can be either depressed or stimulated by the endotoxin of *Salmonella typhi* Our direct observations with radioactive lipopolysaccharide accord with the view that the reticulo endothelial cells assume a dominant part in the disposal of lipopolysaccharide

(2) The other path involves a gradual elimination of radioactive lipopolysaccharide from the plasma, one part of which (i e , $\equiv PO_4$) appears in the urine Possibly this process may be mediated by the serum phosphatase, which we have shown to be active in splitting the lipopolysaccharide in vitro The fate of the non radioactive remainder of the molecule has not yet been investigated

The toxic component of endotoxins is clearly distinct from the known phospholipid, polysaccharide, and protein fractions and contains a relatively large amount of phosphorus [9,10] The recent work of Westphal and Lüderitz [11] has characterised this substance as a second, highly insoluble, phospholipid Tal and Goebel [10] found that the toxic component was detoxified by mild acid hydrolysis, and that the only apparent change was the liberation of dialysable phosphate Whether the phosphatase reaction which we have described plays a rôle in the destruction or detoxification of living gram-negative bacteria in vivo is an important point to be determined

We acknowledge a grant towards the cost of animals from the Medical Research Council The autoradiographs were prepared by Mr A Beasley, of the pathology department, St Mary's Hospital

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Reviews of Books

Body Fluids in Surgery

A W WILKINSON, CH M , F R C S E , senior lecturer in surgery, University of Aberdeen Edinburgh E & S Livingstone 1955 Pp 212 16s

THE past ten years' progress in the study of body chemistry may have been discouraging to those who have no mind for electrolytes , but no-one can deny it has been of considerable benefit to patients Inevitably the work has been reported diffusely in innumerable articles, and the assimilation of the new knowledge is made much easier by monographs on the subject This book is an outstanding example in every page there is evidence that Mr Wilkinson is a surgeon who lives and thinks in terms of body-fluids and electrolytes , the subject pours out of him without effort and with clarity, since he writes well without prolixity

The material is rationally ordered, starting with water, followed by sodium, then potassium and acid-base balance, with good descriptions of the clinical states associated with their disturbance The second half of the book deals with electrolytic imbalance associated with injury, shock, and gastro intestinal disorder, and with diseases of the heart, liver, and kidney A chapter on treatment completes it

Every surgeon will welcome this book, but it will find particular favour with those of pre-war vintage, since their training lacked an understanding of body chemistry and for them the subject is therefore harder to grasp The subject is now placed at their command in a book written by an expert to make experts

Modern Public Health for Medical Students

I G DAVIES, M D , F R C P , professor of public health and preventive medicine, University of Leeds London Edward Arnold 1955 Pp 487 30s

AUTHORS of textbooks on public health for undergraduates must make a choice Should they write a flowing, readable, and interesting narrative (an illustrated essay on the mystique of community health) and leave the student, once enthused, to extract the facts for himself ? Or should they produce a textbook giving the largest possible number of facts ? Professor Davies has chosen the latter course and produced a comprehensive and accurate textbook with all—indeed in some sections, more than all—the undergraduate needs to know about this subject

The nineteen chapters begin with a mainly historical introduction and finish with international health, accidents in the home, and health education Perhaps, as environmental sanitation is entirely omitted, a better title would have been A Textbook of Social Medicine, but within these limits the student, whether undergraduate or postgraduate, will find all he wants There are particularly good chapters on the measurement of health, diseases of social importance, and handicapped persons The index unfortunately fails to live up to the comprehensiveness of the text

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In England Now

A Running Commentary by Peripatetic Correspondents

My friend Ananias failed his finals so often that we thought he'd receive his M.B. posthumously. However, once qualified he prospered steadily. Yet at this year's reunion dinner he ate two helpings of everything, touched me for a fiver, and blamed it all on a Tibetan ape.

'My brother left it with me after his last leave. Height 5 ft. 6 in., colour of hair brown, so rare that the Zoo pundits had never heard of it, and eyes like two saucers of strong tea. I was loth to harbour it. Already, because I was of non-domesticated habit, the dramatis personæ of my household came and went rapidly, and I didn't feel that an ape around the place would retard the process. But I was wrong. Obispo, as I called him, was adored by my housekeeper, and she taught him to clean shoes and lay the table. In the evenings he used to sit and watch me drink gin, and I found him a very sympathetic audience.

"One night, when Bevan's Hard Bargains had really been after their pound of flesh, I had my feet up on the mantelpiece and was giving Obispo a soul-searing account of the day. It was the look of him, sitting there gravely in my chair, chewing my stethoscope, and listening with his enormous eyes like a psychiatric consultant, that gave me the idea. If he could listen to my woes, he could listen to those of my patients.

"I gave him my cram course in medicine, and in three days he could feel a pulse and hold a pen; in five he could pretend to write, and in ten he was wearing horn-rimmed spectacles, a white coat, and a stethoscope, and taking his first surgery. He was terrific. There he sat, apparently taking notes and nodding his head solicitously. When the patient had to stop for breath, he'd gaze soulfully over his specs and loose off a sigh of sympathy that would have blown over a bus. I made up bottles of bromide and rang the changes on the colouring; for good value, I occasionally made one gently effervescent and sealed the cork with collodion, thus ensuring that the owner was clear of the premises before the explosion. The neighbourhood was awe-struck by these detonations, and decided that the Indian doctor's medicines were constructed of rare and costly 'Imalayan 'erbs.' We were really public benefactors, as everyone's neurotics assembled at our Wailing Wall.

"One day I decided Obispo had better get registered, so I cabled my brother, who sent a magnificent yakskin diploma in an obscure Tibetan dialect and four colours. It made Obispo M.D. Shangri-la, and entitled him to a salute of 21 jinghals and grazing rights for 8 yaks on the front lawn of the Great Palace at Lhasa.

'By this time, the surgery routine was running like clockwork. We'd had a few snags, of course, such as Obispo's lack of inhibitions over scratching himself, and also a little tension concerning some bananas in a patient's shopping basket. And the occasion when he drank a quart of surgical spirit and took the surgery hanging from the chandelier by his feet. However, my remarks about Yoga and the Mysterious East soon reassured the faint-hearted. More irritating to me was his trick of pointing out paragraphs in textbooks in such a way as to imply that I had made a misdiagnosis, and he took to leaving *Boyd's Pathology* about, kept open by a gin bottle at the chapter on hepatic cirrhosis. But the real trouble came while I was on holiday. Before I went, he brought me a heap of documents to sign. I learned too late that among them had been a letter he'd typed to the executive council to say I was resigning and appointing him as my successor.

'Appeal to the executive council? My dear fellow—they've just made Obispo chairman.'

* * *

When we bought our lovely old Devonshire cottage, covered in roses and creepers, I was indignant when my hard-headed lawyer brother said "all thatched houses are verminous." But I must admit that, at first, during the nervous hours of the night I used to hear sounds like outsized burglars heavily armed with coshes, tramping about under the steep-pitched roof over my bedroom ceiling. These were exterminated by lumps of bread spread with poison and thrown up through a trapdoor, and they have never returned. Then after the first autumn frosts myriads of little scampering footsteps could be heard up and down and along the alley-ways inside the old cob walls in the larder and even in the rooms. Poor dears, they met untimely deaths in traps, and now rats and mice are no more. Then I found miniature serpents climbing up the walls and even sometimes cosily tucked into blankets. I don't know what they are called and I don't need to know, because they too have disappeared.

The next plague was silver-fish, darting swiftly out of cupboards. These were more difficult to eradicate, but I seldom see one now. Spiders are, I am afraid, chronic, but then I rather like them; they seem to be part of the household. There are none of the fat Miss Muffet variety, but only those with a delicate air and legs like a film star's eyelashes. Last of all are the tortoiseshell butterflies. They hibernate high up on the dark beams of the staircase, and during the winter just hang there with folded wings, motionless as mummies; but with the first warmth of spring, they will awake and fly in and out of the windows bringing sunshine with the beauty of their wings into every room.

* * *

If you must dislocate your shoulder, the thing is to do it in the presence of a surgeon and an anæsthetist. It happened in this fashion to me, albeit late at night and in a country village. The patient was promptly laid on a bed in the local doctor's house and given intravenous pethidine, nothing stronger being available. Traction was exerted and I heard the anæsthetist remark "You'll have to put your foot in it, Charley," but this step proved unnecessary. With Kocher's method at the second shot there was an audible click and a sharp stab of pain, and the head of my humerus was back where it ought to be. The operation had been watched by august spectators—a principal medical officer from the Gold Coast Ministry of Health, and a member of the territory's medical disciplinary committee. Afterwards we all motored 30 miles to Korlebu, roused the surgeon's wife, and enjoyed five cups of her strongest tea.

* * *

The time has come when physicians should band together and defy the serious menace to their art which noisily fills our skies. It is virtually impossible now to use the stethoscope without the disturbing buzz of aircraft overhead. As one strains ecstatically for the rarest rub or the most musical of murmurs, one's senses are instantly shattered by the irreverent coughing and spluttering of these infernal engines. And the poignancy of the moment is the greater when one has just taken infinite pains and achieved infinite unpopularity in commandeering silence from the ceaseless chattering and sluice clatter that pervade all hospital wards.

The solution clearly does not lie with peaceful approaches. I have waited impatiently for a lull before running from patient to patient with chest-piece poised aloft. I have closed windows, I have bought thick rubber tubing, I have wound cotton-wool round my ear pieces, and I have shaken my fist in the air—all to no avail. No sooner do I reach for my stethoscope when a distinct drone revives my frustration. And as I stand by helpless while opening snaps and bronchial breathing go undetected, the drone becomes a crescendo of deafening vibrations, enough to discomfort Laennec in his place of rest.

The problem is urgent, for if a solution is not found soon, we shall have to throw away our stethoscopes and carry mechanical phonograms instead. Even so, we shall have to learn how to decipher the graphic squiggles of aeroplanes from those produced within our patients' chests.

* * *

PRESCRIBERS' NOTES

Where are the Snows?

Gold pencil, a tablet for writing, and then
They came as a Boon and a Blessing to men.
First the *Basis*, next *Adjuvant*, then the *Corrective*,
All inside the *Vehicle*—dog cart or brougham?
And, just to ensure they were doubly effective—
Well wrapped in dog Latin you couldn't see through 'em.
To those who were not getting rapidly well a glance
At your Prescription was good as a tonic.
Whereas nowadays, in this Age of Inelegance,
Ordered by telephone, tab. Supersonic
Is all you can hope for, except for the fact
That your doctor, like you, doesn't know how they act.

Concerning a further advance in the treatment of bucco-pharyngeal INFECTIONS

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conversion of linoleic to arachidonic acid Further, vitamin E, which is a powerful antioxidant and therefore protects E F A, is largely removed from low extraction flour *and what remains is destroyed by the "improvers."* The dietary intake of E F A and of unnatural fats in this and other countries during the past years is at present being examined by Miss Dorothy Hollingsworth, Dr J N Morris, and myself

EFFECTS OF E F A -DEFICIENCY

What are the consequences of deficiency of E F A in man? We can only surmise by arguing from the effects of such deficiency in lower animals First, deficiency would be likely to be at least five times commoner in males than in females Secondly, we might expect deposition of cholesterol since cholesterol esterified with unusually saturated or with unnatural fatty acids is probably disposed of less readily, diets high in saturated or unnatural fats or cholesterol or deficient in vitamin B_6 would enhance this Thirdly, E F A -deficient animals *are much more sensitive to noxious agents such as ultra*-violet light (mild doses of which we found to produce complete necrosis of an irradiated paw[14]), to X-irradiation[15] including probably its carcinogenic action, and perhaps to chemical carcinogens[16] In your columns Dr Nyrop has argued[17] for E F A -deficiency increasing the sensitivity, of males particularly, to a chemical carcinogen in tobacco smoke and so contributing to bronchial carcinoma, and in general I endorse his views Aortic atherosclerosis is unusually common in persons dying of bronchial carcinoma Are there not other forms of cancer the incidence of which might be similarly increased? For instance, deaths from leukæmia have *increased rapidly in the past two decades, are somewhat* commoner in males than in females, show peaks of incidence (particularly in the case of lymphatic) in persons under 5 and over 45 years, are commoner in the U S A and Denmark (a country with a highly developed medical service including radiography) than in England, are commoner in the rich than in the poor and (in the U S A) in white than in coloured persons, and are nine times more frequent amongst U S A radiologists than amongst other physicians[18] If the more highly civilised and wealthier peoples are becoming increasingly sensitive to the carcinogenic effects of X rays through deficiency of E F A, the above facts become explicable provided those young children who died of leukæmia were irradiated when their pregnant mothers had diagnostic radiography, a chemical carcinogen could hardly be responsible for their deaths But a chemical carcinogen in food, susceptibility to which has been increased by E F A -deficiency, might account for the susceptibility of males in particular to carcinoma of the stomach

EPITHELIUM AND NERVOUS SYSTEM

Seborrhœic eczema is a disease predominantly of males and appears to be increasing in incidence It resembles histologically the lesion found in E F A deficient rats, some cases are alleged to respond to vitamin B_6 by inunction but not by injection, and inunction of an antagonist of vitamin B_6 produces dermatitis[19], it is not impossible that this therapeutic effect is achieved by local conversion of linoleic to arachidonic acid, and that some cases of seborrhœic dermatitis are E F A deficiency Similarly the dermatitis that sometimes follows the local application of detergents may arise through these extracting E F A from the skin In lower animals, in which we have carefully studied the skin lesion of E F A deficiency and found a dramatic increase in permeability of th epidermis,[7,8] we believe there is a structural fau perhaps through failure of phospholipids containing E F A to polymerise and form the impermeable barrier i the stratum granulosum Phospholipids are rich in unsaturated fatty acids (though not so rich as cholesteryl esters), and although *we found them to be* normal in amount in the epidermis of E F A deficient rats they were abnormal in composition since the epidermal content of dienes and tetraenes had been enormously lowered In the E F A deficient dog[21] the iodine number of serum phospholipid fatty acids is lowered, as is that of serum cholesteryl ester fatty acids, whereas the iodine numbe of serum glyceride fatty acids is normal So, as in th case of esterified cholesterol, we have an abnormal typ of phospholipid being formed which may not only cause a structural defect in the skin which is responsible for th great increase in permeability but may also be outstandingly important for four reasons

First, the nervous system is rich in phospholipids containing polythenoid fatty acids, and these are found togethe with highly unsaturated cholesteryl esters in myelin, th presence of abnormal types of the compounds that are know to be important to it would be unlikely to leave functio undisturbed disseminated sclerosis is a disease of highl civilised countries being almost unknown in India an China, and other diseases in which the ectodermal neurogl is affected may be relevant, since serum E F A fall in acut infections it is not impossible that postinfective encephalomyelitis should be considered in this context, early mil dementia appears to be becoming commoner in males

Secondly, duodenal ulcers are increasing particularly i males, and in lower animals ulcers of the gut can be produce by feeding saturated fat

Thirdly, the mitochondrial membrane probably contain phospholipids, and derangement of this through deficiency o E F A might be responsible for the uncoupling of oxidativ phosphorylation found in such deficiency[22]

Fourthly, it is known that after a meal rich in fat th blood is more coagulable,[23] and recently it has been shown that the substance concerned is almost certainly phosphatidy ethanolamine

CORONARY THROMBOSIS

Phospholipids are increased in the serum of person with acute myocardial infarction, and if this compoun contained unusually saturated or abnormal fatty acids, would be expected to persist in serum for a longer tim *and might therefore be a factor in causing* thrombosis whether coronary or cerebral, in persons with athero sclerosis which I have concluded above may well b caused by cholesterol esterified with abnormal fatt acids Eighteen months ago, when we had obtained som evidence of the production of abnormal compounds called attention[25] to the correlation in this countr between the dietary intake of vegetable fat and death from coronary thrombosis "I believe the answer ma *be that the level of total dietary fat is related to* atheroma but that the level of dietary *vegetable* fat is related t clotting upon atheromatous plaques, and hence t coronary thrombosis" In general it is the vegetable fat that are hardened and may give rise to abnormal phospholipids But at that time we had been fortunate in having Dr Ancel Keys recently to work with us and I had bee impressed in general with his belief that total dietar fat, of whatever kind, was related to atheroma thoug we differed about its relation to coronary thrombosis an about Eskimos who have high dietary fat and allegedl little atheroma Since then I have come to realise tha Keys's hypothesis is not correct what matters

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THE LANCET
LONDON SATURDAY, APRIL 7 1956

Inflammation and Cortisone

Interest in inflammation is as old as medicine Celsus, who described its four cardinal signs (Galen added the fifth), and all physicians for centuries later considered inflammation as a disease, and their treatment was guided by this idea John Hunter was probably the first who saw inflammation as a defence against a variety of injuries The first half of the 19th century brought a number of accurate observations and experiments, among which those of Addison and of Waller[1] were prominent, and they culminated in the classical work of Cohnheim[2] The descriptions by him and his predecessors of tissue changes in inflammation were based on in-vivo microscopic observations of transparent tissues, such as tongue, web, and mesentery of the frog The main vascular events were firmly established by Cohnheim, and Metchnikoff's work on phagocytosis[3] brought further progress In the years that followed there was much controversy between those who, like Metchnikoff, believed in a central cellular defence mechanism and those who laid more stress on humoral factors, Lewis's[4] brilliant work on the triple response to mechanical injury and the immediate release at the site of injury of a histamine-like substance, convinced many physiologists that histamine was responsible for the vascular changes of inflammation Rous and Gilding[5] however, showed that there were differences between the vasodilatation produced by scratching and that produced by histamine For some time interest also centred on hyaluronidase This enzyme, which hydrolyses hyaluronic acid, a constituent of connective tissues, is produced by some bacteria and was believed to be important in breaking down the host's local defences, but experiments showed that there was no relation between the virulence of bacteria and their ability to form hyaluronidase[6,7] Meanwhile, another question under investigation was whether the accumulation of inflammatory exudate was the result of increased venous pressure or of increased capillary permeability Dyes, such as trypan blue, Evans blue, or isamine blue, which, when injected intravenously become protein-bound and normally do not pass out of the circulation, were much used in these inquiries Ramsdell[8] who introduced this technique, held that accumulation of dye in an inflamed area indicated endothelial capillary damage, and this view is now generally accepted It was soon found that histamine was not the only substance which increased capillary permeability, and Menkin's work[9] of the past two decades drew attention to other substances found in inflammatory exudates which cause emigration of leucocytes and increased capillary permeability Menkin isolated from inflammatory exudates a peptide with these actions, which he called leucotaxine Spector,[10] working in Cameron's department, found that in rats enzymatic digests of various proteins caused (1) increased capillary permeability, (2) swelling of endothelium and (3) emigration of leucocytes Only peptides of 8–14 amino acid units produced all three effects, and so did the crystalline pancreatic-trypsin inhibitor, which has a molecular weight of 6000 Of great interest and possibly related to the mechanism of inflammation is a finding reported recently by Jepson et al[11] They discovered a pain-producing substance which is formed in human plasma merely by contact with glass This substance is very similar to or identical with bradykinin, a peptide generated from bovine plasma or α_2-globulin and from human plasma by the action of snake venom or trypsin The significance of these findings in explaining the mechanism of inflammation lies in the possibility that mere contact of plasma with a foreign body or damaged endothelium, or with any tissue other than normal endothelium, may produce a bradykinin-like peptide

Interest in the mechanism of inflammation was renewed when it became clear that there was a close relation between cortisone and corticotrophin (A C T H) on the one hand and the course of infections on the other Reviewing this subject in 1952 Thomas[12] was able to collect 115 published reports of animal experiments and observations on human beings Among the earliest workers, Finland et al[13] described dramatic improvement in pneumonia and Smadel et al[14] and Woodward et al[15] recorded similar benefit in typhoid fever, but they found bacteræmia at the same time as clinical improvement The experimental and clinical work which followed showed clearly that cortisone made many infections worse Although inhibition of antibody formation was often but not invariably reported, most workers nowadays lay more stress on changes in *non-specific general* and particularly local defence mechanisms Investigations of the Shwartzman phenomenon and observations of the course of inflammation in the living animal have been particularly helpful Thomas et al[16,17] found that cortisone-treated rabbits showed no local reaction twelve hours after an intradermal injection of toxin while in the control animals erythema and œdema developed After eighteen to twenty hours there was still no erythema or œdema in the treated animals, but many small petechiæ appeared In other experiments, when cortisone (25 mg daily) was given for four days, the intravenous injection on the third day of meningococcal toxin was followed within

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Although we still use large quantities of aspirin in this practice, when gastric irritation or sensitivity appear, with their sinister implications, panadol becomes the drug of choice, and having used it now for two years we find it a satisfactory analgesic which is tolerated better than tab codein co or aspirin, side effects being negligible

Hawick Roxburghshire R R HAMILTON

DOMICILIARY CONSULTATION IN PSYCHIATRIC PRACTICE

SIR,—I was interested in Dr Skottowe's letter (Jan 14) and in Dr Hopkins's reply

If the universal overcrowding of mental hospitals is to be alleviated, some calculated risks must be taken in returning relatively stabilised schizophrenics to the outside world But this will be of little use until the community has been trained to accept people with some degree of emotional handicap, as they now accept people with some degree of physical handicap

In this country the Canadian Mental Health Association is doing a great deal to educate the public along these lines

The association engages speakers, holds discussions, and encourages visits to the Provincial mental hospitals and clinics. A recent departure is the setting up, by the association of a social club for patients in Regina It is used by patients living in the city who have been either in one of the mental hospitals or in the Munroe Wing (a small psychiatric unit attached to the Regina General Hospital) Although the idea of the social club for discharged patients is far from new, this is, as far as I know, the first example of such a club being run by a voluntary organisation This scheme receives considerable support and encouragement from the doctors working in the Provincial psychiatric service, but no doctor actually attends the centre, as it is felt that it would be undesirable for those using it to feel that this was merely an extension of the institution which they have just left The centre is in the charge of a psychiatric social worker, who carries out counselling and if necessary, suggests to a patient that he should again seek medical advice

Munroe Wing,
Regina General Hospital
Regina Saskatchewan Canada

JOHN D LUCY
Director

STAPHYLOCOCCAL INFECTION AFTER CARDIAC SURGERY

SIR,—Reading your annotation of Feb 11, I was struck by the fact that there is no mention of oral sepsis Fleming and Seal[1] make only an indirect reference to dental *extractions* as an ætiological factor in streptococcal bacterial endocarditis, the state of the mouth not being mentioned in the cases described Again in the full survey of wound infection in a thoracic surgery unit by Blowes et al[2] the gums are not considered as a portal of entry

Oral sepsis is no longer regarded as the cause of all the ills to which the body is heir, but it is generally agreed to be an important factor in bacterial endocarditis The pioneer work of Okell and Elliott[3] and of Round et al[4] provides experimental evidence of bacteræmia occurring *without operative interference* which has been confirmed but never refuted Most patients with heart lesions and many patients awaiting a thoracic operation have periodontal disease often in an advanced form The organisms in the gum pockets of these patients may pass into the blood through the pumping action of chewing or grinding The mouth flora will include *Streptococcus viridans* as well as staphylococci both coagulase positive and negative, which are likely to bear some relation to the bacterial flora of the ward after some time in hospital If a dental extraction can lead to infection of a diseased endocardium, surely dental bacteræmia can occasionally infect a valve damaged by tearing, the cardiac suture line or the dead spaces which may occur in thoracic surgery Fleming and Seal presume that the organisms gain ent at the time of operation A study of the case histories do not justify this presumption, normal convalescence bei apparently abruptly disturbed It is more reasonable postulate that, the penicillin cover for the operation ha ceased, severe bacteræmia develops when the patient be to masticate more vigorously, the mouth being relative unhygienic, as it is, despite nursing care, after all ma operations

There are ample possibilities of infection witho implying that all are due to oral sepsis My purpo is to draw attention to the mouth as a portal of entr A great effort is being made to provide full dental trea ment for patients in all hospitals, and it is importa to appreciate that the dental service can do more tha just ward off toothache Efficient preoperative dent prophylaxis—that is, scaling and polishing, wheth by dental surgeon or dental hygienist—can be a important factor in the prevention of postoperativ complications

London W 1 B W FICKLING

BILLROTH-I AND POLYA OPERATIONS

SIR,—I have read with interest the comments o Professor Goligher and his colleagues (Feb 4) on th veteran contest of Billroth-I versus Polya operation

I am sure they are right that if there is trouble from leaku anastomoses, at least one way out of it is to compromise wi living, undernourished, dumping, bile vomiters, in the good proportions which a Polya procedure will provide, rather tha to encourage mortality from leakage Even then it woul appear that the duodenal closure must be carefully done o leaks abound One wonders whether, when there are instanc of separation of the anterior part of the anastomosis wi leakage into the peritoneal cavity leading to disaster, the may not be an equal or greater number of separations on th lesser curve, or at the more difficult posterior part of th anastomosis (comparable to the formation of any penetratin posterior duodenal ulcer) with sealing and no leakage, but resulting large gap between mucosal surfaces leading t subsequent ulceration

I agree also that " it was surprising to find that the majorit [of recurrent ulcers] were on the lesser curve of the stomach More than 100 of my own Billroth I series of two third resec tions have been operated on for over three years, like the own series, but with, so far, no recurrent ulceration on th lesser curve The recurrence rate after the standard Billroth operation for duodenal ulcer does appear to be, in mo surgeons' hands, on the high side (my own being 6%), bu the 15% described by Goligher et al seems exceptionally hig Capper and Welbourn[1] have done much to show that the ra of recurrence depends chiefly on the amount of stomac resected, and with the extra gap to be filled followin resection of a duodenal ulcer and the necessary accompanyin length of duodenum, there is a tendency to skimp the resectio to avoid tension with resulting leakage at the anastomosi even though with full mobilisation really high resection feasible It is always difficult when several surgeons ar involved in a series to know exactly how much stomach eac has resected In my personal series I have found that m assistant at times recorded a resection less high than I hav credited myself

Radiographic examination in my own cases has show distortions of the lesser curve, but these have all been th "puckering and distortions" which Goligher et al mention and twice I have even sought these lesser curve "ulcers" at operation by direct inspection of the interior of the stomach with disillusioning results Increasing experience makes m feel that with the very best of radiologists the interpretatio of the shadows of barium in the stomach and duodenum ar often less accurate than the interpretation of the telescop appearance of the planet Mars It may be possible that som of the lesser-curve recurrences were really original concomitan gastric ulcers which possibly were not sought at the primar operation for it appears that as Goligher et al did no inspect directly for the "ulcer" at the second operation they may not have done so at the first operation either further analysis by Capper and Welbourn[2] of the results o many partial gastrectomies for ulcer by numerous surgeon in these subjects This is, I think, less likely to happen in America"

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[1] Fleming H A Seal J A F *Thorax*, 1955 10 327

[2] Blowers R Mason G A Wallace K R Walton M *Lancet* 1955 ii 786

[3] Okell C C Elliott S D *Ibid* 1935 ii 869

[4] Round H Kirkpatrick H J R Hails C G *Proc R Soc Med* 1936 29 1552

[1] Capper W M Welbourn R B *Lancet* 1951 ii 193

[2] Capper W M Welbourn R B *Brit J Surg* 1955 43 24

In our own medical schools, though "fear of examination failure with resulting withdrawal of financial support is very great,' much remains still of that carefree attitude to life for which the British medical student has always been famed By contrast, the American student is a very serious person and works much harder "He has had plenty of fun at college and is now ready and able to take things seriously" His devotion to his studies does not seem to arise either from fear of examinations or merely from awareness of competition with his colleagues "In the schools I have visited perhaps there is still some apprehension about anatomy and other preclinical subjects, but I think it is mild and probably will soon be as negligible as that felt for final examinations" Dr ELLIS is impressed by the American student's readiness to speak his own mind "to any teacher at any time,' his critical attitude, and the uninhibited manner and clarity with which he expresses himself

The main reason why the American student works hard is that he is impelled to do so by "that most powerful incentive to work—interest in it The interest that the average student in any faculty in any university takes in his work must be in large measure merely a reflection of the interest his teachers take in him" and Dr ELLIS speaks enthusiastically of the interest taken in the individual student by the majority of teachers in American medical schools No doubt there are still many places where "teaching is regarded as synonymous with talking, where, nameless in a crowd, the student must fall back on his books, only to impair his education, eyesight, and sanity in a hopeless fight to achieve "complete coverage" But the present trend is away from this In many medical schools "the process of teaching is regarded as imparting inspiration and guidance to learning, with the imparting of factual knowledge only so far as is required by the former where such an attitude of mind exists on the part of the teachers there is little need to look further for incentive to hard work on the part of the student and the curriculum is by comparison almost unimportant"

All systems, however, are liable to the defects of their qualities Dr ELLIS feels that some American medical schools, though undoubtedly right in putting the chief emphasis on education, do not give their students enough technical training "Medical education, while being subject to the general principles of all education, is also subject to the peculiar needs of training for work in the profession of medicine" facility in the technique of clinical methods and practical skill in obtaining information from the patient is vitally important, and Dr ELLIS suspects that American students are weak in this respect He attributes this weakness first to a lack of sound introduction to clinical methods at a time when their whole attention can be focused on it, and secondly to the absence of constant and prolonged practice of it

> "It is not that American medical students take poor histories and make poor examinations, it is that they appear to suffer from a lack of balance between their knowledge of medicine and their knowledge of diseased people This second knowledge can surely only be acquired by the steady application of clinical methods (with increasing skill) to patients This constitutes experience, and when there is lack of balance between knowledge and experience there is an increased feeling of insecurity in dealing with patients"

This feeling of insecurity might explain why the final-year American student is sometimes unable to make use of his own knowledge—why he is so often overcome by a sense of inadequacy when faced with the problem of the "whole man" rather than a particular disease Dr ELLIS points out that, though postgraduate training could do much to remedy this defect, it is still outside the control of the American medical schools It is a great thing that the new graduate should leave his school with the ability to learn and a will to go on learning, but he will be handicapped until he acquires clinical skill to match his knowledge

Dr ELLIS would probably agree with us that, if American teachers tend to neglect technical training in favour of basic education, we in this country have hardly yet begun to realise how far we are guilty of the opposite error To those who regard American medicine as excelling mainly in the use of techniques, and to those who think of American medical schools as huge and impersonal, it will come as a surprise to hear how deeply American teachers are concerned with fundamental principles and how much thought time, and trouble they devote to their students as individuals

Protection and Liberty

LENDING money to friends is said to be a sure way of losing their friendship, and the same applies to helping races or individuals whom we may think need our care and protection most of the horrors of history have sprung directly from well-meaning efforts to change people against their will The obligation to try to help certain types of people, even against their wishes, is inherent in our social structure, but those who spend their lives protecting their neighbours from themselves need expect little thanks from the objects of their solicitude and must be prepared for the criticism of those who prefer the touchline to the centre of the field

Assuming that we know what is best for our neighbour, we must be prepared to answer two questions on our stewardship in what circumstances can we force him to follow our advice, if not our example, and at what point should we retire and leave him to look after himself? As a nation we have long been the self-appointed protectors of many races, and today our problem is when and how to withdraw without undoing the good work we have done We fear to hand over our garden while the serpent is at large But we should not forget that most peoples prefer their own misgovernment to good government by others, and think that they can deal with snakes as well as anyone else

At home we have to face the same problems in our dealings with some of our fellow citizens In our society everyone is legally under care until he comes of age, but his emancipation is normally only a matter of time Some 3 per 1000 of the population, however, are liable to qualify for compulsory care because they are judged to be mentally defective, and though for low-grade defectives the need for care arch, is rarely found The true congenital flat foot is easily diagnosed very early in life and here the problem of treatment is entirely different

It is my experience that unless we distinguish most carefully the deformity which is present and give it its correct descriptive title, we shall be tempted to give *treatment which is incorrect, inadequate, and too* complex

Manchester, 3 W SAYLE-CREER

CHRONIC PAROXYSMAL HYPOGLYCÆMIA

SIR,—I should like to thank Mr Altounyan for reporting (Feb 11) the interesting history of a case of hypoglycæmia due to an islet-cell tumour of the pancreas, with symptoms for fifteen years prior to operation It is a pity that a histological report was not available at the time of writing, but presumably the case was one of benign adenoma

I should, however, like to take issue with the terminology used in the title of the paper

The term ' chronic paroxysmal hypoglycæmia " is non descript, cases of this sort should be regarded as examples of " hyperinsulinism," as we have recently pointed out[1] This will avoid unnecessary terms, and enable similar cases to be more easily categorised

Further, Mr Altounyan uses the subtitle " Whipple's syndrome " Whipple's disease (intestinal lipodystrophy) was described by *G H* Whipple in 1907[2] Whipple's triad of criteria for the diagnosis of hyperinsulinism were propounded by *A O* Whipple in 1935[3] If an eponym is to be employed, preference could be given to Wilder, who described the first case in 1927[4], Harris, who first used the term in 1924[5], or Campbell, who did early work on the symptoms of hypoglycæmia in 1922,[6] and was associated with the first successfully operated case in 1929[7] With such a large field, it is I suggest, preferable to avoid an eponym Most workers are content with the term hyperinsulinism

Diabetic Department,
King's College Hospital,
London, S E 5 H D BREIDAHL

MYXOMATOSIS

SIR,—Dr Brailsford (Jan 14) states " The Ministry of Agriculture has unsuccessfully used extermination measures for fifty years, at very great cost in value of herds of cattle and flocks of poultry, to get rid of swine fever, foot-and-mouth disease, and fowl-pest, but it has learnt little or nothing of cure of these conditions though smallpox, cholera, typhoid, plague, and tuberculosis have largely been eradicated without the aid of unprofitable destruction of this type "

The veterinary profession, when dealing with the food producing animals, has two prime duties (1) to stamp out any source of infection which may be transmitted to the human population, and (2) to increase the productivity of these animals in order that the nation's larder may be preserved There are two methods at hand for prevention of disease (*a*) vaccination, and (*b*) slaughter and the rigid isolation of the affected area Most bacterial diseases are controlled by vaccination, but most virus diseases have to be controlled by slaughter because of the peculiar characteristics of many viruses existing in several strains and provoking only a short-lived immunity It is true that we have learned little or nothing of the cure of our virus diseases, but then, has anyone ? We cannot cure foot and mouth disease, swine fever, or fowl pest I am sure Dr Brailsford would agree that there is similarly no cure for the common cold, influenza, or poliomyelitis We can and do protect against swine fever by vaccination (there is no official slaughter policy against this disease) and we have eliminated foot and mouth disease as an enzoötic by slaughter We have completely eliminated such diseases as glanders, cattle plague and rabies by slaughter, and are now eliminating tuberculosis from our cattle population

It is to be hoped that members of the veterinary profession will never tolerate the slaughter of animals when control by vaccination is an alternative

Liverpool K L VAUGHAN

GONADAL DYSGENESIS AND TESTICULAR TUMOURS

SIR,—The recent finding that nuclear sex can be easily determined by the examination of vaginal smears[1-3] has enabled us to investigate systematically cases of primary amenorrhœa In the course of this work we have come across a patient with a quite unusual clinical picture[4], to our surprise the cell nuclei in the vaginal smear were chromatin negative

A 27 year old single woman consulted us on account of hirsutism She had gross features and pronounced virilism Investigation revealed a calcareous tumour in the minor pelvis, adrenal cortical dysfunction, and increased urinary excretion of 17-ketosteroids At laparotomy, a solid, fist size tumour at the site of the left gonad was removed together with the uterus, fallopian tubes, and right gonad Histopathological examination disclosed that this gonad was rudimentary (" streak ovary "), and the tumour was a dysgerminoma Postoperatively intensive X ray treatment of the pelvis was started, and the patient is still well after two years Ethanol extract of half the tumour mass contained no 17 ketosteroids and but little œstrogenic substance After irradiation, and possibly as a consequence thereof, the 17-ketosteroid excretion level diminished

Dysgerminoma is known to be endocrinologically inactive We therefore assume that in this patient the virilism was caused by dysfunction of the adrenal cortex similar to that in the adrenogenital syndrome The fractionated 17-ketosteroid pattern was in full accordance with this assumption

This case thus presents a striking syndrome, consisting in the combination of (1) gonadal dysgenesis, proved by the rudimentary gonad and the male nuclear sex, (2) dysgerminoma, and (3) adrenal dysfunction

The evaluation of recent developments in embryological endocrinology, and study of other cases recently reported, soon convinced us that this peculiar syndrome was not to be regarded as a purely fortuitous coincidence Patients with so called " ovarian " agenesis have been shown to be mostly male *It is assumed* that in these patients the male gonad, its anlage, or an essential component, must have been destroyed by some obscure early intra-uterine lesion, resulting in completely female sexual development Although dysgerminoma occurs mostly in normal women, attention has since long been focused on its association with gonadal anomaly and hypoplasia Novak[5] points out that " dysgerminoma is the most common tumour of pseudohermaphrodites, as it is of males with cryptorchidism " Cryptorchidism also represents a distinct gonadal aberration, occurring in males Concerning the accompanying adrenal dysfunction Novak[6] and Ber[7] have described cases with hirsutism and virilism, entirely comparable to ours, and dysgerminoma itself is generally believed not to be the source of androgens It is tempting to assume that the early *intra uterine injury may damage, not only* the sole gonadal anlage, but more or less the entire urogenital ridge This could explain the most varied combined

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1 Breidahl H D Priestley J T, Rynearson E H *J Amer med Ass* 1956 160 198
2 Whipple G H *Bull Johns Hopk Hosp* 1907, 18 382
3 Whipple A O *Surgery* 1944, 16 289
4 Wilder R M Allan F N Power, M H Robertson H F *J Amer med Ass* 1927 89 348
5 Harris S *Ibid* 1924 83 729
6 Fletcher A A Campbell W R *J metab Res* 1922 2 637
7 Howland G Campbell W R Maltby, E J, Robinson W L *J Amer med Ass* 1929 93 674

1 Carpentier, P J, Stolte, L A M, Visschers, G P *Lancet* 1955, ii 871
2 Carpentier P J Stolte L A M, Visschers, G P *Ned Tijdschr Geneesk* 1956 100 154
3 Carpentier, P J Stolte, L A M, Visschers G P *J clin Endocrin* (in the press)
4 Plato, W P *Acta Endocr Copenhagen* 1953, 14 227
5 Novak E Gynecological and Obstetrical Pathology Philadelphia and London, 1946, p 342
6 Novak, E Gray, L A *Amer J Obstet Gynec* 1938 35, 925
7 Ber, A *Acta med Scand* 1949, 133 411

region need vaccination. The board suggests that hospital management committees should appoint some one to "persuade the staff to be vaccinated", and there can be little doubt that suitable propaganda within the hospitals would increase very considerably the number of those protected. It was also suggested that the practice in many hospitals before 1948 of making vaccination a condition of employment might be reintroduced.

The matter is closely linked with infant vaccination: the rate in this country is now only 34%. Primary vaccination in adults carries a greater risk of complications than in infants, and there is some doubt about the wisdom of vaccinating large numbers of adults, unless there is immediate danger. But nurses and particularly nurses in infectious diseases hospitals, run special risks, and we share the misgiving of the Sheffield board at their vulnerability. The annual reports of the Ministry of Health have repeatedly drawn attention to this serious position, and the Ministry has just produced a revised version of the memorandum[12] on smallpox vaccination. Yet apparently not enough has been said, for clearly not enough has been done. Air journeys from smallpox-endemic areas take less time than the incubation period of the disease. There have been 23 importations of variola major in the past ten years, and there will undoubtedly be more; it is very probable, also, that unrecognised cases will once again enter hospital. *All* the staff *must* be protected.

AMŒBÆ PRESENT?

EVERY morning a long file of black soldiers in white pyjamas used to approach the laboratory down the avenue of palm-trees. Each bore before him a bedpan decently shrouded in a "cloth, distinctive". They were the inmates of the dysentery ward bearing their daily offerings. After a few weeks it was easy to demonstrate without hesitation the amœbæ of all sorts, both ambulant and encysted. But the mind goes dim as quickly as the eye, and most pathologists who thought that they "knew the amœbæ" would admit that when they see a suspicious object under the microscope today their hand reaches for the textbook and its pictures. Though these will refresh the memory, for the student of tropical medicine no book can replace the teaching of the master at the bench—and weeks, months, and years of experience. The tricks of the trade are many and hard to put on paper. Some rely for detection upon the flash of the refractile amœba as the microscope is brought into focus; others on a background of weak eosin to distinguish protozoon from trash. Arguments on the proper strength of the iodine solution to display nuclei have never stopped. Some put great faith in concentrating the cysts by changing the specific gravity of the substrate; others say that the examination of up to *ten* natural specimens yields more profitable results. When the masters disagree the pupil may do worse than to follow undeviatingly the methods of one of them until he knows enough to disagree. Into a few pages of the newly founded *Central African Journal of Medicine*[13] Sir Philip Manson-Bahr has distilled a life time's knowledge of amœbiasis. Here are the wisdom of experience and methods proved by time. Many a solitary doctor in the further parts of the world will, having read this article, turn back to the bench with renewed enthusiasm; but the author still would be the first to admit that without a microscope and ample material the student will learn little by reading alone. It is probable that this difference between experience and booklearning explains the wide range of estimates of the occurrence of cysts of *Entamœba histolytica* in this country. The practised eye in the hospital for tropical diseases sees things overlooked in most laboratories. It is time for a clear answer to the question, "How many 'normal' people in this country are passing cysts?" and, as a corollary, "Why do we see so few patients with the classical disease?"

PROSPECTS FOR LABORATORY TECHNICIANS

DURING the past twenty years laboratory technicians have become more numerous and more necessary, more skilled and more responsible, and they are now essential members of the team headed by the pathologist. Similar changes have taken place elsewhere, in pharmaceutical manufacturing houses and in Government departments, and many of the young men who would once have taken an apprenticeship now stay at school a year or two longer and then enter some laboratory. If the National Health Service is to get its proper share of the best men for its laboratories, the financial prospects it offers should broadly resemble those in industry and in comparable grades of the Scientific Civil Service. It may be useful to compare the salaries offered to men of comparable education and skill for jobs of similar responsibility, in the National Health Service (under the new grading and salary structure recently announced[1]), in a large pharmaceutical manufacturing firm, and in a large institution of the Scientific Civil Service.

Entrants, who are expected to have the General Certificate of Education with passes at ordinary level in four subjects, including English, mathematics, and a science, have salaries nearly £100 per annum less in the National Health Service than in industry or in the Civil Service; the difference falls to £75 a year by the age of 21, but it is not until at least five years after entry, when the associate examination of the Institute of Medical Laboratory Technology has been passed, that the scales coincide. In the National Health Service there are two marks of efficiency, the intermediate and final examinations of the Institute of Medical Laboratory Technology, which do not exist in the Civil Service grade of scientific assistant, though in industry the supervisor's assessment of merit, on which salary increases depend, probably plays an equivalent part.

The selection of supervisory technicians varies greatly. In the National Health Service they are selected from those who have passed the final examination of the I.M.L.T. in a second branch, some six years or more after entering the laboratory; and to gain this advancement (and a further promotion to chief technician five or ten years later) the technician *may* have to move his home. In industry promotion is by selection, and if a move is necessary the employers often give financial help. In both cases, the senior or supervisory technician can expect a maximum salary of between £800 and £1000. The Scientific Civil Service selects its supervisory technicians, who are called experimental officers, by open competition at ages between 18 and 31, from those who passed either the G.C.E. at advanced level in two mathematical *or* scientific subjects, the intermediate B.SC., or the Higher National Certificate, or who hold a pass degree—or who have attained equivalent standards, according to age at entry. Scientific assistants, the junior grade, are considered only when they are recommended by their present department or have attained the requisite educational standards. Successful candidates can rely on attaining a gross salary of £935 in thirteen years, and some may enjoy accelerated promotion. A very few may be promoted to higher grades whose duties have no equivalent in the hospital service.

The range of salaries offered to technicians in the National Health Service under the new agreement is thus roughly comparable with those elsewhere; but there is arch, is rarely found The true congenital flat foot is easily diagnosed very early in life, and here the problem of treatment is entirely different

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[12] Ministry of Health. Memorandum on Vaccination Against Smallpox. H.M. Stationery Office. Pp. 8. 6d.

[13] *Cent. Afr. J. Med.* 1955, 1, 269.

[1] Whitley Councils for the Health Services (Great Britain). Professional and Technical Council 'B'. P.T.B. circular 53.

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H D BREIDAHL

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[5] Harris S *Ibid* 1924 83 729
[6] Fletcher A A Campbell W R *J metab Res* 1922 2, 637
[7] Howland, G Campbell W R Maltby E J Robinson W L *J Amer med Ass* 1929 93 674

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[4] Plate, W P *Acta Endocr Copenhagen* 1953 14 227
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[7] Ber, A *Acta med Scand* 1949, 133 111

The Widdicombe File

XXXII THE BASE DEGREES BY WHICH WE RISE

DEAR BARBARA,

Thank you for sending me such a helpful account of the Faculty of Omphaloscopists and their exams No, I'm not proposing to chuck pathology and turn omphaloscopist at my time of life It is merely that I am trying to make up my mind about some problems of organisation and exam structure that are worrying pathologists these days and your Faculty is an accepted model of efficiency in these matters and it seemed worth finding out more about it Perhaps you'd like to know a little about us in return (I ought by the way to say that the worried pathologists include several more or less official committees, but I know what the committees are up to only at very much umpteenth hand, and speak only as the most private of private individuals)

You might ask *then* what sort of representative organisation we pathologists have, what sort of regulations there are as to admission to our branch of the profession, and what examinations there are which the aspiring pathologist must take And I would answer you, with only a little exaggeration, as to the first, none, *as to the second, none, and as to the third*, none again This will not be believed in Venice ? Yet it is true

Unlike nearly every other specialty, including yours, pathology has no exam structure If the recent graduate wants *to* become an omphaloscopist, he knows he must pass *as* soon as he can his D OMPH Later, if he aspires high, he can go for his F F OMPH R C S The array of similar diplomas—D M R, D A, D C H, D P H, D OPHTH D OBST R C O G, D P M, and so on—with a variety of higher degrees to match, speaks for the generality and popularity of the system Failure to acquire the correct diploma is the clearest of red lights against persevering in any of these *specialties* *But not so the young pathologist* The D C P and D PATH exist, but hardly do more than exist so far as this country is concerned—I'll come to them later—and higher degrees are by no means necessary at any stage There are several distinguished *professors of the subject* who take a simple pleasure in flaunting their bare M B Consultant jobs admittedly go nowadays usually to people with some sort of higher degree, but the higher degree may be one of several *most* diverse sorts and there is no agreement as to which, if any, is most worth having

Our absence of exams is matched by our absence of professional organisation (the two things of course nearly always go *together—admission to the cult* by ordeal is as characteristic of professional bodies as of primitive souls) We have the Pathological Society, in professional standing as high as any of its kind in the world Like all successful societies, it is getting too big like all *successful fields* of science, pathology is getting too big for one society, and *only* the last ditch determination of a few diehard general pathologists to understand every paper delivered, or ask questions until they do, preserves its meetings from unintelligibility By and large, however, it is still the respected fulcrum of pathology as a science in this country But with the political aspects of pathology it will have nothing to do Like Gallio, it says

> ' that is a question of wages and names
> And I know the strife it brings
> I will not pass upon any of your claims
> I care for none of these things "

Firmly and *loftily*, it insists it is a Scientific Society, unconcerned with the affairs of the market place Pig-headed, perhaps, but also longheaded When scientific societies start playing politics, usually a rush of splinter groups starts, and soon it is one of the splinter groups that is the real scientific society, and the parent body is a mere *talking* figurehead But, as a result of the political nihilism of the Pathological Society, its main splinter party, instead of being a ginger group of young pathologists, is ambitious of turning into a Representative Body The Association of Clinical Pathologists has remained a second eleven scientifically, but it is willing, unlike its senior partner, to recognise that pathology is not only a science but a way of earning a living (Do not think one must therefore despise the A C P Our two societies represent the mundane and the lunar, the *yin* and the *yang*, of a scientist's existence today he must give his work, and he must be paid for his work) Willing though it may be to organise us, it is not yet very successful it is handicapped not so much by being young and brash and *too openly technological* in its approach, but because many pathologists—including many of the older and most influential—just frankly do not want to be organised and those few who enthusiastically believe in organisation have the *most diverse views* as to how it should be done

This agnosticism about organisation, this rottenness at the core (as you, Barbara, with your well drilled omphaloscopists, must think it), has many roots For one thing, we include, to our great benefit, the best array of out and-out individualists—not to say eccentrics—to be found in medicine For another, organisation entails an admission that ours is a specialty like any *other, whereas all true pathologists* know in their hearts that pathology is not a specialty in medicine, but *the* basic science of medicine (To claim that we are *not* merely consultants, but consultants' consultants, smacks a little of pride) It is to be noted that the urge to organise comes mostly from the clinical pathologists, to whom avowedly pathology is just another ancillary diagnostic service for the hospital

Various sorts of organisation have been suggested A College of our own ?—we can't afford one A Faculty ?—but of what ? The Academy of Medicine, uniting the four Colleges, seems still a pipe dream We could hardly become a faculty of the Obstetricians or the G P 's There remain the Physicians and *the Surgeons* The R C P won't have us (or anyone their constitution remains and will remain Linacrean) A pity this there's much to be said for it on both sides but the College remains as narrow in some of its ideas as the preposterous finger's breadth off Trafalgar Square to which it clings so sentimentally It is perhaps overstating the case to apply to them Eliot's

> " *Do not let me hear*
> Of the wisdom of old men, but rather of their folly,
> their fear of possession,
> Of belonging to another, or to others "

But they seem sometimes, whatever their merits as *individuals*, as a College to be a little over preciously concerned with their integrity The case is otherwise with the R C S The Surgeons are broader-*minded* (perhaps just richer) *than* the Physicians, and would probably have us But *timeo Danaos* there is the *old* Spanish proverb to be remembered " Take heed of an ox before, a mule behind, and a College *of* Surgeons on all sides " Moreover, while it is legitimate for Anaesthetists and Radiologists and Omphaloscopists to fall in behind the surgeon's antique *drum*, it would be more than a little infra dig for *the* basic science *of* medicine Shades of papa Virchow !

Exams *are at* present the crux of the matter The young man entering pathology, needing a motive (whether he realises it or not) to preserve in him his studently habit of work, sees with mixed feelings his contemporaries systemic lupus erythematosus, or in a symptomatic and self-limited fashion as in certain cases of drug allergy, among which the lupus-like syndrome arising in some hydralazine hyperreactors is notable[18] One is led to wonder whether a similar chain of events might take place also in selected "hyperergic" (joint pains!) cases of viral hepatitis but, to prove this, further investigations are needed In our own control material which has been collected for more than five years, nothing more than occasional nucleophagocytosis has been observed whether in chronic or acute hepatitis, both by the anticoagulant and defibrinated techniques

Clinica Medica dell Università
Genova Italy

ALBERTO M MARMONT

VANISHING LUNGS

SIR,—Your editorial,[19] which gave a very concise yet informative account of this fascinating subject, referred to a recent article[20] by one of us May we indicate some aspects which have so far not been adequately considered?

You emphasised the practical problem of abnormal air-spaces appearing in areas of tuberculous processes healed under the influence of chemotherapy These have raised the difficult question of "open" healing of tuberculous cavities, which in turn has led to the current dispute over resection versus *conservative management of such residual lesions* Here the work of Medlar[21] must be carefully considered

The concept of "open" healing of tuberculous cavities has not been borne out in Medlar's extensive and very careful histological studies In true tuberculous cavities Medlar could find no evidence of "open" healing, and he considers that in such cavities the potentiality for recrudescence remains persistently high In a large number of resected specimens showing openly healed cavities Medlar found what he judged were abnormal air spaces of non-tuberculous origin These he prefers to designate "developmental bronchiectasis" From his findings he is convinced that these pre-existed in the area adjacent to healed tuberculous lesions, where their presence is purely coincidental

We are now detecting the "vanishing lung" phenomenon increasingly often, and this remarkable increase, associated with many different pulmonary conditions, cannot be explained by Medlar's interpretation It is hardly conceivable that in so many cases pre-existing developmental anomalies could merely by chance be associated with lung areas affected by various other pathologic conditions

The concept of "developmental lung defects" was described by us[22] long before Medlar reported his studies We regard his findings *as conclusive confirmation of our concept of the* rôle of "acquired lung defects" in the pathogenesis of observed abnormal air spaces of the lungs We believe that such defects are due *to disturbance of the visceral function* of the lungs[23] caused by *damage* to the lung parenchyma in many different disorders These are quite like the "developmental defects" produced by *pathological changes in the* lungs during the postnatal period of development or during the period of the involution in advanced age The "vanishing lungs" phenomenon observed *in the whole gamut of pulmonary* diseases,[24] is reasonably explained by our concept of "lung defects" of developmental, acquired, and involutional origin

The practical problem of clinical management of abnormal air spaces is obviously far more complex No clinical criteria exist by which we can definitely *ascertain the nature of abnormal air spaces* in any given instance In cases of pulmonary tuberculosis the sputum is usually negative as a result of prolonged chemotherapy *It is certainly not possible to distinguish radiographically* between thin-walled tuberculous cavities and abnormal air spaces of non-tuberculous origin As we have indicated in these cases even the histological features *are subject to different interpretations* Those who oppose resection may now find support from Medlar's interpretation Assuming the presence of developmental anomalies which have long pre-existed, they are justified in treating such residues expectantly, and rely on long-term chemotherapy to take care of the tuberculous foci We advocate resection because in our experience when "lung *defects*" become clinically manifest it is usually because of progressive distension due to complicating obstructions[22] which are apt to give trouble later With Medlar we believe that recrudescence of true tuberculous cavities *is common* even after prolonged chemotherapy

In some instances obstruction by unsuspected early bronchogenic cancer has been revealed by resection of such abnormal air spaces Accordingly we feel that the *patient is better rid of areas of "vanishing lung"* sooner rather than later

New York

ISRAEL RAPPAPORT
EDGAR MAYER

RUPTURED UMBILICAL HERNIA

SIR,—I was much *interested in Dr de Glanville's* article (Dec 24) *because I had a case of spontaneous* rupture in an infant, which has been reported elsewhere[25]

The condition is rare but not quite so rare as Dr de Glanville suggests *5 cases were reported in this* country between 1868 and 1900,[26–30] 3 of these being described in your columns Johnson[31] in describing a case listed 17 others that had been reported, including the 5 from this country already mentioned Further cases have been reported by Turco[32] and Stein and Straus[33] This brings the total to 29, including Mr G F Parker's case[34] and Dr de Glanville's 2 cases Of these, 3 have been in infants, 2 in children, and the remainder in adults *But rupture in adults, following* ulceration of the coverings, has probably been much commoner than these figures would indicate

Whittington Hospital,
London, N 19

S L STRANGE

MEDIASTINAL SURGICAL EMPHYSEMA

SIR,—Following Mr O'Donoghue's account (Jan 28) of surgical emphysema due to a perforated duodenal ulcer, the following case report may be of interest

A man, aged 37, was admitted with the typical history and signs of a perforated peptic ulcer of two and a half hours duration At operation a small anterior duodenal perforation *with only moderate surrounding induration* was found, there was little peritoneal soiling The perforation was closed with an omental plug Postoperative progress was satisfactory until the third day, when lower abdominal distension began to develop Since this was thought to be colonic a flatus tube was passed, and then a turpentine enema given, but without relief *Oral fluids were discontinued and hourly gastric suction and intravenous therapy re commenced* The abdomen became more distended over the next two days, and on the fifth day it was noted that the patient had surgical emphysema of the abdominal wall which had spread through the mediastinum to the root of the neck Radiography confirmed the presence of mediastinal emphysema and showed free gas in the peritoneal cavity *there was no evidence of pneumothorax*

It was decided to drain the peritoneal cavity under local anæsthesia and some gas and fluid were evacuated through a suprapubic stab *No improvement resulted*, and the patient's general condition continued to deteriorate He went into severe peripheral circulatory failure and died on the sixth postoperative day

Necropsy showed that the *perforation* had given way completely and there was now a hole about $^1/_2$ in in diameter

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[18] Heinn M J Parkin T W, Hargraves M M, Odel, H M *Arch intern Med* 1955 95 857

[19] *Lancet* 1955 ii 660

[20] Rappaport I *J Amer med Ass* 1955 158 1436

[21] Medlar E *Amer Rev Tuberc* 1955 71 158

[22] Mayer E, Rappaport I *Dis Chest* 1952 21 146 Mayer E, Rappaport I *J Amer med Ass* 1953 153 700 Rappaport, I Mayer E *J Amer geriat Soc* 1954 2 581

[23] Rappaport I *Dis Chest* 1954 25 1

[24] Rappaport I Mayer E *Amer J Surg* 1955 89 1002

[25] Strange S L *Postgrad med J* 1956 32 39

[26] Leonard C *Brit med J* 1868 i 39

[27] Keetley *Lancet* 1884 ii 270

[28] Pilkington, H *Ibid* 1890, i 1005

[29] Lawson G *Ibid* 1890 ii 560

[30] Hemsted, H *Brit med J* 1900 ii 1640

[31] Johnson J T *Trans sth surg gynec Ass, Nashville, Tenn* 1902 14 257

[32] Turco A *Boll Soc piemont Chir* 1937, 7 412

[33] Stein L I Jun Straus I H *Illinois med J* 1951 99 117

[34] *Lancet* Jan 14 1956 p 107

The other is our professors Our professors possess a unique point of vantage between the preclinical and clinical fields You can divide university chairs into two main groups—those in subjects like physics and Greek, where the mere name of professor silences argument, and those in subjects like art or law, whose professors may be excellent fellows but whom one doesn't by mere virtue of their professorships regard as the best painters or counsel The preclinical subjects fall into the first group, the clinical into the second. It is not so long ago that most clinical chairs were mere pickings of the senior honorary, often a sort of graceful retirement for one who had shot his bolt (and made his pile) Even in these days of successful professorial units the independence of the others is jealously guarded (probably rightly, in the long run - a whole department of medicine is too much for one man to run) The one professor on the hospital staff who is really boss of his own whole department is the Professor of Pathology (one can say the same of many bacteriologists and some biochemists, but then this whole argument applies, mutatis mutandis, to them also) Now nearly every pathologist starts his career in a teaching department, and is well known in consequence to at least one chief And every appointment in pathology has on its selection committee at least one professor of the subject and though the local professor has only sometimes the appointment in his pocket he has at least a pretty strong veto in most cases Every candidate is then either a protege of his own, or of one of his twenty odd fellows and at least a good second-hand judgment is available in every case That is not to say selection committees never err (he who would believe that has never been an unsuccessful candidate) but the close nexus of informed opinion makes the external evidence of degrees and the like less necessary than it is in less well-knit branches of the profession

In fact, when you boil it down to its bones, we are governed more efficiently and ruthlessly than by an official College, even if almost unconsciously, by a junta consisting of nearly all our professors (we have remarkably few easy-chair men at the moment) with a few readers and some six or eight of the more active heads of non-teaching labs It s all very undemocratic and irregular And the Minister, who likes a Negotiating Body to negotiate with, may ultimately make us regularise the position But for the present it works—works in fact rather well

I began by setting forth to you, Barbara, our disgraceful state of anarchy with respect to exams and organisation and the like I've examined for you some of the alternatives and shown that our anarchy is an aristarchy and that we are little the worse in anything except self conceit for lack of degrees It is a prime function of the pathologist to recognise, more precisely than anyone else, the moment when normal hyperplasia goes beyond the limits of health Isn t it just possible that our passion for postgraduate degrees and diplomas and all that they imply is becoming just a little pathological ?

Yours

PETER DAVEY

F P Path S (God forbid!)

Medical Congresses

GASTROENTEROLOGY

THE fifth Pan-American Congress of Gastroenterology was held in Havana, Cuba, from Jan 20 to 27 Delegates from the Latin American countries, U S.A , Great Britain and France joined members of the Cuban Society of Gastroenterology in discussing diseases of the liver and biliary tract, spleen, pancreas, and intestine

Non-tropical Sprue

Dr G B J GLASS (U S A) described the measurement of the hepatic uptake of radioactive vitamin B_{12} in the diagnosis of non tropical sprue The absorption and consequently the hepatic uptake of vitamin B_{12} may be defective in many conditions but sprue is unique in that the hepatic uptake remains insignificant when intrinsic principle is administered simultaneously A tracer dose of 0 5 µg of CO^{60} B_{12} is given orally with 75–100 ml filtered gastric juice This is followed by a purgative after eight hours and an enema twenty four hours later Two days after the tracer dose evidence of radioactivity is sought over the abdomen and over the liver There is no evidence of hepatic uptake of vitamin B_{12} in non-tropical sprue

Dr D ADLERSBERG (U S A) emphasised the value in idiopathic sprue of steroid hormone therapy, and in particular of the latest of these hormones—prednisolone and prednisone In 74 cases 15 mg by mouth daily led to improved absorption of fats and vitamins, with a corresponding lessening of steatorrhœa Unfortunately relapses invariably occurred one to six weeks after cessation of treatment, and other complications were ulceration and perforation of the intestine silent bone fractures and infection including pneumonia

Excretion of Uropepsin

Dr SEYMOUR J GRAY (U S A) described the dominant influence of the adrenal cortex on the stomach Secretion of gastric pepsin is closely mirrored by urinary excretion of uropepsin, which can be measured by a simple colorimetric method Changes in uropepsin excretion closely follow changes in ketosteroid excretion In healthy people the uropepsin level rises after administration of corticotrophin or cortisone increased excretion is not influenced by vagectomy Similar increases follow the stress of pain, trauma, surgery, myocardial infarction burns, or even emotion Uropepsin levels are low in Addison's disease, and a rise to normal follows treatment with cortisone Low levels are also found in myxœdema pernicious anæmia, carcinoma of the stomach, and cirrhosis of the liver, and after gastrectomy In contrast, uropepsin levels are high in patients with peptic ulcers This quantitative test has therefore been employed in distinguishing benign from malignant gastric ulcers, and in differentiating the bleeding of œsophageal varices from that of peptic ulcers

Serum-iron Levels with Jaundice

Dr V BEATO and Dr M ESCALONA (Cuba) have found the fasting serum iron level of some help in distinguishing obstructive from hepatocellular jaundice Compared with their normal values of 96–160 µg , the serum-iron level is often elevated in hepatitis, but is usually unchanged in obstructive jaundice and hepatic cirrhosis They suggested that the test may be helpful in cholangiolitic hepatitis when other liver-function tests are negative

Portal Cirrhosis

Dr B SEPULVEDA (Mexico) stressed the synergistic role of alcoholism and malnutrition in the ætiology of portal cirrhosis In a series of 119 patients with this disease alcohol or malnutrition alone was a contributory factor in 6% and 3% respectively, but combined they were significant factors in 83%

Œsophageal Varices

Dr R YAZIGI (Chile) underlined the poor prognosis of the cirrhotic with intractable jaundice His figures also revealed that in a series of over 600 patients with portal cirrhosis only 36% bled from proven œsophageal varices Bleeding varices need expert management early to reduce the mortality of 40% cited by Dr C FLOOD (U S.A), who suggested that this high figure was due to severe hæmorrhage before the patient reached hospital, or alternatively to complicating hepatic coma That hepatic coma is a significant factor was made clear by his much smaller mortality-rate of 17% for bleeding due to extrahepatic portal hypertension In his hands management *is based on* early blood transfusion and early balloon tamponnage to stem the bleeding In contrast, Dr R R LINTON (U S A) advocated immediate ligation of the œsophageal varices Of a small group of patients treated in

Obituary

JOHN ALEXANDER SINTON

V C, O B E, M D, D Sc Belf, F R S, D L

Brigadier Sinton, who died on March 25, was the first man to gain both the Victoria Cross and the fellowship of the Royal Society The first of these distinctions was awarded in 1916 for his personal qualities and the second in 1946 for his scientific attainments

He was born in British Columbia in 1884 of Ulster parents but he was educated at Belfast In 1908 he graduated M B with first-class honours at Queen's University, and he held appointments in the pathology department there and at the Liverpool School of Tropical Medicine As he did not join the Indian Medical Service until 1911, his age at entry was above average and his opportunities for appointment to the highest ranks were correspondingly reduced In his earlier years in India he was medical officer to the 31st Bengal Lancers, where he was enormously popular with all ranks and their families Soon after the outbreak of war in 1914 he saw active service in Mesopotamia and he was four times mentioned in despatches before the engagement in 1916 in which he was awarded the V C for "outstanding courage and devotion to duty" He was invalided to India in 1916 and served on the North-West Frontier until 1921, for his work there he was appointed O B E and again mentioned in despatches A third of his working life was thus spent on active military duty in war

In 1921 he began in earnest his career in medical research when he was seconded to the Indian Research Fund Association to take charge of a special inquiry into the treatment of malaria Later, a malaria treatment centre was started at Kasauli, Punjab The experiments carried out there under his direction placed the therapy of malaria, and particularly the evaluation of antimalarial drugs, on a new and rational basis One of the most important results of this work was the recognition of the value of pamaquin in the prevention of relapse in *vivax* malaria He was not, however, wholly preoccupied with his studies on the treatment of malaria and he also took charge of the Central Malaria Bureau and later the entomological section of the Central Research Institute, Kasauli

In 1927 a separate malaria research organisation was set up in India and Sinton became first director of the Malaria Survey of India He gathered round him a team of outstanding workers and was their undoubted leader and inspiration until he retired in 1936 The headquarters of the survey was in Kasauli, in which pleasant hill-station the British Army had its Malaria Treatment Centre, where cases of persistently relapsing malaria (almost exclusively *vivax* infections) were sent Sinton worked in close collaboration with the staff of this unit and A H Q in devising carefully controlled trials of different courses of treatment which it was hoped might effect radical cure Many unsuccessful attempts had been made with quinine in different combinations and dosages, but when plasmoquine was investigated it soon became evident that this drug possessed the unique property, hitherto unsuspected even by the makers, of destroying the phase of *Plasmodium vivax* which survives between relapses A series of trials led to the evolution of courses of treatment with combined quinine and plasmoquine, or, later atebrin and plasmoquine, which were adopted by the Army in India and reduced relapsing malaria to negligible figures This had an ironic if somewhat obvious sequel For lack of suitable cases, the Malaria Treatment Centre had to close, and no further controlled experiments in the chemotherapy of malaria could be carried out in these favourable surroundings In all this work Sinton played a leading part His shrewd brain was quick to grasp the significance of the results of plasmoquine treatment, and to press home the necessity of finding out by controlled trials the best way of using it Strangely enough the conclusions of the Kasauli group did not find favour in the eyes of the malaria subcommittee of the Health Organisation of the League of Nations, and plasmoquine was not widely used except in India—where it was adopted as the standard treatment—and indeed did not attract much attention until the work was repeated and the result confirmed by United States investigators during the late war

Sinton had wide knowledge and experience of all aspects of the prevention of malaria and organised many control schemes throughout India He was an able entomologist, and added much to our knowledge of the mosquitoes and also of the sandflies of India During these years he published over 200 scientific papers, many of them in the *Records of the Malaria Survey of India*, a journal which he himself founded in 1929 to provide an outlet for the work of his own organisation It soon became a journal which accepted work on malaria from all over India and beyond, and under his editorship the journal (now the *Indian Journal of Malariology*) quickly won international fame

After he retired from the Indian Medical Service in 1938 he was appointed Manson fellow of the London School of Hygiene and Tropical Medicine and adviser on malaria to the Ministry of Health But on the outbreak of war the following year he was recalled to India and posted as quartermaster to a military hospital in India a post which, reputedly, he held with outstanding success He was demobilised in 1940 on reaching the age of 55 Soon afterwards he was recalled from retirement and appointed consultant malariologist to the East African Forces and later to the Middle East Forces, where his duties were exacting The potential danger of a malaria outbreak in certain areas was great, and detailed organisation was necessary to have everything in readiness As all supplies had to come round the Cape, and 6–9 months elapsed between the placing of an order and the receipt of the goods, careful advance planning was necessary Into this Sinton threw himself with characteristic energy, and the insignificant incidence of malaria in this Force was, in no small measure, due to his expert guidance He was retired for the second time in 1944, but after serious outbreaks of malaria among our troops in Sicily and Italy he was again recalled and appointed consultant malariologist to the War Office

After his final retirement in 1945 Sinton went to live on a small isolated estate in Northern Ireland and cut himself off completely from his previous activities Instead he began to take part in public affairs, especially in those of Queen's University, of which he became a pro-chancellor He was also high sheriff of the county of Tyrone and a member of the National Arbitration Tribunal He received many academic distinctions, including honorary degrees, the Chalmers medal, the Mary Kingsley medal, and, ten days before his death, the Manson medal

To the man who had this varied and distinguished career two of his friends have paid tribute H W M writes

"Sinton had an exceptionally quick intellect and a flair for getting to the heart of any problem He was a man of the highest integrity and of great physical and moral courage He always did what he felt to be right no matter how unpopular his actions might prove to be he loathed expediency These characteristics and his uncompromising attitude sometimes brought him into conflict with higher authority, and this may help to explain the paucity of official recognition of the great work which he did On the other hand, no one could have been kinder or more understanding and considerate to his older and younger colleagues, and all who worked with him had the greatest respect and affection for him He would take endless trouble to help others, and on many occasions he abandoned his own research work for days or even weeks on end to obtain information requested from him

J S K B recalls him as tall, spare, active with unflagging energy

"Sinton (he continues) threw himself with enthusiasm into whatever work he had in hand, and did not waver until it was completed He was forthright and outspoken and did not suffer fools gladly He loved argument, and his eyes shone with the light of battle He was indeed a formidabl adversary, particularly as he was almost invariably right But he was the kindest and most generous of souls whose mind never entertained a mean thought, and whose gosp the powers given by the Act could not be exercised in respect of her, accordingly the Court had ordered her to be discharged

Lord **Goddard**, C J, agreeing, said that it was important to stress the duty of the judicial authority in deciding whether the person brought before him was a mental defective It was not enough that there should be two medical certificates, that they should have been given was a necessary preliminary to his having jurisdiction but they were not conclusive in any shape or form There had to be a judicial inquiry and the magistrate was obliged to see the person concerned In many cases the appearance and demeanour of the patient, coupled with the certificates would be enough, but his Lordship, could not believe that it would ever be sufficient for a patient who was described as a borderline high-grade mental defective that there was room for a difference of opinion amongst experts was shown by the affidavits It was for the magistrate to apply such tests and to call such evidence as he might require and it was important that he should not think that he was merely to act as a rubber stamp In the present case the court could not say that there was no evidence to support the magistrate's finding as to mental deficiency, but his Lordship agreed that the finding that the applicant was found neglected within the meaning of the Act could not be supported No doubt what was done was thought and intended to be for the benefit of the applicant, but persons of whatever age were not to be deprived of their liberty and confined in institutions merely because doctors and officials thought that it would be good for them

Mr **Justice Devlin** agreed

In re Rutty —*Queen's Bench Division (Divisional Court)* Lord Goddard *C J* Hilbery and Devlin *JJ* March 9 1956 J F Platts-Mills (Robert K George) Mrs E Underhill (Robert K George) Rodger Winn (The Solicitor Ministry of Health) V G Hines (W I Piper Chelmsford)

C J **Ellis**
Barrister at Law

A Bequest and Two Claimants

A woman by her will dated Aug 11, 1953, gave her residuary estate to "the Imperial Cancer Research Fund care of the Christie Hospital and Holt Radium Institute Withington Manchester" She died in September 1953, at the time of her death she was resident at Bournemouth, but before 1950 she had lived at Liverpool The evidence was that her father had died at Liverpool of cancer, but there was no evidence that he had ever been treated for cancer at the Christie Hospital The gift was claimed by both the Imperial Cancer Research Fund and the South Manchester hospital management committee which administers the Christie Hospital under the National Health Service

Mr **Justice Vaisey**, giving judgment, said that this was rather an unfortunate case because there was no doubt that the deceased was anxious to promote cancer research Nothing was further from his Lordship's thoughts than to confuse Liverpool and Manchester, but it was alleged that those living in Liverpool knew quite a good deal about what was happening in Manchester, and that might be some explanation of the reference to Manchester in the will

Of the two claimants, the Christie Hospital had, at all material times, carried on cancer research and treatment, while the Fund was only concerned with research It was a puzzle why the deceased had used the words "care of the Christie Hospital " if she merely intended to benefit the Imperial Cancer Research Fund, it might be that those words possessed a significance which he was precluded from giving them In the decision of the House of Lords in National Society for Prevention of Cruelty to Children *v* Scottish National Society for Prevention of Cruelty to Children ([1915] A C 207) were a number of observations which applied precisely to the present case, Lord Loreburn had said there that the accurate use of a name in a will created a strong presumption against any rival who was not the possessor of the name mentioned in the will, which could not be overcome except in very exceptional circumstances In that case, as here, the name given was the true name and the name by which the institution was described in its Royal Charter His Lordship felt considerable doubt whether the deceased did not really contemplate cancer research at this particular place, but the words "care of" were not very helpful to the second claimant because they were used every day merely as part of an address He thought that the gift to the "Imperial Cancer Research Fund care of the Christie Hospital " was a gift to the research fund, although it was a curious way of doing it, a possible explanation was that the deceased gave that address because she felt sure that they would know where to send it He had come to the conclusion that her residuary estate should go to the first claimant, the Imperial Cancer Research Fund, under the gift contained in her will

In re Scanlon Deceased *Chancery Division* Vaisey J Feb 14 1956 Counsel and Solicitors T L Dewhurst (Bell Brodrick & Gray for Oscar H Whittingham Bournemouth), R R A Walker (Wilde Sapte & Co) Raymond Walton (Sharpe Pritchard & Co for P W H Revington, Manchester)

Irene Moses
Barrister at Law

Mental Defectives on Licence

The Board of Control are concerned about the number of patients who are kept on licence for long periods, and they have revised[1] the suggestions for the periodic review of these patients which they offered superintendents and hospital management committees in 1949 The board would normally expect that a patient should be discharged after a trial on licence for twelve months at most unless there are "overwhelming reasons to the contrary," and they ask that superintendents and H M C s should review the circumstances of patients at the end of one year on licence with a view to discharge Where it is not found possible to recommend discharge of a patient after eighteen months on licence, the board ask that a report giving the reasons should be sent to them Reports for patients who by March 1, 1956, had already been on licence for eighteen months or more should be sent as soon as possible and not later than Sept 30 1956

Special Articles

SCOTTISH STANDING ADVISORY COMMITTEES

The Secretary of State for Scotland has appointed new members to the standing advisory committees to hold office until Dec 31, 1958, and has reappointed other members whose terms of office have expired Medical members have been appointed or reappointed as follows

Medical Advisory Committee —Dr A P Meiklejohn (Edinburgh)

Dental Advisory Committee —Dr W M Gibson (Glasgow)

Nursing and Midwifery Advisory Committee —Dr N I Wattie (Glasgow)

Pharmaceutical Advisory Committee —Dr I M Macleod (Inverness)

Advisory Committee on Hospital and Specialist Services —Dr James Milne (Glasgow)

Advisory Committee on Local Authority Services —Dr Richard Scott (Edinburgh)

Advisory Committee on Health Services in the Highlands and Islands —Dr C S Sandeman (Durness) chloride anæsthesia for tiding over or for curing local pain—served us repeatedly Apart from ordinary practice, it won two 'firsts' for his old medical school, the Royal College of Surgeons in Ireland—the one a light weight boxing title in the British and Irish Inter'varsity contest where a thumb, dislocated outwards to a right angle, was made viable for a final win, the other when a key man in a short-handed basket ball team tore an adductor muscle and then returned to score after it was 'frozen'

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[1] H M (56)25

'His kindliness was unfailing and his wit imperturbable Handing a prescription to someone of like humour during the blitz, he added 'You may not need this' as a V1 bomb came in a bee line His presence and his manual skill gained his patients' fullest confidence My own heartfelt relief at his return when I did a locum for him echoed their immense esteem His sole concern was with his patients' welfare, and in this best of senses it is true that 'no city has given birth to a man, more munificent in heart, more ungrudging in hand Sand escapes our numbering, and who shall count the glad assuagement that he brought?' "

HENRY JAMES CRAIG GIBSON

M A Glasg, M D Edin, J P

Dr H J C Gibson, medical superintendent emeritus of Dundee Royal Infirmary, died at his home in St Andrews on Jan 28 at the age of 67

He was the only son of the Rev J D W Gibson of Carmichael, Lanarkshire, and he was educated at Merchiston Castle School and at Glasgow and Edinburgh Universities After qualifying in 1914, he held house-appointments in Edinburgh Royal Infirmary On his return from war service in 1919 he took up a career in medical administration, and in 1920, while principal medical officer of Craiglockhart Poorhouse and medical superintendent of Craiglockhart Hospital, Edinburgh, he graduated M D With his appointment as medical superintendent of Dundee Royal Infirmary in 1922 he began his life's work During the 31 years of his administration the infirmary not only kept pace with the rapid developments in the older branches of medicine but successfully entered new fields The smoothness of this transition and the lively interest and support that the citizens of Dundee and its surroundings gave increasingly to their hospital were due in no small part to his energy and tact

Lannan

His colleagues hold that "his integrity and the breadth of his knowledge and experience were prime causes of the harmonious relations existing between the honorary and the salaried staff and the board of directors, and respect for his sense of judgment and his transparent honesty more than once kept bitterness from a discussion Those going to him on some official errand in which personal issues were involved found a wise counsellor and often a kindly friend His direction of the infirmary though close and detailed was based on trust of the staff and he was rarely disappointed"

Dr Gibson was always conscious that his first duty lay to the infirmary, but he served on several committees connected with nurses' salaries and other matters His initial opposition to a health service derived chiefly from his fear that the individual patient would suffer in the increasing complexities of a vast organisation, but when the scheme was introduced he endeavoured to carry over into it the best of the traditions of the voluntary hospitals He was for a time on the board of management of Dundee Royal Infirmary The interest of St Andrews University in its main teaching hospital also commanded his willing cooperation His work was widely appreciated in the university, and in 1948 he was appointed lecturer in the history of medicine In this year his history of the Dundee Royal Infirmary was published privately

His chief relaxation lay in classical studies and he made contributions to a new Oxford Latin dictionary on the basis of his studies of Latin medical works, a translation and critical examination of Anthimus gained him the history of medicine prize of Glasgow University in 19 After he retired to St Andrews in 1953 he was elected a member of the Royal and Ancient Golf Club and he also served on the council of St Leonards School Unfortunately within a year of his retirement illness curtailed his new activities, but it called out the cheerful quiet courage that illuminated his character

W G C writes

Perhaps Dr Gibson's influence was most clearly seen in the general methodical management of the patients and the hospital services, for he had the orderly brain of a business man as well as the clinical acumen of a trained physician In Scotland we have always liked our medical superintendents and men like Dr Gibson, held in respect and affection both by lay members of the board and by the medical staff justify our ideas A medical superintendent has hard tasks, and hard masters and servants, especially when voluntary contributions necessitated purse cutting, and it says much for Dr Gibson that he could refuse or agree without offence for we soon came to realise that he saw beyond the immediate request, and we saw too that his guiding interest was the true welfare of the sick

When the infirmary was taken over by the board of management, he was invaluable in advising and helping the young board Here, too, he faithfully served the hospital he loved and it was hard for him to see expansion and development outside his own domain Changes had come and he found it difficult to accept them But he left a most valuable history of the infirmary, which will show for succeeding generations the great place a local hospital had in the hearts of the people and the great voluntary services rendered by the staffs and contributors Perhaps we are gradually returning to more local administration and more local pride in our institutions If so it will be because, to many of us, places run by such men as Dr Gibson remain as happier memories

In 1917 he married Miss Christine Wilson, who survives him with a son and daughter

ERNEST JENNER WRIGHT

M B E, M R C S, D T M

Dr Jenner Wright, honorary consulting physician to the government of Sierra Leone, and a former specialist physician in the Colonial Medical Service in Sierra Leone died in Freetown in December He was 63 years of age

His father was a well-known African barrister and he was educated in Belgium He studied medicine in London at St Mary's Hospital Medical School and qualified in 1914 Two years later he joined the Colonial Medical Service and settled in Freetown As his appointments show, he won recognition as an outstanding clinician but he also found time for research into the deficiency diseases D G F M, as his contemporary in West Africa, though in another Territory, writes

"He was the first in West Africa to recognise the syndrome we know today as ariboflavinosis, with its associated neurological manifestations, as a nutritional disease He first described it in 1926 in the Annual Medical and Sanitary Report of Sierra Leone, and in 1930 it was again described in his privately printed *A and B Avitaminoses of Sierra Leone* and was mentioned in Leitch's *Dietetics in Warm Climates* His work will remain a lasting contribution to our studies in tropical nutritional diseases Later Wright, like his contemporaries, became greatly interested in the theory of the late Alfred Clark, who believed the cause of pellagrous deficiency diseases was a toxic one Clark held that the foods prepared from the staple foodstuffs such as manioc maize the millets, and sorghums still contained traces of cyanic glucosides, and these acted as respiratory inhibitors of cellular metabolism to meet this, by detoxication of the cyanic substances, there was an excessive demand on the sulphur of body protein

"Jenner Wright's name is honoured in West Africa as one of its greatest doctors He has earned a wider fame in the annals of nutrition as a contributor to our knowledge of one of the great tropical deficiency diseases"

After he retired in 1940 he served as chairman of various wage boards He was interested in numismatics and old books, and his library and collection of West African coins were extensive He leaves a widow and three daughters, one of whom is a doctor

Letters to the Editor

DEFICIENCY OF ESSENTIAL FATTY ACIDS AND ATHEROSCLEROSIS, ETCETERA

SIR,—Scant attention seems to be paid by the medical profession and by food administrators to a very important change in the dietaries of the more civilised countries that has been occurring over recent decades with increasing intensity. I refer to a chronic relative deficiency of the polyethenoid essential fatty acids (E.F.A.). It is true that the matter was raised in your columns a year ago, but then no less a person than a professor of nutrition stated[1] that such deficiency rarely if ever occurs in man; Professor Yudkin, however, has the disadvantage of not having worked upon E.F.A. Our own experimental work, humble in scope, combined with a careful assessment of the literature, has led us to exactly the opposite conclusion. The causes of death that have increased most in recent years are lung cancer, coronary thrombosis, and leukæmia; I believe that in all three groups deficiency of E.F.A. may be important. Your readers with stereotyped minds should stop reading at this point.

The most important E.F.A. is the vitamin arachidonic acid with four double bonds (tetraenoic). This can be formed in the body from the dienoic linoleic acid, also a vitamin, but vitamin B_6 is needed for the conversion.[2] The body probably has some slight ability to synthesise E.F.A., and these unsaturated fatty acids are of course easily oxidised. Oleic acid, with one double bond, can readily be synthesised in the body and for convenience I shall include it below in the term "saturated fat." For a reason that is obscure the requirement of male animals for E.F.A. is at least five times that of females.

Eighteen months ago Dr. V. Basnayake and I made the surprising discovery that in the rat, fed a diet entirely free of fats and of sterols but adequate in other respects, there was a large deposition in the epidermis of cholesterol (or more accurately of Liebermann-Burchard-positive sterols) and this was mainly esterified; after about 7 weeks of the deficient diet the esterified cholesterol was more than doubled. Alfin-Slater and others[3] had slightly earlier found accumulation of esterified cholesterol in the liver of rats on a fat-free diet, but their work had not then appeared in print; and two groups of workers[4 5] have shown that linoleic acid lowers serum-cholesterol in man. Obviously in our experiments the cholesterol was being synthesised in the body and its accumulation might have arisen for one of three reasons; these we discussed when we reported[6] our observations to the 2nd International Conference on Lipids in Ghent last July.

First, there is an enormous increase in permeability of the skin in E.F.A.-deficiency[7-9] and there is an increase in capillary fragility,[9] and therefore cholesterol might pass more readily from blood as has recently been supposed to occur in atherogenesis[10]; this we rejected because the great increase is in the epidermis and not in the dermis.

Secondly, the epidermis might be synthesising unusual amounts of esterified cholesterol; but liver-synthesis is normal in E.F.A.-deficiency.[3]

Thirdly, the cholesterol might be esterified with unusual fatty acids and might therefore be less readily disposed of from tissues.

We obtained evidence that this is true. Cholesterol is normally esterified mainly with unsaturated fatty acids[11] and when—as in our experiments—these are extremely deficient in the body it is esterified with much more saturated fatty acids synthesised in the body from carbohydrate. Thereby, I believe, abnormal esters are produced which tend to be deposited in tissues. Such deposition would be enhanced by a diet relatively high in saturated fat or high in cholesterol (which increases the dietary requirement of E.F.A.[12]). A diet deficient in vitamin B_6 and relatively low in arachidonic acid would act similarly, and this I believe may be the reason for the occurrence of atherosclerosis in pyridoxine-deficient monkeys[13] and possibly for the occasional hypertension in pyridoxine-deficient rats, which however we have never observed—probably because we give such rats large amounts of E.F.A. Atherosclerosis might therefore be regarded as a chronic deficiency of the vitamin arachidonic acid, this deficiency occurring in the body under the following conditions: (1) on diets very low in E.F.A. and adequate in aliments, but such diets would be exceedingly unusual; (2) on diets high in cholesterol and fairly low in E.F.A.; (3) on diets high in saturated or unnatural fats and fairly low in E.F.A., where the fats would be acting as an antivitamin; and (4) on diets deficient in vitamin B_6 and fairly low in arachidonic acid. Are such diets encountered?

DEFICIENCY OF E.F.A.

For many years and particularly in recent years animal fats and more especially vegetable fats have become increasingly oxidised and deprived of E.F.A. before being eaten. Vegetable oils, in many cases rich in E.F.A., are hardened by hydrogenation; margarine and shortenings are produced by hydrogenation of cottonseed and soybean oil, some peanut-oil, and certain other oils; during this hydrogenation much of the E.F.A. are destroyed and unnatural *trans* fatty acids are formed. Unnatural fatty acids are formed not only during hydrogenation but also during the practice of deep frying. Whale-oil is sometimes added to margarine, and this, like other marine oils of plant and animal origin which contain a variety of highly unsaturated fatty acids, is deodorised and hardened by hydrogenation. Some people who consume high-fat diets, such as some Norwegians and also Eskimos[14] uncontaminated by so-called civilisation, fare well by taking marine foods. The extraction-rate of bread is important in this context. The unsaturated fatty acids occur in the germ—wheat-germ oil is an excellent source—and therefore only small amounts survive in 70%-extraction flour. Of this remnant part is destroyed (as indeed is part of that in 80% extraction flour) by the use of the so-called "improvers." Those that are bleaching agents, such as agene and chlorine dioxide, are all powerful oxidising agents, and the other improvers are also oxidisers. As well as the chemical improvers, substances with surface active properties are added in baking, such as glyceryl monostearate, stearyl tartrate, and polyoxyethylene stearate; nothing is known of the effect of these upon the metabolism of E.F.A. Vitamin B_6 is mainly present in high-extraction flour, which is an important dietary source. Therefore the use of 70%-extraction flour tends to produce E.F.A.-deficiency partly by having a low content of E.F.A. and partly by having only about a third of the vitamin B_6 present in wholemeal flour, this vitamin being needed for the

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[1] Yudkin, J. *Lancet*, 1955, i, 46.
[2] Witten, P. W., Holman, R. T. *Arch. Biochem.* 1952, 41, 266.
[3] Alfin-Slater, R. B., Aftergood, L., Wells, A. F., Deuel, H. J. jun. *Ibid*, 1954, 52, 180.
[4] Friskey, R. W., Michaels, G. D., Kinsell, L. W. *Circulation Res.* 1955, 12, 492.
[5] Bronte-Stewart, B., Eales, L., Antonis, A., Brock, J. F. *Lancet*, Jan. 14, 1956, p. 101.
[6] Basnayake, V., Sinclair, H. M. Proceedings of the 2nd International Conference on Lipids Chem., 1955.
[7] Sinclair, H. M. *Biochem. Soc. Symp.* 1952, 9, 80.
[8] Basnayake, V., Sinclair, H. M. *J. Physiol.* 1954, 126, 55P.
[9] Kramar, J., Levine, V. E. *J. Nutr.* 1953, 50, 149.
[10] Wang, C. I., Schaefer, L. E., Adlersberg, D. *Circulation Res.* 1955, 3, 293.
[11] Kelsey, F. E., Longenecker, H. E. *J. biol. Chem.* 1941, 139, 727.
[12] Bromer, W. W., Day, H. G. *Chem. Engng News*, 1953, 31, 3064.
[13] Rinehart, J. F., Greenberg, L. D. *Amer. J. Path.* 1949, 25, 481.
[14] Sinclair, H. M. *Proc. nutr. Soc.* 1953, 12, 69.

Notes and News

THE HOUSING PROBLEM IN THE TROPICS

MODERN industry, with its demand for urban labour forces and better communications, can have profound effects when rapidly introduced into a predominantly agrarian community, and in some of the tropical and subtropical countries of the British Commonwealth the advantages of industrial development are offset by the disadvantages of breaking down tribal barriers and customs, disrupting family life, and weakening the productive resources of the countryside by attracting workers to the towns.

For the creation or preservation of a stable community, which will use its resources fully, good housing is of paramount importance. As Sir Selwyn Selwyn Clarke[1] puts it, "unsettling thoughts and desires to emigrate to other countries or to crowd into cities are much less likely to occur in the minds of those whose roots in their traditional ancestral lands are renewed and reinforced through the replacement of a leaky and insanitary hovel by an attractive dwelling in which they can feel a justifiable pride." But, he says, attention has to be paid to designing and siting the houses in line with local customs and activities, and so far as possible with individual tastes. Villages and townships should be planned to keep pace with housing development, with social centres, schools, shops, and clinics; while the establishment of crafts and small industries will further help prevent the drift to the towns.

In underdeveloped areas, land tenure is always a controversial subject; but, in Africa particularly, there are signs that government policy is changing towards giving Africans the land they occupy. Supporting this policy, the East African Royal Commission of 1953–55 contended that reserves, tribal boundaries, and the present system of land tenure perpetuated primitive methods of cultivation, which was bad for the economy and which depressed the standard of living. But, though the commission suggested certain safeguards in the transference of land between races, Sir Selwyn doubts whether these are adequate so long as the peasant, chief, or headman may sell his land to wealthy individuals or finance corporations, thereby alienating it from the community which formerly possessed it. He makes three proposals to avoid this: (1) the holder should utilise the land to the common good; (2) he should not be allowed to transfer ownership except by permission of the tribal council or coöperative; and (3) on his death his land should go to one son. (At present land is often divided among so many heirs that each becomes the owner of an inconvenient fragment.) If a man dies childless, his land should revert to the tribe or coöperative, which would be responsible for re-allotting it and making provision for his widow.

Sir Selwyn believes that housing is as much a public concern as water supplies, roads, schools, and hospitals, and like them should be a communal responsibility. In his view the State should house those who are too poor to make adequate arrangements for themselves. In underdeveloped territories the best means of doing this, he suggests, is for the central government to assume responsibility for planning and financing housing schemes and to leave the local authorities on the spot to implement, supervise, and maintain them.

Turning from housing to houses he has some equally shrewd and practical suggestions. He is insistent that there should be no more back-to-back single-room shanties but instead three-room family houses each with kitchen, bathroom, and closet. As rule-of-thumb measurements he suggests that the floor area of a living-room in the tropics should not be less than 120 sq. ft., with a window opening not less than a tenth of the floor area. But he recognises that hygiene is less likely to be accepted when it runs counter to tradition. Thus ventilation and light will be more easily introduced into a Moslem household if the window of the women's room opens on an inner courtyard and a latticed vent is placed on the outer wall. He points out that the success of a housing scheme, as of so many other projects, depends on a good start. Building materials, whether they be bricks and mortar or bamboo, palm fronds, and dried mud, are not enough. The success of a housing scheme will depend on carefully selected tenants being taught "the use and abuse of housing by a capable, energetic and tactful housing estate manager."

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[1] *New Commonwealth*, Dec. 12 and 26, 1955, pp. 577 and 632.

THE DRUG BILL

THE Committee of Public Accounts[1] has lately expressed concern at the prices paid for proprietary preparations and basic drugs, which "include a profit margin substantially in excess of that hitherto accepted as appropriate for Government contracts." A Treasury minute[2] on the committee's report expresses awareness of the need to complete promptly the negotiations with the Association of British Pharmaceutical Industry. These negotiations still centre on proprietary drugs—a field in which very great difficulties have been encountered. "It is necessary to reconcile the particular interest of the Health Service in obtaining economical supplies of drugs with the wider public interest in the continuance of a developing pharmaceutical industry." If, says the Treasury, the present negotiations cannot be concluded satisfactorily, the committee's suggestion of annual rebates from manufacturers whose prices have been shown to be excessive will be explored.

A NEW KIND OF NURSING COURSE

As a result of the Scottish Health Services Council's report[3] on the job analysis prepared by the Nuffield Hospitals Trust an experimental training course for 75 students is to be held at Glasgow Royal Infirmary. The first 25 students will begin next September. The aim of the course will be to develop leadership and judgment. It is to be financed by the Department of Health for Scotland and the Trust. It has been approved by the General Nursing Council for Scotland.

The course will be suitable for university graduates and for girls with a good higher leaving certificate or other education qualification. They should be between 18 and 25 years of age. There will be no fee, the usual training allowances (£240 during the first year of training and £250 during the second year, with a deduction of [illegible] for board, lodging, and uniform) will be paid. The students will not be required to sit the preliminary State examination and they will take their final State examination after two years of concentrated study. But they will not be eligible for registration until they have completed a third year of hospital experience during which they will act as staff nurses.

HOSPITAL COSTING

THE Minister of Health[4] has accepted the main recommendations of the working party which devised a system of costing the departments and services of a hospital.[5] These recommendations are to become effective from April 1, 1956. The new method should, in the Minister's view, "be a substantial further aid to efficient and economical administration."

A STUDY OF CEREBRAL PALSIED

THE British Council for the Welfare of Spastics has published several useful booklets for parents of children suffering from cerebral palsy. The latest booklet[6] is different, for most parents would find it difficult reading. On the other hand those who have to plan the education of the cerebral palsied, and their psychologists and teachers, will be interested and helped by the study of 168 Liverpool children which is described. One may question such statements as "The lesion in rigidity is believed to be in the cerebellar system," but in her own field the author writes with convincing sincerity. She has found that the Terman-Merill scale is generally satisfactory for testing these children, but she is far from ignoring the effects of such things as mixed laterality, visuo-spatial disability, and emotional disturbance. Although she may differ in details of method from some other psychologists her assessment would pass the pragmatic test—it works.

TRAINING THE BLIND

THE film *Conquest of the Dark* (16 mm., sound, 27 min.) shows the progress of a blind man through the Royal National Institute for the Blind rehabilitation centre at Torquay and the Ministry of Labour training centre at Letchworth. It emphasises the restoration of confidence, competence and sense of achievement. Copies of the film are available from the Royal National Institute for the Blind, 224, Great Portland Street, London, W.1.

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[1] Third Report from the Committee of Public Accounts, Session 1955–56. H.M. Stationery Office 1955. See *Lancet* [illegible]
[2] Special Report from the Committee of Public Accounts, Session 1955–56. H.M. Stationery Office 1956. Pp. 15. 9d.
[3] See *Lancet* 195[illegible], i, 801.
[4] H.M. (56)24.
[5] Ministry of Health. Report of the Working Party on Hospital Costing. H.M. Stationery Office, 1955. See *Lancet* [illegible]
[6] A Psychological Study of a City's Cerebral Palsied Children. By Ella B. Floyer, M.A., DIP.ED., formerly educational psychologist, Liverpool Education Committee. London: British Council for the Welfare of Spastics. Pp. 88. 3s. 6d.

atheroma is, I believe, the amount and structure of the dietary fatty acids

NEED FOR RESEARCH

You will now conclude, Sir, if indeed you have not done so long ago, that I have strayed into the realms of fantasy You will remind me that long ago Sir Thomas Browne wrote "Imagination is apt to rove, and conjecture to keep no bounds" My inclusion of "etcetera" in the title invites the scorn we so readily pour on vendors of patent cure alls I have no wares to sell The experiments to test my hypotheses are simple to devise, and for eighteen months I have hoped to be able to perform them But at that time when Dr Basnayake and I observed as we think the deposition of an unusual cholesteryl ester and the formation of unusual phospholipids we were engaged upon the ninth move of our laboratory, he did the estimations in another department while I did plumbing and carpentry Now we are engaged upon our tenth move which will be followed later by our eleventh Nomadism is incompatible with experimental science And all the time we note that these diseases of civilisation have increased, are increasing and ought to be diminished—diseases which I believe are caused by a dietary high in saturated fats and unnatural fats, and relatively low linoleic and arachidonic acids so that abnormal esters of cholesterol and abnormal phospholipids are formed in the body I have not in this letter been concerned with conditions I believe to be caused by a pure dietary deficiency of essential fatty acids, without any relative increase in saturated or unnatural fat these I consider to include phrynoderma[19] and also vesical calculus so common in the Far East, the latter particularly affecting children under the age of 10 and being far more common in males than in females[26] (7 1, which is about the ratio of the requirement for E F A) My purpose in sending you these speculations, which are supported by experimental evidence, is to try to help to prevent the devastating and usually increasing mortality in highly civilised countries from atherosclerosis and its sequelæ, from cancer of the lung and stomach, from leukæmia, from disseminated sclerosis, and possibly other diseases of civilisation There is a particular urgency in that if any part of my thesis is right it would be unfortunate to adopt flour of a low extraction-rate for three reasons first, the practice would reduce the dietary content of E F A partly because flour of low extraction has most of these removed, much of the rest being destroyed by the so called improvers, secondly, it would remove an important dietary source of vitamin B_6 this vitamin being needed to convert linoleic to arachidonic acid thirdly, it would remove, in presence of "improvers," all the vitamin E which protects E F A, and indeed this protection might account for the unsubstantiated claims of Shute and others that administration of vitamin E is useful in certain of the conditions in which I suggest deficiency of E F A is important You, Sir, have consistently opposed any such retrograde step[27], when Professor McCance and Dr Widdowson on the basis of their short-term experiment upon children in Germany pronounced[28] that "general information and also scientific information had been wrong in laying so much emphasis on the value of high extraction [bread] for all persons under all conditions" you rightly concluded "we maintain unrepentantly that, when it is a question of altering what has been a staple food for a very long time, the onus of proving advantage lies on those who wish to make the alteration not on those who oppose it" To revert to flour of a lower extraction-rate fortified with only three nutrients would I fear be likely to increase these diseases of civilisation in this country And let us not rush into "fortifying" low-extraction flour with arachidonic acid until we are sure that this will not produce cataract or have other disadvantages With no sympathy for long-haired naturalism, I humbly plead that we should give more thought and perform more research before extracting and "improving" wheat, manufacturing unnatural fats that then appear in margarine (which could otherwise be an excellent food) and before foisting upon the public sophisticated fodder which it unsuspectingly accepts "Truth," wisely wrote Leonardo "is the daughter of Time and not of Authority" But time is fast carrying away—unnecessarily—increasing numbers of the greatest persons I am sure you, Sir, will agree that research upon the problems I have mentioned is worth while, particularly at a time when we are trying to determine correct policy regarding the desirable extraction-rate of flour

CONCLUSIONS

In summary my thesis is that the dietaries of the more highly civilised countries are becoming increasingly deficient in the essential polyethenoid fatty acids (the vitamin arachidonic acid which in presence of vitamin B_6 can be formed in the body from the vitamin linoleic acid) and increasingly rich in more saturated fatty acids and unnatural fatty acids which may act as antivitamins This disastrous change arises partly from processes of manufacture such as the hardening of fats, and partly from the use of low-extraction flour "improved" with oxidising agents Since the requirement of males for E F A is much greater than that of females the consequences are more serious in males These consequences may include the following

1 Cholesterol becomes esterified with abnormal or unusually saturated fatty acids and these abnormal esters are less readily disposed of and so cause atheroma

2 Phospholipids (such as phosphatidyl ethanolamine) contain abnormal or unusually saturated fatty acids, and these abnormal phospholipids being less readily disposed of, are retained in plasma and increase the coagulability of blood thereby contributing to *coronary* and cerebral thrombosis

3 The deficiency of normal phospholipids in the epidermis and gut makes these structures faulty, and this may contribute to the incidence of seborrhœic eczema and peptic ulcer

4 The similar deficiency of normal phospholipids (or presence of abnormal phospholipids) in the nervous system causes defective structure including demyelination which may cause disseminated sclerosis and possibly mental disease

5 Deficiency of polyethenoid fatty acids may increase susceptibility to noxious agents including the carcinogenic effect of X irradiation and chemical carcinogens, the former, taken in conjunction with increased presentation of the carcinogen may account for the increased incidence of leukæmia and the latter for the increased incidence of carcinoma of the bronchus and for the predominance of carcinoma of the stomach in males

6 If further experimental work gives any support to these broad conclusions steps should be taken to increase the dietary content of polyethenoid fatty acids, and perhaps to decrease the content of unnatural fatty acids bread and flour of high extraction without added oxidising agents and margarine and shortenings made with less hardening of fats, would be important factors in thus decreasing some very serious diseases of civilisation

Oxford　H M SINCLAIR

PRODUCTION OF CODEINE

SIR,—Dr Williams (March 17) is quite wrong in assuming that because 'Panadol' can be described as *p*-hydroxyacetanilide its properties are likely to be similar to those of acetanilide

There is the same difference between benzene and phenol, but he does not buy 'National Phenol Mixture' for his car One need go no further than p 2 of Martindale to find that *n* acetyl-*p*-aminophenol is but the active principle of acetanilide shorn of all the sinister implications that Dr Williams fears

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26 Ramalingaswami V Personal communication
27 *Lancet* 1955 ii, 235
28 McCance R A, Widdowson E M *Ibid*, p 205

British Empire Cancer Campaign

The Duke of Devonshire has been elected chairman of the grand council of the Campaign in succession to the late *Lord Horder*

Society of Chiropodists

The annual dinner of this society will be held on Friday, April 27, at 7 P M , at the City Hall Cardiff under the presidency of Mr J H Hanby, F CH S

World Health Organisation

The ninth World Health Assembly is to be held at Geneva from May 7 to 18 At the same time the World Federation of United Nations Associations is holding its seventh seminar on the World Health Organisation Further information about the seminar may be had from the federation, 1, Avenue de la Paix, Geneva, Switzerland

Ergonomics Research Society

On April 16 to 19, at Bristol University, this society will hold a symposium on Human Factors in Road Transport Further particulars may be had from H Murrell, Department of Psychology, 22, Berkeley Square, Bristol, 8

European Society of Hæmatology

This society will hold a congress in Copenhagen from Aug 26 *to 31, 1957*, under the presidency of Dr J Bichel The secretary general is Dr Aa Videbæk, Blegdamsvej 11, Copenhagen, Denmark

International Congress of Internal Medicine

The *4th International Congress of Internal Medicine* is to be held in Madrid from Sept 19 to 23 The main subjects chosen for discussion are the rôle of the adrenals in the pathogenesis and evolution of internal diseases, and bronchial asthma and emphysema

Wessex Rahere Club

A dinner of this club will be held at the Clarence Hotel, Exeter, on Saturday, April 28 Membership is open to all Barts men practising in the west country The hon secretary is Mr A Daunt Bateman, 11, The Circus, Bath

N A P T Travelling Fellowship

The Scottish branch of the National Association for the Prevention of Tuberculosis is offering a postgraduate travelling fellowship (£250) Doctors working in Scotland on tuberculosis are invited to apply before June 30 Full details may be had from the Scottish secretary, N A P T , 65, Castle Street, Edinburgh, 2

Reciprocal Agreement with New Zealand

An agreement on social security between the United Kingdom and New Zealand came into operation on April 1 From that date, people in this country are able to draw National Insurance benefits by virtue of their residence in New Zealand Anyone who wishes further information should apply to a local office of the Ministry of Pensions and National Insurance

Indian Medical Service Dinner Club

The annual dinner of this club will be held at the East India and Sports Club, St James's Square, London S W 1, on Friday June 8, at 7 30 P M Tickets may be had from the secretary of the club, medical board room Commonwealth *Relations Office, Matthew Parker Street*, S W 1

Oxford Medical Publications

Dr J C Gregory has been appointed head of the medical department of the Oxford University Press and will be responsible for Oxford Medical Publications Mr G T Hollis, who has held this position for 27 years has retired owing to ill health but will continue to act as an editorial consultant The department has now moved to Amen House, Warwick Square, London E C 4

International Congress of Gastroenterology

A meeting of the Association des Societes Europeennes et Mediterraneennes de Gastro Enterologie will be held from *July 18 to 21 at the Royal* College of Surgeons of England, Lincoln's Inn Fields London W C 2 under the presidency of Dr Thomas Hunt The subjects chosen for discussion include ulcerative colitis, pre malignant conditions of the gastro intestinal tract and non malignant diseases of the œsophagus Membership is open to all interested and forms of application may be had from the hon secretary, Mr Hermon Taylor *London Hospital, E 1*

General-practitioner Clinical Assistants

4 general practitioners have been appointed as part time clinical assistants to the West Middlesex Hospital, Isleworth and 2 to King Edward Memorial Hospital, Ealing For the 6 posts 26 applications were received

Proposed Closure of a London Hospital

The North East Metropolitan Regional Hospital Board has invited the London Executive Council to comment on a proposal by the board to close St George in the East Hospital London, E 1 *on July 31 this year In a letter to the council* the board points out that since 1948 there has been a shift of population towards the periphery of the region At St George-in-the East the demand has steadily lessened and there has been increasing difficulty in staffing the hospital adequately The board is satisfied that other hospitals (of which there are several) in the area can take over the work without inconveniencing the public At a meeting of the London local medical committee on March 27 the following resolution was passed *nem con*

> That in view of the grave difficulty in securing hospital beds in London for patients who need them probably greater now than at any time since the National Health Service started the London local medical committee protests most strongly against the proposal to close St George in the East Hospital
>
> That the Minister of Health be asked to receive a deputation from the committee

A bibliography on penicillin V is obtainable from the Distillers Company (Biochemicals) Ltd , Fleming Road, Speke Liverpool

Dr Margaret Fitzherbert head of the maternity department of the Princess Tsahai Memorial Hospital has been made a chevalier of the Order of Menelik II by the Emperor of Ethiopia

The selling rights of *Principles of Medical Statistics* by Prof A Bradford Hill F R S are held in the United States and Canada by Oxford University Press Inc 114 Fifth Avenue New York 11 N Y U S A

The Directors of the Nursing Press Ltd have decided to cease publication of the *British Journal of Nursing* after the April issue owing to increased costs of production

Diary of the Week

APRIL 8 TO 14

Tuesday, 10th

ROYAL COLLEGE OF PHYSICIANS OF LONDON Pall Mall East S W 1
5 P M Dr F Avery Jones Clinical and Social Problems of Peptic Ulcer (First of two Lumleian lectures)

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
8 P M *Psychiatry* Dr A R May, Mr M S Folkard Dr R K Freudenberg Mr J P S Robertson Changing Concepts of the Function of the Mental Hospital

Wednesday, 11th

ROYAL SOCIETY OF MEDICINE
4 30 P M *Physical Medicine* Dr H D Darcus Dr D A Brewerton Methods of Increasing Muscle Strength

MANCHESTER MEDICAL SOCIETY
4 30 P M (Medical School University of Manchester) Dr F R Ferguson *Reflections on Therapy in Neurology*

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St Vincent Street Glasgow C 2
5 P M Dr Frank E Adair (New York) Some Newer Considerations of Breast Cancer

Thursday, 12th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P M Dr Avery Jones Clinical and Social Problems of Peptic Ulcer (Second of two Lumleian lectures)

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn Fields W C 2
5 P M Dr Leon Gillis Amputations in Children (Hunterian lecture)

ST GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner S W 1
6 P M Sir Stewart Duke Elder The Eyes of Invertebrates (Thomas Young lecture)

ALFRED ADLER MEDICAL SOCIETY
8 P M (11 Chandos Street W 1) Dr A Joyce Martin Lysergic Acid Outpatient Therapy in a Day Hospital

LONDON COUNTY MEDICAL SOCIETY
8 P M (St Andrew's Hospital Devons Road Bow E 3) Mr J R M Whigham Gastric and Gall bladder Surgery

Friday, 13th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330 Gray's Inn Road W C 1
3 30 P M Mr W D Doey Respiratory Paralysis in Poliomyelitis

Saturday, 14th

ASSOCIATION OF CLINICAL BIOCHEMISTS
10 A M (University of Glasgow) Joint meeting with Biochemical Society Symposium on Clinical Control of Electrolyte Deficiencies

indicates that there is less postoperative trouble with the Billroth-I procedure, and I feel we should not condemn a cart load of apples because of one dubious basketful.

If leakage is a worrying factor it may be worth trying my present regime of a resection of the duodenal ulcer with low partial gastrectomy of about a third, vagotomy, and Billroth I anastomosis. This is giving promising results both in function and in freedom from recurrence. Of over 100 patients hitherto treated in this way 45 were operated on over two years ago. So far there have been no recurrent ulcers, and the functional results are my best to date. Though it is early days to consider recurrence rate, this operation does not appear to produce regurgitation of bile, possibly because the low resection, and so greater residual stomach, does not open out the œsophago gastric angle as do many high gastric resections. If one feels strongly that it is absolutely essential to anastomose the stomach remnant to jejunum, I am quite sure that the Roux en-Y anastomosis of Schofield and Anderson[3] will almost certainly be followed by freedom from bile regurgitation. I have seen, at a demonstration by Mr Schofield, 12 patients, who had vomited bile severely after Polya procedures, completely cured by this operation.

It would be a pity to retreat once more into a maze of afferent loops, to flounder again into bogs of bile, and then perhaps to sink into unwanted drowsiness and sleep, now that we are just fighting free from it all.

Oxford G. E. MOLONEY

ACUTE TUBULAR NECROSIS OF THE KIDNEY FOLLOWING ABORTION

SIR,—The article by Professor Bull and his co-workers (Jan. 28) raises interesting points, some of which I have discussed elsewhere.[4]

It is notable that in all 13 cases the abortion was induced. It may be inferred that no case following spontaneous abortion was seen. This is in keeping with the other recorded cases of a similar nature. Likewise, I found no case of significant renal failure in over 20,000 consecutive cases of abortion admitted to the three Dublin maternity hospitals. (Induced abortion is very rare in this city.) On these grounds I suggest that the syndrome might be more properly alluded to as "acute tubular necrosis of the kidney following induced abortion."

Of the patients treated by Professor Bull, 8 admitted to injecting a *soapy solution* into the uterus and 1 to the use of a vaginal douche, the nature of which was not stated. The method used to procure the abortion was not given in 3 cases. In only 1 case was an instrument used—and this by a trained nurse; the additional use of a douche, possibly 'Dettol,' seems likely here. The employment of soapy solutions is an impressive feature of the recorded cases of renal failure following abortion, so common indeed that the solutions must be suspected of being directly implicated in the renal damage. Professor Bull and his colleagues may be in a position to provide a control series where the abortions have been procured by instrumentation alone.

Abruptio placentæ is the obstetrical complication with which renal failure is most commonly associated. The placenta is formed about the end of the first trimester; hence *classical examples of abruptio placentæ arise in the middle months of pregnancy.*[4] This is an entirely different clinical syndrome. For this reason the use of the term "abortion" for termination of pregnancy before the period of viability is misleading. A clear distinction should be drawn between the termination of pregnancy before and after the formation of the placenta. This distinction, particularly in the present context, is far more important than the arbitrary period of viability, which has no scientific basis.

In all the fatal cases, and therefore presumably in all those where the patient survived, the renal lesion was *tubular* necrosis as distinct from cortical necrosis. This suggests that the lesion may be due to a toxic agent acting directly on the tubules, whereas in abruptio placentæ the renal damage is presumed to result from vasospasm. If this be so, the tubular lesion in cases of abortion may be always reversible, while steps taken for the relief of vasospasm may be expected to be ineffective.

In conclusion, I suggest that the renal failure following induced abortion is not related to intercurrent factors—e.g., shock—but is due to the direct toxic action of, usually, soap solutions. The syndrome may have no obstetrical basis, the pregnant uterus being merely the portal of entry for a toxic solution. It seems to be the *soap, and not the abortion,* that causes the renal damage.

Dublin K. O'DRISCOLL

A NEW WAY OF TREATING FLAT FEET IN CHILDREN

SIR,—Mr Helfet's article under this title (Feb. 11) interests me greatly; but what Mr Helfet describes is neither new nor a method of treating flat feet. The method of treatment was devised by Mr Franklin Charlesworth,[1] the chiropodist at Hope Hospital, Salford, who has used it for so long that I cannot remember when he started it.

The patients that Mr Helfet describes are not those with flat feet but with feet that are everted, valgus, or pronated.

As some of us in this country have been at pains to emphasise, to apply the term "flat" to these feet is completely erroneous. Many of these pronated feet have such a high arch that they are correctly described as pes cavus. The late Mr C. Lambrinudi, Mr T. T. Stamm, myself, and others have been emphasising that the problem is not that the feet go flat but that they topple over into eversion, and that in association with this eversion there is an interesting and rather complex movement at the subtaloid and midtarsal joints. This causes the inner border of the foot to become convex instead of straight or concave and makes the head of the talus sink a little. In other cases the foot topples over because there is inadequate support by the first metatarsal from atavism—i.e., shortness, looseness or instability, or a permanently elevated position (metatarsus primus elevatus). In all these conditions the lack of support in the forefoot causes the foot to roll over into eversion. Stamm[2] has also given a very vivid description of what he calls the "unscrewed" foot. *In all these varieties it seems that the important defect of the foot is in the forefoot, and it just depends on the minute details of the defect whether the end result is a pronated foot,* hallux rigidus, or hallux valgus.

It has, I think, been amply demonstrated in recent years that correction of pronated feet, when necessary, is best effected by means of some apparatus which holds the heel upright and replaces the defective support of the forefoot. That is what Mr Charlesworth's and Mr Helfet's supports do. The methods evolved by Mr Charlesworth are not expensive. Mr Helfet's methods follow very much those of Mr Charlesworth, and no doubt he will be interested to know following his suggestion in the last sentence of his article, *that* whereas in the past the material used has been plastic-strengthened hessian we are about to embark on trials of resin *impregnated laminated glass fibre.*

I would finally appeal for this to be recognised. A very high proportion of children at and soon after the time they start to walk have what we describe as pronated feet and genu valgum. In the majority it is a passing phase which requires no treatment. In a small proportion these changes will persist. As we are at present unable to tell which child will cure itself and which will not, it is wise to treat each by some simple means. Moreover, this allays the anxiety of the parent, which is perhaps the most important aspect. It is not until the child has reached the age of 6–10 that a persistent deformity needs serious consideration. Treatment then may consist in some form of surgical alteration *to the shoe, the* provision of a suitable light semi-flexible arch support, or a heel seat such as Mr Charlesworth and Mr Helfet describe. If this is persisted in, the majority of children will be cured. A very small proportion will still have the deformity and operative treatment will be necessary; but even at the age of 10–12 a condition of flat feet, using the word "flat" to mean a flattened longitudinal

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[3] Schofield, J. E., Anderson, P. St. G. *Brit. med. J.* 1953, ii, 598.
[4] O'Driscoll, K. *Irish J. med. Sci.* January, 1953, p. 40.

[1] Charlesworth, F. Chiropodial Orthopædics. Edinburgh, 1951.
[2] Stamm, T. T. *Med. Pr.* 1952, 227, 589.

morphological or functional aberrations in structures derived from this source the gonad, the adrenal cortex, and the kidney. Of course, this hypothetical unitarian concept, though supported by several facts must await further investigation and confirmation.

In 1952 Huddleston Slater[8] described an entirely comparable case in which the patient was later found to have male type nuclei.[9]

> The patient was of normal male habitus, had an empty scrotum, and had been submitted to repeated plastic operations for hypospadias. Laparotomy revealed a normally developed uterus and fallopian tubes and, at the site of the ovaries, bilateral tumours. The right tumour was diagnosed as a differentiated arrhenoblastoma (Pick's adenoma tubulare testiculare ovarii), the left as a dysgerminoma with a separate dermoid cyst. Hormonal findings suggested adrenal insufficiency.

Thus, in this case dysgerminoma was associated with another quite rare tumour, which may arise in ovary or in testis and is thus again associated with undoubted developmental anomaly of the gonads in a male. In males adenoma tubulare has been reported almost exclusively in cases of cryptorchidism or hermaphrodism. In females it is said to exert no virilising effect, but some doubt seems now justified as to whether this tumour is ever found in normal females.

Quite recently Greenblatt[10] described a patient (case 6) with feminine appearance and male skin sex, in whom a testis was removed that contained, amid non tumorous areas of immature testicular tubules, nodules of adenoma tubulare. The gonadal structure in this case is of special interest, as it seems to represent a transition between the entirely neoplastic right gonad of the foregoing case, and the non-tumorous, immature, œstrogen producing testes of the so-called "intersex males with purely feminine external genitalia."

These three cases thus present a logical sequence, extending clinically, from almost completely male to almost completely female habitus, and histologically from complete aplasia through tumorous aberration to almost normal immature structure. These facts seem to suggest that early intra uterine injury to the male fœtus may cause either complete destruction with aplasia, or variable damage with eventual tumour formation, or only functional disturbance with no gross morphological aberration of the testis.

Another rare tumour, described as common to ovary and testis, which, in the light of the foregoing, deserves our attention is primary chorionepithelioma of the gonad. The nuclear sex of patients with such a tumour should be carefully studied. This tumour, too, has been reported in conjunction with dysgerminoma, and like dysgerminoma it is often found in young patients.

We can now firmly conclude that some tumours, formerly termed ovarian, are in fact testicular. Some light is thus thrown on the curious identity of dysgerminoma and seminoma. Future studies should be directed to the question whether, taking nuclear sex as a dividing line, histological difference may be found between tumours that were formerly thought to be identical. On the other hand the evidence points strongly to a close pathogenetic relationship between dysgerminoma and adenoma tubulare.

This seems to represent a new step towards the understanding of various morphological and functional sexual deviations. Male individuals in whom a female or pseudohermaphroditic sexual pattern has developed should be carefully investigated for dysontogenetic tumours.

P J CARPENTIER
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Utrecht Netherlands

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8 Huddleston Slater, W B *Ned Tijdschr Geneesk* 1953 97, 646
9 Levij I S *Ibid* 1955, 99 1477
10 Greenblatt R. B *Amer J Obstet Gynec* 1955, 70 1165

"L E -CELL" PHENOMENON IN CHRONIC HEPATITIS

SIR,—The article by Dr Joske and Dr King[1] in which they report finding L E cells in two patients with active chronic hepatitis contains a few points I should like to comment on.

To begin with, it is widely recognised that methods involving the coagulation of blood—such as in the Magath Winkle[2] procedure adopted in this study—have greatly enhanced the sensitivity of the original L E test. Without going here into the reasons for this,[3–7] the question has already arisen whether such techniques should not be used, "because they are so sensitive that they defeat the value of the L E cell as an indicator of acute and subacute lupus erythematosus, or whether the method should be welcomed" as a more sensitive but still reliable diagnostic procedure.[8] Also, the need for quantitation of the intensity of the phenomenon has been repeatedly emphasised, and Haserick[9] has remarked that no "aspecific" case has been reported to date, with a strongly positive (++++) plasma L E test. I can add, from my personal experience, that even the degree of homogenisation of the engulfed nuclei has a very great importance, and that greatly depolymerised inclusions after the customary incubation time, with a marked "jump of coloration"[10] between phagocytosing and phagocytosed nuclear chromatin, clearly indicate a high concentration of the L E factor in the blood, and are almost invariably associated with active lupus. L.E like cells, "tartoid" cells and genuine, but generally not plentiful and seldom totally depolymerised, L.E cells—not to speak of simple nucleophagocytosis—are more frequently met with in non lupus weakly positive tests, especially by the more sensitive (and often more traumatising) defibrination techniques. In our experience, nucleophagocytosis has been frequent in febrile Hodgkin's disease.

I have accordingly suggested[11] that always at least one defibrinated and one anticoagulant test should be done, the latter preferably both by the auto and by the iso-techniques (viz, with the patient supplying both the reacting blood or marrow cells and the active plasma or serum factor, or only the latter, the buffy coat being furnished by another, if possible group compatible, individual, or even by an animal such as the dog or the horse [hetero test]). In the admittedly rare non lupus positive tests, good photomicrographs clearly demonstrating at least a couple of typical L E cells would also be desirable, since so much information as to the reliability of the report may be gained by simply inspecting these cells. Proof of this may be found in the reported finding of L E cells in the ascitic fluids of cirrhotic patients by Leoni,[12] while nothing more than tart cells and the like are depicted in his original article.

Lastly, I agree with Dr Joske and Dr King that the L E phenomenon may be the end product of an auto immune mechanism resulting from true auto-sensitisation, or perhaps simply from antibody-like globulin synthesis with an excessive and disordered immuno allergic background. In fact, I considered this working hypothesis in 1951[13] and submitted it more fully in 1952,[14] 1953,[15,16] and 1955[7,17] This immuno allergic reaction would seem to develop spontaneously (though it is often precipitated by drugs, stress, or infections), and to be self-perpetuating in genuine

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1 Joske R A King W E *Lancet* 1955 ii 477
2 Magath, T B Winkle, V *Amer J clin Path* 1952, 22 586
3 Zimmer F E, Hargraves, M M *Proc Mayo Clin* 1952, 27 424
4 Hargraves M M *Adv intern Med* 1954 6 133
5 Lee, L S Schwartz L I Pariser S *Blood* 1954 9 965
6 Snapper I Nathan D J *Ibid* 1955 10, 718
7 Marmont A *Acta hæmat* 1955, 13 257
8 Sulzberger M B, Baehr, R L *Yearb Derm Syph* 1953–54, p 247
9 Haserick J R *In* Modern Trends in Dermatology Edited by R M B MacKenna London 1952 p 76
10 Marmont, A Fusco F *Stetoscopio Rome* 1951 1 363
11 Marmont A Piuma, M *Boll Soc ital Ematol* (in the press)
12 Leoni, A *Min Med Torino*, 1953, 55, 1022
13 Marmont A Le cosiddette angiomesenchimopatie reattive diffuse Rome, 1951
14 Marmont, A *Schweiz med Wschr* 1952 82, 1111
15 Marmont A *Min Med Torino* 1953, 44 80
16 Marmont A Eighth Congress of Dermatology and Syphilology Nancy 1953 vol 2, p 53
17 Marmont, A *In* Attualità in Ematologia Edited by A Baserga Rome, 1955 p 187

and extreme weakness In some of our cases after a few months the clinical signs of myxoedema are beginning to appear and radio-iodine uptake studies confirm the presence of hypothyroidism

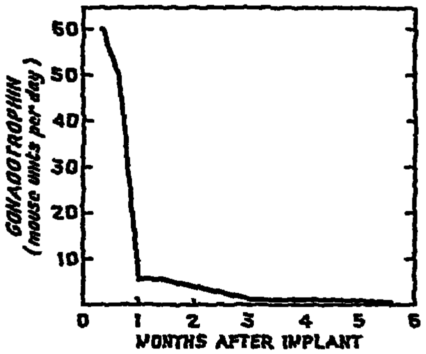

Fig 1—Case 6 urinary excretion of gonadotrophin after pituitary implantation

One of the earliest and most constant hormonal effects has been the development of diabetes insipidus which appears within a few weeks after implantation The severity of the polyuria depends on the amount of cortisone administered, and is usually not great if the dose can be restricted to 25 mg per day It can, moreover be controlled readily by pitressin given either as a snuff or as the tannate in oil The polyuria tends to diminish after a few months

Results

In the 8 cases of malignant disease other than cancer of the breast the treatment has been entirely ineffective This group included 4 patients with malignant melanoma, 3 with advanced carcinoma of the uterus and 1 with sarcoma of the breast All have died of progressive malignant disease Of the 25 patients with breast cancer 9 have died of progressive malignant disease while 9 others have shown no improvement though possibly some of them have been too recently treated for assessment The remaining 7 cases have sustained benefit as follows

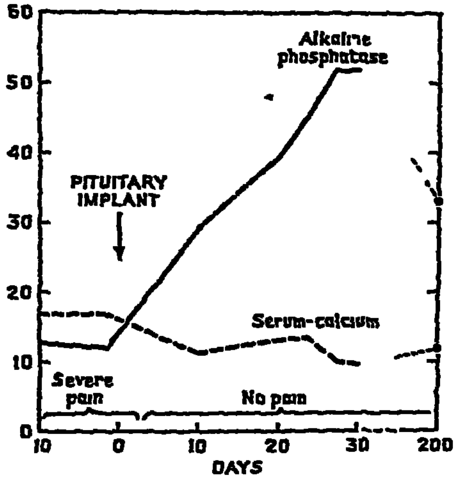

Fig 2—Case 1 blood-levels of alkaline phosphatase (King-Armstrong units) and calcium (mg per 100 ml) before and after pituitary implantation

Case 1 — A woman, aged 48 was admitted bedridden and in great pain from spinal metastases Implantation (10 mC) was performed in February, 1955 Within two days the pain had almost disappeared and within a week she was ambulant Biochemical evidence of bone regeneration was provided by the rising blood level of alkaline phosphatase and the falling level of calcium (fig 2) This patient remained well for six months free from pain and carrying out her household duties In October, 1955, she had new metastatic nodules in the mastectomy scar Bilateral adrenalectomy has now been performed

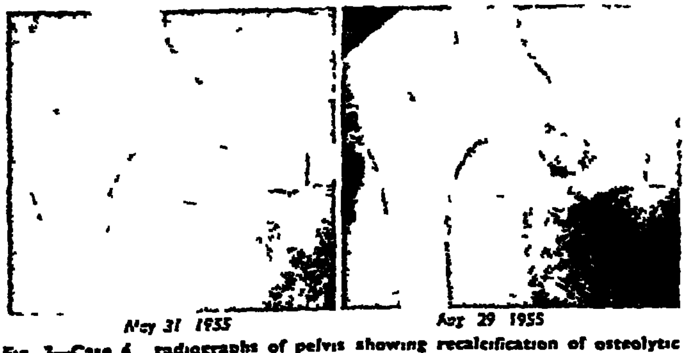

Fig 3—Case 6 radiographs of pelvis showing recalcification of osteolytic metastases following pituitary implantation on May 30 1955

Case 2 —A woman aged 49 with an untreated ulcerating breast cancer of two years duration, abruptly developed jacksonian convulsions originating in the hand area of the motor cortex The convulsions recurred repeatedly with deepening coma Seven days after the onset in March, 1955, 10 mC of radon was implanted The convulsions have not recurred, though she has frequent minor cramps and twitchings The primary growth has shown no change We recognise that there is no indisputable evidence of a brain metastasis, and, if a brain metastasis is present, symptoms due to haemorrhage into it may have undergone spontaneous arrest

Case 3 —A woman, aged 35 with multiple metastases in lymph nodes and bones, was treated by implantation of 1[illegible] mC radon in April 1955 The pain, of vertebral origin, is greatly improved Radiographs demonstrate undoubted recalcification of the vertebra, and the lymph glands appear to be smaller

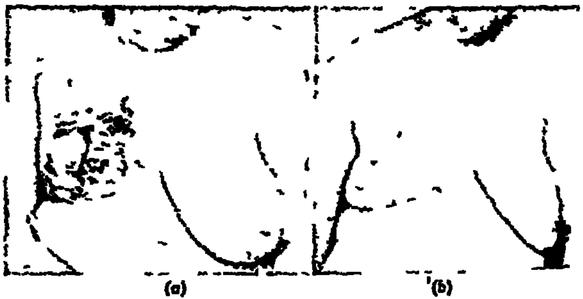

Fig 4—Case 7 clinical condition of breast before pituitary implantation (a) and four months after implantation (b)

Case 4 —A woman aged 53, with multiple pulmonary metastases, was submitted to implantation of 20 mC of radon in May, 1955 The cough of which she complained has ceased and radiographic examination appears to indicate reduction in the size and number of the metastases

Case 5 —A woman aged 63 with ulcerating nodules in a mastectomy scar and enlarged supraclavicular lymph glands was submitted to implantation (20 mC) in May, 1955 The ulcers have healed, and the underlying skin nodules have almost disappeared, and we believe that the supraclavicular glands have become smaller

Case 6 —*A woman, aged 50, with skeletal metastases,* was submitted to implantation (15 mC) in May, 1955 She gained much relief from her severe pain Radiographic examination shows undoubted recalcification of the bones (fig 3)

Case 7.—A woman, aged 66, was admitted with an untreated massive growth of the breast ulcerated over an area 6 in in diameter and with enlarged axillary and supraclavicular glands 15 mC of radon was implanted in July, 1955 The tumour is now half its original size and the ulcer has healed (fig 4) The glands have regressed

Discussion

There is no doubt that in some cases destruction of the pituitary gland by this method results in relief of pain (particularly from skeletal metastases) in recalcification of the affected bones in shrinkage of soft-tissue deposits, and even in a reduction in size of the primary growth We cannot yet determine the extent to which these responses depend on individual variations in 'hormone dependance' of the tumours or on the completeness of the pituitary destruction In all but 1 of the 7 cases described here the 17-ketosteroid excretion has fallen to below 1 mg in the twenty-four hours (see table) which suggests a fairly complete functional pituitary destruction Unfortunately in the unsuccessful cases our data morphological or functional aberrations in structures derived from this source the gonad, the adrenal cortex, and the kidney. Of course, this hypothetical unitarian concept though supported by several facts, must await further investigation and confirmation.

In 1952 Huddleston Slater[8] described an entirely comparable case in which the patient was later found to have male type nuclei[9]

> The patient was of normal male habitus, had an empty scrotum, and had been submitted to repeated plastic operations for hypospadias. Laparotomy revealed a normally developed uterus and fallopian tubes and, at the site of the ovaries, bilateral tumours. The right tumour was diagnosed as a differentiated arrhenoblastoma (Pick's adenoma tubulare testiculare ovarii), the left as a dysgerminoma with a separate dermoid cyst. Hormonal findings suggested adrenal insufficiency.

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[8] Huddleston Slater W B *Ned Tijdschr Geneesk* 1953 97 646
[9] Levij I. S *Ibid* 1955 99, 1477
[10] Greenblatt R B *Amer J Obstet Gynec* 1955 70 1165

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Lastly, I agree with Dr Joske and Dr King that the L E phenomenon may be the end-product *of* an auto-immune mechanism resulting from true *auto*-sensitisation, or perhaps simply from antibody-like globulin synthesis with an excessive and disordered immuno allergic background. In fact, I considered this working hypothesis in 1951[13] and submitted it more fully in 1952,[14] 1953,[15,16] and 1955[7,17] This immuno-allergic reaction would seem to develop spontaneously (though it is often precipitated by drugs, stress, or infections), and to be self-perpetuating in genuine

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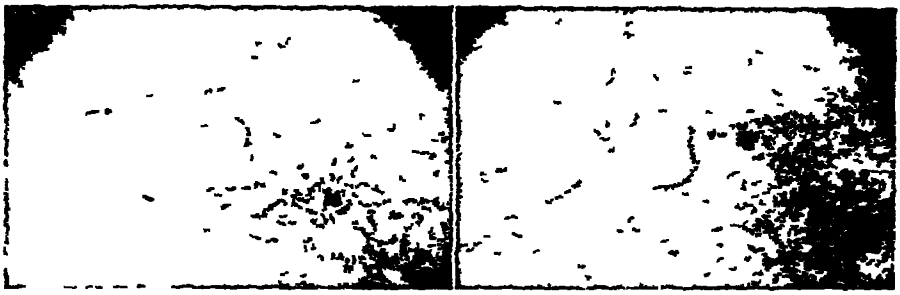


Fig 1—Retinopathy in a case of chronic type-2 nephritis A before treatment, showing papillœdema, retinal œdema, and macular star, B, after treatment with serpasil only

standing pressure was recorded as well, another three readings were taken; and in each case the lowest reading was recorded The pulse-rate was noted while the patient was recumbent

The dispensary held inert tablets corresponding to the three strengths of serpasil employed, and also made some sugar-coated phenobarbitone tablets each containing gr $^1/_2$, and some similar sugar-coated inert tablets In 9 of the cases the patients were watched for several weeks during which they took inert "serpasil" tablets and the sugar-coated phenobarbitone These tablets were then changed over to serpasil proper and inert "phenobarbitone" In all the other cases serpasil itself was given initially (to avoid delay in treatment), and if the blood-pressure fell significantly inert "serpasil" tablets were substituted in the middle of treatment Great care was taken that no patient should know when there was a change of tablets

In all cases, except those already on pentolinium or hexamethonium injections, each patient received initially serpasil 1 mg daily in divided doses, and thereafter the amount was varied according to the response Few patients required less than 0 5 mg a day, and none received more than 2 mg a day The dosage of phenobarbitone, when used, was gr $^1/_2$ t d s In the 12 patients already receiving injections of ganglion-blocking drugs the starting dose of serpasil was usually smaller than 1 mg daily and was gradually increased, according to its effect

Results

Serpasil Only

Of 41 patients to whom serpasil only was administered, the result was good in 17 (41 5%), there was no effect in 16 (39%), and the effect was doubtful or cannot yet be assessed in 8 (19 5%)

In the 17 patients who responded well to treatment, the mean diastolic blood-pressure before treatment was 145 8 mm Hg and during the trial the mean fall in this pressure was 47 4 mm Hg The highest and lowest figures ever recorded for each patient would show an even more impressive fall in pressure, but we have taken the average of readings at several consecutive attendances The use of inert tablets seemed to show without reasonable doubt that the results were in fact due to serpasil

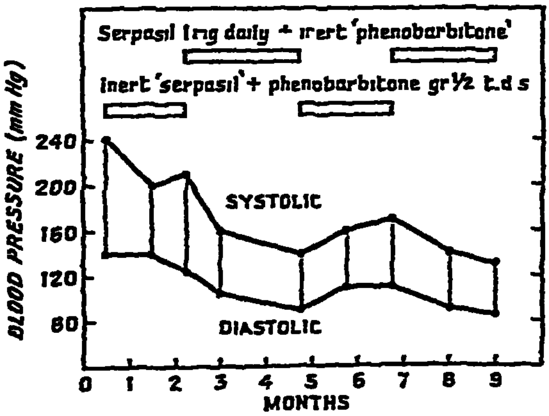


Fig 2—Blood-pressure of a patient receiving serpasil and inert tablets alternately

Serpasil Added to Ganglion-blocking Drugs

Of 13 patients in which administration of serpasil was added to that of ganglion blocking drugs, the result was good in 9 (69 2%), there was no effect in 3 (23 1%), and the effect was doubtful or cannot yet be assessed in 1 (7 7%)

These patients were all being treated with pentolinium or hexamethonium by subcutaneous injection, and their blood-pressure was therefore showing considerable diurnal variation At the time of attendance, the mean diastolic pressure *of this group, taken while recumbent* was 153 3 mm Hg After the addition of serpasil the mean fall in diastolic pressure was 29 4 mm Hg This fall is not so great as in the first group, but in 2 of these cases involved it has been possible to discontinue injections of ganglion-blocking agent, and in 3 others the dose of ganglion-blocking agent has been reduced considerably

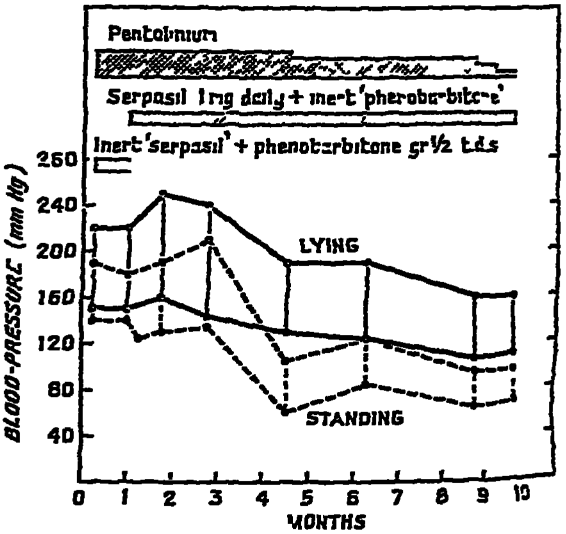


Fig 3—Blood-pressure, showing the effect of adding serpasil to pentolinium.

Further Findings in the Two Groups

Subjectively, most of the 54 patients have felt better after the treatment was started, and headaches have either been relieved completely or considerably lessened. This relief was not always clearly related to a fall in the blood pressure Vision has improved in cases where retinopathy was present, and patients unable to read a newspaper at the start of treatment have later been able to do so We have not been impressed with the objective improvement in retinopathy except in one or two cases, but cases of acute retinopathy most likely to respond to treatment were usually treated with pentolinium and are not included in this series Fig 1 illustrates severe retinopathy with papillœdema in a case of chronic (type-2) nephritis treated with serpasil only before treatment and four months later In this case the initial pressure in hospital was 190/140 mm Hg After in the duodenum. Gas under pressure, free fluid, and pus were present in the peritoneal cavity, and the presence of surgical emphysema in the mediastinum was confirmed. A careful search was made for the route of escape of the gas, but no completely conclusive evidence was discovered. There was a tiny tear in the attachment of the right coronary ligament to the diaphragm, though it was impossible to be quite sure that this was not a result of post mortem manipulation. There did seem to be a concentration of gas bubbles along the inferior vena cava. It must be presumed that the gas had in some way reached the retroperitoneal tissues through a small tear, and then tracked up along the vena cava.

The source of the intraperitoneal gas remains unknown. It could have been swallowed—which seems unlikely in view of the considerable intraperitoneal tension. It could have arisen by bacterial action in the peritoneal exudate—but no gas-forming organisms were cultured. Or it could have escaped from the bowel, the rising pressure in the lumen having possibly contributed to the breakdown of the perforation.

My thanks are due to Mr H A Haxton for permission to publish this account.

Crumpsall Hospital,
Manchester. P B LACY

INGUINAL HERNIORRHAPHY

SIR,—May I examine Mr Haxton's exposure (Feb 11) of the "fallacy" contained in my article? He states that my argument is undone by a failure to note that the linea alba is elastic in its length.

Although I do not believe it, I propose to accept Mr Haxton's suggestion for the sake of argument. The argument is that if the linea alba is elastic the whole of the lower third of the abdominal wall can descend, thus collapsing the "arch" of the conjoined tendon on to the inguinal ligament. Elasticity, however, is a passive quality needing the action of a dynamic force to demonstrate it. In this case the muscles provide the dynamic force. To achieve the desired effect a muscular mechanism for stretching the linea alba longitudinally in its lower half is needed; but I cannot invent such a mechanism. The lower half of the rectus abdominis, the most hopeful mechanism, fails because although stretching from the pubis to the lowest intersection, at the umbilicus, its pull is balanced by the upper half of that muscle, which, as far as I know, is not relaxed synergistically. In the upright position, therefore, the elasticity of the linea alba would be unused, as I am unaware of any evidence showing that the lower half of the rectus abdominis can overpower the upper half.

Let us assume, however, that the lower half of the rectus abdominis can overpower the upper half and stretch the linea alba downwards from the umbilicus, the active stretch occurring between the umbilicus and the xiphoid. This action is opposed by the contraction of those fibres of the internal oblique arising from the anterior superior spine and running horizontally to be inserted into the linea alba—unless it is suggested that they are synergistically inhibited. If these internal oblique fibres contract they will tend, as they become taut, to fix the point on the linea alba into which they are inserted, in both the coronal and the sagittal planes. Whether they are powerful enough to balance the rectus abdominis I do not know, but they would embarrass its action. The only muscle that could act without this embarrassment is the pyramidalis—a puny fellow. Therefore, even though the linea alba could be stretched very easily, it would avail the "arch" of the conjoined tendon little or nothing. As far as I know the pull of the external oblique and the internal oblique, above the level of the anterior superior spines, balance each other, and, therefore, can be discounted.

The last possibility of utilising the hypothetical elasticity of the linea alba is to return to Keith's original concept—that as the muscle fibres in the "arch" contract, it must approximate in length and position to the inguinal ligament. From observation I can state that the power of these "arch" fibres is so poor that they are unable to act in the way needed, even when stimulated alone, with the rest of the abdominal muscles relaxed.

Although the linea alba stretches with pregnancy it scarcely "twangs" back to "normal" with parturition, and I am sure that if Mr Haxton repeats my simple experiments he will find my observations substantially correct.

Tutnall, near Bromsgrove,
Worcs. F S A DORAN

MEMORIAL TO SIR HUGH CAIRNS

SIR,—The Society of British Neurological Surgeons has decided to commemorate the name and work of the late Sir Hugh Cairns. The memorial will take the form, in part, of a lecture to be given in London or Oxford from time to time by eminent men whatever their country. For this it is necessary to provide an endowment fund to cover an honorarium and travelling expenses.

Our society, knowing the high esteem in which Sir Hugh Cairns was held by people in many walks of life, believe that these might wish to show their respect and, where appropriate, their gratitude by subscribing to this object. The magnificent work done by Sir Hugh in organising, with the warm coöperation of the Army authorities, the special neurosurgical skills to be applied immediately behind the battle marked a lasting advance, we venture to believe, in military surgery.

Subscriptions should be sent to the hon treasurer of our society, Mr J B Pennybacker, the Radcliffe Infirmary, Oxford.

GEOFFREY JEFFERSON
President
D W C NORTHFIELD
Hon secretary
J B PENNYBACKER
Hon treasurer

Parliament

QUESTION TIME

Unemployed Doctors

Replying to a question, Mr JOHN BOYD CARPENTER, the Minister of Pensions and National Insurance, said that on March 19 there were 35 doctors registered at appointments offices in receipt of unemployment benefit.

Lung-Cancer and Smoking

Mr W D CHAPMAN asked the Minister of Health what action he had now decided to take, following the reports of his advisory committees, to inform the public about the dangers of lung cancer from smoking.—Mr R H TURTON replied: I have this very important subject under urgent review. Mr CHAPMAN: Will the Minister try to tell us how quickly he can make up his mind on this very important issue and try to give us a date? Will he also take note of the feeling which exists that there should be a national campaign and that the matter should not be left to small bodies and local authorities but should be officially sponsored by his Ministry? Will he make a note of the fact that he should try to emphasise in propaganda that one of the things which people can best do to help themselves is to give up smoking in the dangerous years between 40 and 50 when they become more susceptible to the disease?—Mr TURTON: I am studying the very points which the hon Member has mentioned.

Dr BARNETT STROSS: Has the Minister yet consulted the Minister of Education to ensure that the facts are taught throughout all schools, and not only to boys but to girls as well? Will he bear in mind that this might well be the most fruitful field if the facts as we have received them are correct? Mr TURTON: The first step is to find out exactly what the facts are at present as regards research.

Overtime for Nursing Staffs

Mr ARTHUR BLENKINSOP asked the Minister what representations had been received from regional hospital boards regarding extra payments for overtime for staffs in mental and mental deficiency hospitals.—Mr TURTON *replied*: Two regional boards have expressed concern at the failure to reach agreement on overtime rates for nursing staff. Mr BLENKINSOP: Does the Minister not agree that in view of the expressed willingness of the regional hospital boards to make some extra payments for this purpose it is vital that the procedure of the Whitley Council should be speeded up?—Mr TURTON: I understand that the claim for enhanced overtime rates has been rejected by the management side of the Whitley Council.

head is slightly raised and turned to the side away from the operator

The head is draped, and an incision is made ½ in posterior to the outer bony margin of the orbit, upwards to the outer end of the eyebrow, and then along the margin of the origin of the temporalis muscle for approximately 3 in This incision is carried through the galea, and the scalp flap is reflected downwards and backwards The temporal fascia and temporalis muscle are then incised with the diathermy knife and the muscle is reflected in the same way as the scalp flap, by means of a rugine Up to this point the operation follows the lines already described in our lateral approach to the frontal sinus (Rowbotham, Clarke, and Hammersley 1955) With the perforator and burr an opening is now made into the orbit through the orbital plates of the sphenoid and zygomatic bones, thus exposing the layer of periorbital fascia Mr Hammersley's drawing (fig 1) shows the operation field at this stage

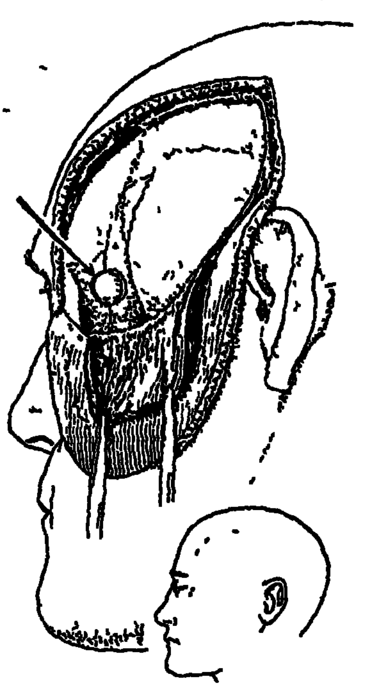


Fig 1—Exposure of periorbital fascia through burr-hole opening Small drawing shows line of skin incision

The bony opening is then enlarged with nibbling forceps, so that the roof and lateral walls of the orbit are removed In this process the dura mater of both anterior and middle cranial fossæ is uncovered The margins of the *superior orbital* fissure are preserved as is the annulus of Zinn In mild cases no more bone is taken away, but if the exophthalmos is severe the outer bony margin of the orbit is unhesitatingly removed The periorbital fascia is now freely incised, allowing the orbital contents to bulge out, and, after complete hæmostasis has been secured, the temporalis muscle, galea, and skin are closed in layers with interrupted silk sutures The wound is drained for twenty four hours

Using standard neurosurgical techniques, the operation is not difficult and can be quickly performed

During operation, and for a few days afterwards, great care is taken to protect the eye, and a pressure pad over the closed lids should be kept in position The help of an experienced ophthalmologist is of great value at this stage

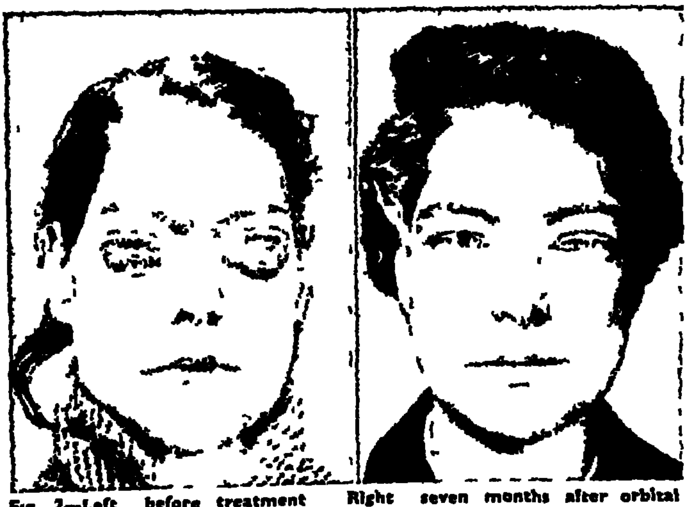


Fig 2—Left before treatment Right seven months after orbital decompression

Results

In every case the exophthalmos receded and has not recurred, no eyes have been lost A very striking finding has been the complete relief of pain in every case All our patients have commented enthusiastically on this and have considered the operation well worth while on this ground alone In no case did ophthalmoplegia progress after operation, in the 6 instances of severe ophthalmoplegia associated with diplopia there was some improvement after operation, but demonstrable ophthalmoplegia is still present This finding agrees with that of Poppen (1950), who found in his series of cases that long standing severe ophthalmoplegia was not dispelled by decompression

One of the most satisfactory cases is shown in fig 2

This woman, aged 38, first noticed exophthalmos, a small goitre, and symptoms of thyrotoxicosis in February, 1954 In August of that year thyroidectomy was performed, but despite alleviation of most of her symptoms, the eye condition progressed and she was referred to us in March, 1955 She was led into the clinic in great pain, with tears pouring down her cheeks The left cornea was completely opaque, and the right was in a similar condition except for a very small part of each upper quadrant (fig 2) The resting pulse rate was 120 per min and the basal metabolic rate +58% She was seen by Dr G O Richardson, who advised that she should be given thyroid gr 4 daily Mr J M L Howat performed immediate bilateral tarsorrhaphy

Three days later the right orbit was decompressed and after an interval of five days the left orbit was similarly treated Reduction in the exophthalmos was immediate and striking, with accompanying complete relief of pain The patient's condition in October, 1955, is shown in fig 2 The visual acuity in the right eye is 6/18, and the left cornea is clearing A few adhesions between the lids—the result of tarsorrhaphy—are still present but she can see to do her housework and look after her young family The thyrotoxicosis is controlled with carbimazole

One patient, a man, died during operation on the left orbit, the right having been decompressed a few weeks earlier

He was 67 years of age, with very severe exophthalmos Thyrotoxicosis had been treated with thiouracil to the point where myxœdema had developed Auricular fibrillation was under treatment with digoxin. Death was attributed to heart failure

This patient was an acknowledged poor operative risk, but in retrospect we feel that the myxœdema may not have been taken sufficiently into account We now do not operate in such cases until we are satisfied about the control of the thyroid deficiency

Pathology

Orbital biopsies have been carried out only occasionally, because of the danger of inflicting serious damage and because of the difficulty, in many of these cases, of identifying structures accurately In every case at operation the tissues within the periorbital layer of fascia were found to be under great tension The extra-ocular muscles were bulky and pale and there seemed to be an excess of orbital fat

In 5 patients pieces of *lacrimal gland* were removed 3 of these specimens showed chronic inflammatory changes with lymphocytic infiltration

In 5 specimens of *levator palpebræ superioris* muscle there was infiltration by lymphocytes, plasma cells, and mast cells The sarcolemma nuclei were proliferating 1 specimen of muscle had undergone replacement by fibrous tissue

Orbital fat was examined in 6 cases with normal findings in 5 In the 6th case the fat was œdematous

Our findings therefore agree with the generally accepted view that in this condition there is in life was to give ungrudgingly of his best a loyal friend, in whose company one could never be dull "

Brigadier Sinton is survived by his widow and their only child, who is the wife of a medical research-worker in West Africa

FREDERICK JAMES FITZMAURICE BARRINGTON

M S Lond , F R C S

Mr Barrington, of University College Hospital, who died on March 23, was a remarkable man He was an outstanding genito-urinary surgeon, to whom colleagues turned for help in difficult cases yet his writings were almost confined to his physiological researches He hardly ever wrote about surgery, nor did he speak publicly at meetings But the keen observation which enabled him to establish a reputation as an experimental worker was applied to every clinical case just as sharply , and, with his impeccable memory, it formed the basis of his immense clinical knowledge

The combination of laboratory research with practical surgery is often held up to young men as an ideal, but it is seldom persisted in by surgeons as they get older The picture of such a combination does not call to mind the idea of a good practising doctor but Barrington was a very good doctor His private practice was never large he was not much interested in it, and a shy abrupt manner did not help But he gave regular and devoted care to his hospital patients "To deputise for him in the outpatient department when he was away was a humbling experience Every old patient whose need was not too urgent used to get up and go away" Students saw him as a rather remote and monosyllabic personality , but to anyone who wanted to learn, and was prepared to listen, he was an exciting instructor Formal speech came to him with difficulty, and his lectures were dry in manner, lacking the vivacity of his conversation But the material of his lectures was magnificent, and notes of them were really valuable, because there was no book to take their place His operating technique was swift gentle and confident, and his cases did remarkably well The regularity of his success seemed to be based on the extreme care taken at every stage—the decision what to do, when and how to do it, followed by the aftercare never deputed

In the period 1914–41 he published what Fulton has called a series of classic papers on the physiology of micturition. These provided the foundation and most of the superstructure of our knowledge of this function and consisted in an able experimental analysis of the chain of reflex reactions that together subserve micturition Barrington never received the academic recognition these researches deserved, though those who have worked in this field have never doubted their originality and their importance "Though an unselfseeking man, he was acute enough to know this but great enough not to fester about it " His industry was immense and his knowledge of the genito-urinary anatomy of the mammalia extensive F M R W recalls how, from the pathological department of the Zoo, he used to return to the medical school "proudly bearing trophies of terrifying dimensions and of surprising origins '

Having qualified in 1907 and held a Beit fellowship, Barrington served during the first world war in cruisers in the Royal Navy, and then returned to a post on the surgical unit at University College Hospital, shortly afterwards being elected to the staff as urologist He was also appointed to St Peter s Hospital. On the outbreak of the second world war he joined the Emergency Medical Service staff at Colindale Hospital and lived at The Woodlands ' As air-raid casualties were admitted in only small numbers, a large genito-urinary unit was developed, drawing patients from University College Hospital and St Peter s and St Paul's Thus he was able to carry on his usual activities in comparatively rural surroundings, and living there with other medical staff proved congenial to him , characteristically he would remark that he had not been "so comfortable since the last bloody war " He was difficult to get to know, but once he had established a link—and usually one relating to some outdoor pursuit—that person, whatever his age, became his friend he was thereafter referred to by Barrington as "old so and so," and however youthful was treated from then on as an equal

Though his main interest outside medicine was in ornithology, he was also a keen botanist and zoologist

' During the late war," writes W E S , " he made detailed annual lists of birds and wild flowers seen at Colindale, which it was possible to print on the patients' press Characteristically he took no interest in garden flowers, regarding them as false and artificial He also enjoyed shooting and sailing and was always glad to accept an invitation for a cruise when he would spend long hours at the tiller observing sea birds, or to visit some place of interest in the country

"Apart from good dining, he cared little for personal comforts, and there was much of the ascetic in his nature five centuries earlier he would no doubt have been a monk He never drove a car, and walking even in London, was his favoured mode of transport His spare figure, with cropped head always hatless and coatless, carrying an attache case containing cystoscope, binoculars and macintosh, striding along in the Harley Street area, was familiar to many Although undemonstrative, his was a generous nature, as many hospital servants and the like in trouble well know '

It will be evident that Barrington was a many-sided man To some he was the experimental physiologist To U C H students he was " Snorker ' , he was " Fitz " at St Peter's , and he was known to many through his love of natural history He had, in fact, innumerable interests—though these did not include committees and administration

' Shy with strangers, he enjoyed with gusto meeting his friends, and there are many who will find life duller and less interesting because no longer will they see that shy angular figure One met him perhaps after a long time his face lit up some pertinent characteristic greeting would be followed by some tale or observation and after parting one had another memory of Barrington and almost always with laughter in it '

F M R W writes of the " generations that have come to know him, love him and trust him over the forty years of his association with University College Hospital and since

' Despite his somewhat farouche manner, and an occasionally alarming vocabulary drawn from the more vernacular variants of the special terminology of his branch of surgery, and at times liberally adorning his postprandial conversation no-one could be more gentle, kind, and thoughtful than he was There was neither guile nor malice in him In a sense he remained a boy all his life He loved the open air, was a keen bird watcher, and an enthusiastic, if, at times a frightening shot At a memorable Christmas shooting party at Sir John Rose Bradford s hospitable home in Wales many years ago he and I tied for bottom place "

" Although in a sense a lonely man, he was nevertheless a friendly and a happy one, and inspired great affection in very many who knew him We shall miss him deeply *Requiescat in pace* ' "

He died suddenly, in the company of friends A memorial service will be held at St Pancras parish church at 12 noon on Thursday, April 19

JOHN EDWARD O'LOGHLEN

L R C P I

Dr O'Loghlen, who died on March 8, had been in practice in South London for over twenty years and was a founder member of the College of General Practitioners After qualifying in Dublin in 1912 he continued his studies in London, Vienna. and Budapest, and he held hospital posts in Winnipeg and under the Metropolitan Asylums Board before he settled in practice in Clapham. As the stimulating letters which he contributed to our columns showed, he still found time to read widely and shrewdly in Continental as well as English journals

A K H. writes " Characters are rarer now in Medicine One of these (and a good friend) was lost to us when J E O Loghlen died It was he who taught me the importance of a close and wide knowledge of anatomy to a general practitioner, who more than anyone needs it for dealing with pain in all its moods and tenses, whether treating a disease himself or passing it on appropriately O'Loghlen felt acutely the discouragement that four changes in nomenclature have laid on those of our generation who wish to renew their anatomical youth

" Our own debt to him is great Seven years of postgraduate study in Vienna had sharpened his clinical eye and his knowledge of innumerable wrinkles One of these—his use of ethyl

DETAILS OF 14 INFANTS WHO DIED BEFORE THE AGE OF 7 DAYS WITH INTERSTITIAL EMPHYSEMA OF THE LUNGS AN MEDIASTINUM

Case no	Maturity at birth (weeks)	Condition at birth	Labour	Meconium or mucus on face at birth	Duration of symptoms	Symptoms	Age at death (hr)	Pn- thra
1	43	Normal covered with meconium	Normal	+ +	15 hr	Cyanotic attacks	24	L F
2	40	Normal	Normal		Found dead	Nil	12	L
3	40	Cried well	Normal	?	16 hr	"Whimpering"	48	L
4	40	Normal	Normal		10 hr		14	
5	42	Covered with meconium, recovered spontaneously	Normal	+ +	3½ hr	Cyanosis	21½	L - I
6	41	Asphyxia	Normal	+ +	30 min	Restless	7½	L
7	40	Normal	Normal	+	?		22	L - I
8	40	Normal	Normal		24 hr	Sloughy breathing	49	I
9	40	Normal	Normal	?	23½ hr	Cyanosis	24	
10	42	Cried spontaneously	Normal		3 hr	Cry less strong	4	L - P
11	40	Mouth full of meconium	Difficult	+ +	24 hr	Cyanosis	24	L
12	40	1–2 min before cry	Normal		Found dead	Vomited ? meconium	36	L - I
13	40	Cyanosed	Normal		30 min	"Grunting"	5½	!
14	40	Cried well after short interval	Normal	+	4 hr	"Queer noise"	10	L

were on "premature" infants and 52 on "full term" or "postmature" infants None of the premature infants died of spontaneous interstitial emphysema, although several had small amounts of emphysema produced by artificial respiration The following list shows what was considered to be the major cause of death in the 52 full term infants

Cause of death	*No of cases*
Gross congenital deformity	22
Hæmolytic disease	2
Obstetric and birth trauma	6
Thrombotic lesions	2
Infection	1
Hyaline membrane	3
Interstitial emphysema	7
Single causes	3
Cause not found	6
Total	52

This list demonstrates the known relative importance of congenital deformities and the now small importance of primary infections in the newborn Interstitial emphysema of the lung and mediastinum was the commonest single cause of death among the normally formed mature infants

Clinical History

Details of the 14 infants who died of interstitial emphysema, pneumothorax, and air block are recorded in the accompanying table

Some typical individual histories follow

Illustrative Case-reports

Case 1—A first male child, normal delivery, maturity 43 weeks At birth he was covered with tenacious meconium After being "cleaned up" he was thought to be fit, and his condition did not disturb the hospital attendants At 9 hours of age he had a cyanotic attack Three further cyanot attacks occurred before he died at the age of 24 hours This infant had no artificial respiration At necropsy a left sided pneumothorax was found The nasal passages and the trachea contained much greenish meconium like material There was bilateral interstitial emphysema of the lung, with much a at the hilum and around the vessels in the mediastinum Microscopy confirmed the presence of meconium in the alveolar ducts

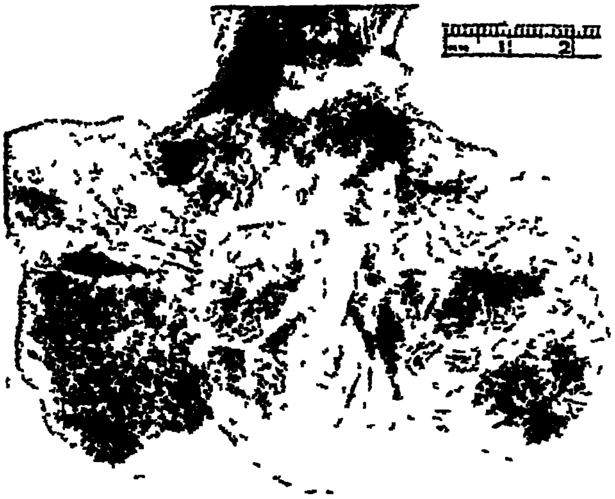


Fig 1—Heart and lungs showing extensive interstitial emphysema in both lung and large vesicles at root of left lung

Case 2.—A full term child born naturally The liquor was slightly green At birth the baby cried normally and appeared

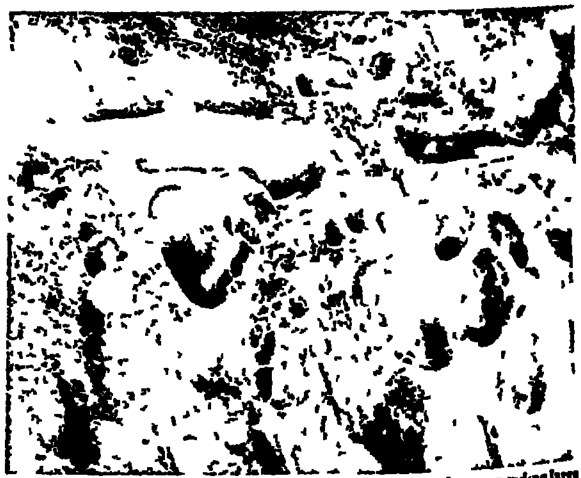


Fig 2—Transverse cut across root of lung, showing air surrounding large vessels

normal, but there were small amounts of meconium stained fluid over the face The infant was left in its cot and was considered to be completely normal, but was found dead at the age of 12 hours Necropsy revealed a left sided pneumothorax and extensive interstitial emphysema of both lungs and the hilum Microscopy showed keratinised squames obstructing the air passages

Case 3—The family doctor in sending the infant to hospital wrote "Baby born 8 P M Sunday night, second of twins born very quickly, vertex presentation Alleged to have cried well, but when seen by me at 9 P M was only whimpering was blue in hands and feet Improved in a few hours Today he has become increasingly blue *I hope it reaches you alive*" The child was dead on admission, then aged 2 days

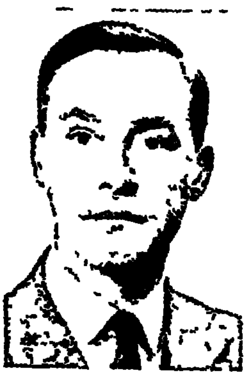
Case 4—A mature infant delivered naturally after normal labour attended by a private doctor The infant cried immediately after birth and in a few moments gave what the doctor described as "*a good yell*" Neither the doctor nor the midwife was in any way worried about the infant Three hours later the mother noticed that the infant was moaning After a further three hours, when she went to change the napkin, she saw that the infant was pale and blue When the infant was 13 hours old, she noticed a little blood

COLIN MACKAY KESSON

M D Glasg, F R F P S

Dr Kesson, assistant physician to Stobhill Hospital, Glasgow, died on March 8 He qualified from the University of Glasgow in 1939, and proceeded to the degree of M D in 1944 Four years later he became F R F P S

S A writes



[Elmore

In Colin Kesson there was something of the inscrutable, an element of mystery which created the impression of aloofness His demeanour was grave and his habit thoughtful beyond his years Such were his inherent qualities and upbringing that his name became synonymous with the virtues of deep earnestness and complete integrity His personality revealed in startling fashion the kinship of antagonistic emotions—when a gust of laughter would sweep him away and bring release from the thraldom of sombre reality In conversation he was an intent listener, but he showed , extreme diffidence in offering his own opinions unless given time for mature consideration Only those who were near him realised his intense interest in clinical medicine and the shrewdness of his judgment He had the gift of identifying himself with the patient's hopes and fears with great deftness he could strip a problem of its academic trimmings and place the patient as an individual—human and unique—in the foreground of the clinical picture For a few years he watched with philosophic calm the ebbing away of his cardiac reserve and he died in the moment when he was attaining to full maturity as a senior physician But his courage was in keeping with his record of service at Stobhill General Hospital, and it will be remembered as a fitting memorial to a gentle personality a patient teacher, and a doctor who was devoted to his calling

BERTRAM SAUNDERS

M D Aberd

Dr Saunders, who died in the Middlesex Hospital on Feb 21 at the age of 91, graduated M.B at the University of Aberdeen in 1894 After taking his M D in 1897 he came to London where he was a contemporary of Sir John Bland-Sutton as a postgraduate student at the Middlesex Hospital He held resident appointments at the North East Hospital for Children, Hackney Road and the City of London Hospital for Diseases of the Chest For many years he practised in Foley Street, a few yards from the Middlesex Hospital, and G D H, one of his younger colleagues there writes "With his old-world courtesy and kindly smile Dr Saunders was a familiar figure in the neighbourhood Towards the end of his life he had known hard times, but his great fortitude and optimism helped him to make little of this and remained with him until the end"

JOHN GORDON

M D Leeds, M R C P, D P H

Dr Gordon, reader in clinical bacteriology in the University of Leeds, died on March 6 He qualified at Leeds in 1918 and took the D P H three years later In 1925 he graduated M D with distinction A year earlier he had become lecturer in bacteriology in the university Most of his work was done in association with Prof J W McLeod, F R S He carried out many original investigations and published a large number of papers, particularly on complement and bacterial respiration He leaves a widow and two daughters

R A H writes

John Gordon was a man who was widely loved by his medical colleagues and also by the hundreds of students who passed through his hands In all his dealings he was strictly honest and thus his advice was always sought and listened to with deep respect At first sight he appeared to have a rather shy personality, quiet in speech and manner and sometimes diffident, but at heart he was a warm and likeable character In his subject he was a remarkable man He had a phenomenal memory, and having read widely in bacteriology he possessed a wealth of information which was always at the disposal of those who worked with him

Dr ARTHUR FELIX

Prof A Pijper, who met Dr Felix at the Lister Institute in 1928, writes

I can still see him, waving a paper of mine in which I had advocated complement fixation for typhoid diagnosis and taking me to task because I had not seen that my complement fixators were practically the same as O agglutinins and "why don t you people read what I write ?" The next few days I had private tuition in the mysteries of H and O and I went back to spread the gospel of receptor analysis in Africa This led to much correspondence between us, at first in German, which in the early '30s somewhat abruptly changed into English The correspondence became even more voluminous when I tried to sort out tick bite fever and murine typhus and louse typhus in South Africa, I could never have done it without Felix's constant advice and his invaluable cultures Then came his finding of the Vi antigen and the carrier that had Vi agglutinins and I hurried to confirm this on the few carriers I knew When I told him this he wrote back with characteristic generosity ' better publish quickly, I have a paper ready with several times the number of your carriers, and I shall hold back my paper, for if yours comes out after mine, it might fall rather flat '

Felix felt at home in Britain the local humour suited him, witness the remark in one of his publications that his earlier papers had "genossen allgemeiner Nicht Beachtung ' He was quick to adapt himself I remember a meeting of a research club in London where his work came under fire and the chairman asked him to say something Felix got up, smiled, shook his head, and said ' I have not the English" He acquired "the English" very rapidly ' In his last years he devoted himself with great enthusiasm to Craigie s discovery of phage typing and again we had many years of the most pleasant coöperation Personally I always looked upon Felix as an inspired man That was the only way in which I could explain how and why he collected and hung on to those famous cultures Ty 901, Ty 2, X 2, X 19, and many others, without which modern bacteriology is unthinkable And he did this, with his remarkable tenacity, through a whole world war, in a laboratory in a railway carriage, through a home coming to a totally disordered Austria, and through many years of a somewhat roving existence with scanty recognition until the Lister Institute gave him what was due to him He greatly enjoyed working there in the same way as he was quietly very proud of his election as an F.R S

Mr **FRANCIS JARDINE**, consulting surgeon to the Edinburgh Royal Infirmary and a former president of the Royal College of Surgeons of Edinburgh, died on March 27 at his home at Elie

Births, Marriages, and Deaths

BIRTHS

BINNS—On March 27, at Kingsbury Maternity Hospital London, N W 9, to Mary wife of Dr T B Binns—a daughter

JEFFERSON—On March 26 at the Radcliffe Infirmary, Oxford to Eirlys (formerly Hughes), M R C P D C H wife of Antony Jefferson F R C S a sister for Ann and Jane

SHARPEY SCHAFER—On March 28, at St Thomas s Hospital S E 1 to Dr Sheila Howarth wife of Prof E P Sharpey Schafer—a daughter

DEATHS

ROBSON—On March 22, at Bournemouth Thomas Robson M D M R C P senior physician Royal Victoria and Bournemouth Hospital and Christchurch Hospital (Corrected notice)

SANDS—On March 10, at St Ebba's Hospital, Epsom, Dalton Eric Sands, F R C P E

Appointments

AITCHISON J D, M B Glasg M.R C P, F R F P S asst cardiologist Aberdeen general hospitals

CADOGAN G S, M B Madras D.P M asst psychiatrist, Rainhill Hospital Liverpool

MAVOR R H M M B Glasg, F R F P S asst chest physician Aberdeen special hospitals

MURRAY R O, M B Camb D M R part time consultant radiologist Royal National Orthopædic Hospital London

STELL, E M B, D A part time asst anæsthetist, Chester group of hospitals

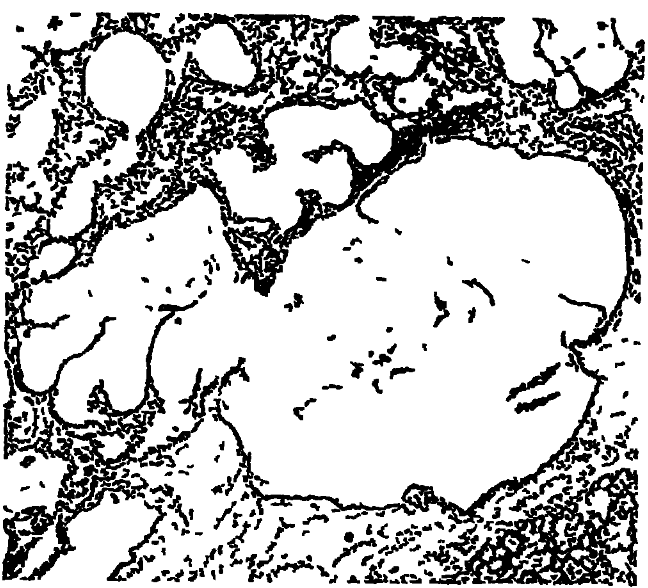


Fig 6—Distended alveoli at site of rupture into interstitial tissue of lung

found radiographic evidence of pneumothorax in 6 children in a series of 702 consecutive normal babies Holt and McIntosh (1953) state that "about 10% of newborn infants have small collections of air in the mediastinum" On the other hand, Keeffe and Jones (1951) found no case of pneumomediastinum or of pneumothorax in the routine anterior and lateral radiographs of over 4000 newborn infants Possibly the incidence of interstitial air will vary with different obstetric practice, but a general impression is gained that a variable amount of interstitial air causing no symptoms may be expected in perhaps 1 in 200 normal infants

The interpretation of free air in the thorax is difficult, for, if one accepts the findings of Davis and Stevens (1930), it would be expected to be present and of no lethal significance in about 1% of all newborn infants However, apart from the numerically greater prevalence (about 10% at necropsy), the importance of air in the thorax largely depends on its position a relatively small amount of air choking the vessels at the hilum of the lung and producing "air-block" is of considerably greater importance than an extensive pneumothorax or a large mass of air extending widely through subcutaneous tissues

Though most workers agree that a small amount of air in the chest does no harm to the infant, DeCosta (1940) was able to review about 50 case reports where this air produced symptoms which required treatment 13 cases of pneumomediastinum were reported between 1941 and 1949 (Heald and Wilder 1949), and 2 of them were fatal

Though the number of cases of spontaneous interstitial emphysema, air block, and pneumothorax reported in this country is extremely small (Rothman 1937, Yudkin 1947), this disease appears to be increasing in relative importance in normally formed mature infants within the first week after birth

The relatively high prevalence in my series is undoubtedly due to the inclusion in my material of the majority of infants dying within the City of Sheffield and to the increasing cooperation of the home doctors by their sending infants into hospital for necropsy instead of certifying the cause of death as atelectasis or as bronchopneumonia

Clinical Manifestations

The clinical histories of interstitial emphysema and death from air block seem to be consistent The children are either mature or postmature Though they cause no alarm at birth they often have much mucus in and around the nose and mouth, and they usually cry lustily Death in these cases has been preceded by either cyanotic attacks or a change in respiration, which usually becomes noisy

These symptoms have previously been well described

One of the first cases ever reported (Ruge 1878) was just like the present series It was a full term baby requiring no resuscitation, it cried lustily during the night (8–12 hours after birth) but later became cyanosed, and died next morning on the way to hospital

Silver (1939), describing the 6th recorded case, pointed out the activity of the infants and observed that infection was not an important factor in causing interstitial emphysema until after this age group

Salmon and Forbes (1943) described 3 cases of pneumothorax, all in infants who cried spontaneously In 2 of the cases meconium and much mucus were a feature at birth

Strain and Connell (1950) described an infant with spontaneous pneumothorax at the age of 4 days The infant cried spontaneously at birth and had had no artificial respiration The symptoms were cyanotic attacks The child recovered

As Salmon (1947) pointed out, the clinical picture of air-block in the newborn is unlikely to be simple The condition is the result of another disorder producing interstitial emphysema In infants with spontaneous emphysema something has produced the excessive production of mucus or the discharge of meconium during labour, and thus, though these infants are clinically apparently normal at birth, they probably have received some subclinical stress during labour

Ætiology

In the present cases microscopy revealed in the small air-passages keratinised squames derived from the fetal skin There was no evidence of infection of the respiratory tract The rupture of the alveoli into the interstitial tissue appeared to be related to the presence of mucus-carrying squames in the terminal bronchioles and alveolar ducts The interstitial air appeared to be compressing blood vessels, particularly in the hilum of the lung No air embolism (Lindblom 1924) was seen in this series of infants

Fisher and Macklin (1940) described a girl dying with interstitial emphysema in which the vessel sheaths were "air burrows in which collapsed vessels look insignificant," and Macklin and Macklin (1944) followed this with their classic study of the mechanism of death in interstitial emphysema of the lung and mediastinum They consolidated the concept of "air block" whereby death occurs from heart failure due to the obstruction to pulmonary blood flow by the pressure of air round the vessels and in the vessel sheaths The production of interstitial emphysema requires the partial obstruction of a segment of the respiratory tree and an increased expiratory effort In the cases described here the respiratory blocking appeared to be due to mucus and inhaled amniotic debris, and the expiratory force that of lusty crying

Following the work of Macklin and his colleagues, Salmon et al (1947) described 6 cases of death from air block in the newborn An interesting observation in 1 of their cases was that "although the infant's mouth and pharynx were full of mucus and meconium, respiration was prompt and spontaneous" They observed that death in these infants was from acute cor pulmonale due to compression of the pulmonary vessels causing pulmonary hypertension

Published reports on interstitial emphysema in the newborn go back to Guillot (1853) but the more recent papers contain unjustifiable statements, such as "Pneumothorax in the newborn results from the trauma of birth" (Strongin 1938) Keeffe and Jones (1951) state that, in all published cases of pneumothorax some form of artificial respiration had been administered Salomonsen (1952) states that "interstitial emphysema of the lung and mediastinum (air-block) commonly

A HOSPITAL ROMANCE

The Feminine Touch, a film from Ealing Studios which opened in London last week, is an embarrassing mixture of a little fact and much fiction The original intention may have been to show, in a lighthearted way, how the student nurse lives and works—a subject likely enough to seize the interest of the many who have ever crossed a hospital's threshold But then it seems, the producer's heart misgave him this, he may have thought, is no subject to lure the public from their home screens Anyhow, almost all else is sacrificed to follow the romance between the blonde probationer and the house-physician Despite brave talk of vomiting patients a revealing glimpse of a sluice room and one or two trips into a ward to meet selected patients, this is simply another boy-meets girl story Perhaps after all, that was the producer s intention, but we should at least have been spared the matron s Nightingale voice in this incongruous setting Acting honours are shared by Diana Wynyard an old trooper who plays the winsome matron with a blush that may owe something to Technicolor and Mandy, a young one, whose stalwart sincerity is proof against this incursion into Ealingland

AN INTERNATIONAL POSTBAG

An international corresponding club has been formed by workers in preventive and social medicine Its 42 members are drawn from teaching and research departments in fifteen different countries The club publishes twice yearly a bulletin to which members send news of the work in progress in their departments Copies, which are available to non members at 5s or $1, are issued alternately from the Department of Social and Industrial Medicine, University of Sheffield, England, and from the Department of Preventive Medicine and Public Health Cornell University Medical School, 1300, York Avenue, New York U S A

University of Cambridge

On March 10 and 24 the following degrees were conferred

M.D—G S Brindley K C Dixon. P H Friedlander, L G Higgins D S H W Nicol J P K. Preedy P G Tasker

M Chir—D W T Roberts T M Robinson W F W Southwood

M B—Katrine M Perry R L Rothwell Jackson.

M B, *B Chir*—F E Loeffler

University of London

Dr John Marshall, senior lecturer in neurology in the University of Edinburgh, has been appointed to the University readership in clinical neurology at the Institute of Neurology

Dr Marshall after graduating M B in the University of Manchester in 1946 held registrarships at the National Hospital Queen Square, London and in the department of neurology of the Royal Infirmary Manchester He has also served as a senior medical specialist in the R.A M.C with the rank of major He took the M R.C.P in 1948, the M.D in 1951 and the D P.M in 1952 Besides his university lectureship he holds the appointment of consultant neurologist to the Scottish South East Regional Hospital Board He has published papers on disseminated sclerosis sensory disturbances in cerebral wounds and on Raynaud s disease

The title of reader in dental surgery (preventive dentistry), has been conferred on Mr R D Emslie, M.S, in respect of his post at Guy's Hospital Medical School

University of Leeds

At recent examinations the following were successful

M.B Ch.B—Margaret E Carter R S Kocen (with honours) I D Adams Michael Barton I S Berg, John Clifford Doreen Crawshaw W B Davies, James Dowson H G Egdell, G H Elsworth, D M. Fletcher D C Fluck Martin Gittleman N M Harland P J Holland Michael Ibberson S I Jacobs Evelyn M M Jones, R W Kershaw E P Langworth J M. Littlewood L W Lowe, Elizabeth J Marsh D M Morgan M A Pace Jean M Phillips Gwendolen R Plumbly B H Rance M D Rawson (Distinction in Surgery) S S Richardson A V Sheard Kurt Simon, B A. M. Smith R G Spector Wee Foh Ta-Min S I Thackstone, D H Thomas G B Walker J M Wilde Pamela M Zinkin.

D.P M—Dorothy J Galbraith Frank Lake L C Wilson

University of Sheffield

Dr Robert Kilpatrick has been appointed lecturer in pharmacology

University of Durham

Dr C H Tonge, senior lecturer in anatomy, has been appointed reader in oral anatomy in the Newcastle division of the university

The court has approved the creation of the new post of professor of dermatology in the division

University of Liverpool

On March 27 the degree of M D was conferred on Cynthia J Discombe and the degree of M CH ORTH on I K Sharp

University of Birmingham

On Thursday and Friday, April 26 and 27, Dr H L Kottmeier, head of the gynaecological department of Radiumhemmet, Caroline Institute Stockholm will give the Ingleby lectures on Carcinoma of the Cervix and Corpus On May 14 15, and 16, Prof P B Medawar, F R.S will deliver the William Withering lectures, on Transplantation and Immunology

University of Reading

Dr Alick Elithorn has been appointed part time lecturer in psychopathology

University of Edinburgh

On July 6 the honorary degree of LL D is to be conferred on Prof G R Cameron, F R S

University of Glasgow

On June 20 the honorary degree of LL D will be conferred on Dr H C Cameron, Dr Edward Glover, and Dr T J Honeyman

University of Dublin

At a recent examination for the diploma in gynaecology and obstetrics the following were successful

Ram Lal Chugh Surendra Nath Das Bimla Devi Dugal A M MacIntosh, Mira Vinayak Muzumdar Attiya Sabir Kantilal Manmohandas Soparkar

Royal College of Physicians of London

Prof F T G Prunty will give the Humphry Davy Rolleston lectures at the college, Pall Mall East S W 1, on Tuesday and Thursday, May 15 and 17 at 5 P M, on Chemical and Clinical Problems of the Adrenal Cortex

Royal College of Physicians of Edinburgh

Prof F H Smirk will deliver the George Alexander Gibson lecture to the college, 9, Queen Street, Edinburgh, 2, on Tuesday, May 8 at 5 30 P M His subject will be the Treatment of Hypertension

Royal College of Physicians of Ireland

On March 28 the following were admitted to the licence of medicine and midwifery of the college

R R Bazeley C J Curran Usha Devi Gautama P W A D Keating Margaret M Kelly O E McCutcheon Mary R. McLoughlin W M. Reid Harry Sternberg G R Withers

Faculty of Anaesthetists

The 8th anniversary dinner of the faculty was held at the Royal College of Surgeons of England on March 21 The Minister of Health Mr R H Turton, proposed The Faculty, and the dean Dr Frankis T Evans, replied The guests were welcomed by Dr Ronald Woolmer, director of the faculty s new research department and his toast was acknowledged by Mrs Pandit, High Commissioner for India, and by Lord Adrian, O M, F.R S

Transfusion and Hæmatology Congress

The International Society of Blood Transfusion and the International Society of Hematology will hold their congress in Boston between Aug 27 and Sept 5

Medical Artists' Association of Great Britain

Forms of application for the examination for membership of this association may be had from Miss Susan Robinson (medical artist), West Middlesex Hospital, Isleworth The last day for entries is Saturday, May 26

Medical Art Society

This society is holding an exhibition at Walker s Galleries, 118 New Bond Street, London W 1 Until April 21 it will be open from 10 A.M to 6 P M (Saturdays 10 A M to 1 P M)

International Association of Gerontology

This association is holding a congress at Merano, Italy, from July 14 to 19, 1957 In connection with the congress an international symposium will take place in Venice on July 20 and 21 on medico social aspects of senile nervous diseases. Further particulars of both meetings may be had from the secretariat, Viale Morgagni 85, Firenze, Italy

TABLE I—CLINICAL DETAILS

Case no	1	2	3	4
Age (yr)	4½	8	2½	9½
Sex	M	M	M	M
Duration of disease (mos)	4	56	3	24
Blood pressure (mm Hg)	110/75	120/70	100/70	120/80
Albuminuria (g daily)	1–4	1–2	1–2	1–4
Urine	Casts no blood cells	Occasional casts, no blood-cells	Occasional casts, epithelial cells	Occasional casts, no blood-cells
Degree of oedema	Severe + ascites	Severe + ascites	Severe + ascites	Severe + ascites
Dosage of prednisolone (mg daily)	60 × 5	60 × 10, 40 × 10 20 × 10, 10 × 10	60 × 10 40 × 10, 20 × 10, 10 × 10	60 × 10, 40 × 5 20 × 10 10
Weight before diuresis (lb)	40	72	29	67
Weight after diuresis (lb)	31	57	22	53
Time since diuresis (mos)	5	4	3	1

remain free from oedema sixty to a hundred and eighty days after diuresis

The serum-albumin level rose rapidly in all 4 cases (fig 2) During diuresis the serum-albumin level was below 1 g in all 4 patients, but the level rose rapidly thereafter The higher level has been sustained by each patient (table II), but in general the optimal electrophoretic pattern was reached at the end of prednisolone treatment, and somewhat lower levels persisted thereafter The gamma globulin level rose in each case during treatment and was sustained Blood cholesterol levels fell from above 260 mg to below 150 mg in all 4 patients and have remained within normal limits The nadir of weight loss having been passed, these patients gradually gained weight without any return of oedema, probably owing to eutrophy and protein anabolism

TABLE II—RESULTS OF INVESTIGATIONS

Case no	Date	Serum protein level (g per 100 ml)				Blood cholesterol (mg per 100 ml)	E S R (mm in 1 hr)
		Total	Albumin	α and β globulins	γ globulin		
1	Sept 28, 1955	4 2*	0 8*	3 4*	0 5*	358*	114*
	Oct 9, ,,	4 8	0 4	3 6	0 8	307	
	,, 13, ,,	4 5	0 7	3 4	0 4	219	
	21, ,,	5 9	1 4	3 8	0 6	183	42
	Nov 22, ,,	7 4	3 1	3 4	0 9	150	14
	Jan 3, 1956	8 3	3 6	3 2	1 5	140	15
2	Nov 8 1955	4 8*	0 6*	3 4*	0 8*	265*	46*
	,, 19, ,,	6 0	0 9	4 0	1 0	260	
	29, ,,	6 2	2 9	2 1	1 1	120	14
	Dec 9, ,,	7 2	2 8	2 8	1 6	100	16
	,, 19, ,,	7 4	3 4	2 0	2 0	100	10
	,, 29,	7 4	3 1	2 7	1 6	95	9
	Jan 30, 1956	6 2	2 7	2 2	1 3	91	7
	Feb 24, ,,	5 4	2 1	2 2	0 8	100	7
3	Nov 22, 1955	5 0*	0 6*	4 0*	0 3*	310*	116*
	Dec 1, ,,	5 7	0 6	4 1	1 0	280	43
	,, 12, ,,	6 8	2 9	3 3	0 6	165	15
	22,	6 9	3 0	2 7	1 3	127	4
	Jan 6 1956	7 1	2 8	3 0	1 3	100	2
	,, 26, ,,	6 7	3 1	2 3	1 3	103	6
	Feb 21 ,,	5 6	2 7	2 1	0 8	105	8
4	Feb 3, 1956	4 8*				407*	
	,, 10, ,,	4 6	0 7	3 3	0 6	230	41
	,, 17, ,,	6 1				176	
	,, 21,	5 7	2 6	2 4	0 7	90	16

* Level before prednisolone treatment

Discussion

Nephrosis is not rare, during the past eighteen years (1938–55) 120 children with nephrosis have been admitted to the Royal Hospital for Sick Children, Glasgow In a long-term follow up of 208 cases Barness et al (1950) found an eventual mortality of 50%, and this mortality has probably been little affected by modern treatment (Barnett et al 1952) In dealing with such a chronic and unpredictable disease it would be foolish to place reliance on a small number of cases treated for a short time Nevertheless the immediate results of prednisolone treatment are encouraging and significantly superior to those obtained with either corticotrophin or cortisone The fact that prednisolone consistently reduced th albuminuria, and caused diuresis and thereafter clinic and biochemical improvement in these patients sugge that it may prove to be valuable in therapy Th treatment is given orally is of great advantage in dealin with small children, particularly when oedema is presen

The general impression is gained (figs 1 and 2) th the patient receiving the longer courses of prednisolo improved more rapidly The mode of action of predn solone is not known, but it seems likely that albuminur is decreased either by a direct action on the nephron by the blocking or destruction of an extrarenal fact (such as an abnormal antigen antibody reaction) pr voking albuminuria It is unlikely that the action is o of simple blocking or antagonism, since the clinic improvement may take place after the hormone treatme has been stopped In addition it is possible that predn solone, which has no salt retaining activity (Bunim et a 1955), may depress the endogenous production of adren hormone and cause sodium and water diuresis resemblin a temporary " addisonian crisis " The improvement i case 2, who had had nephrosis for five years, was unex pected and the persistence of slight albuminuria w surprise

Too much attention has been paid to altering th oedema, the ascites, and the blood cholesterol and serum

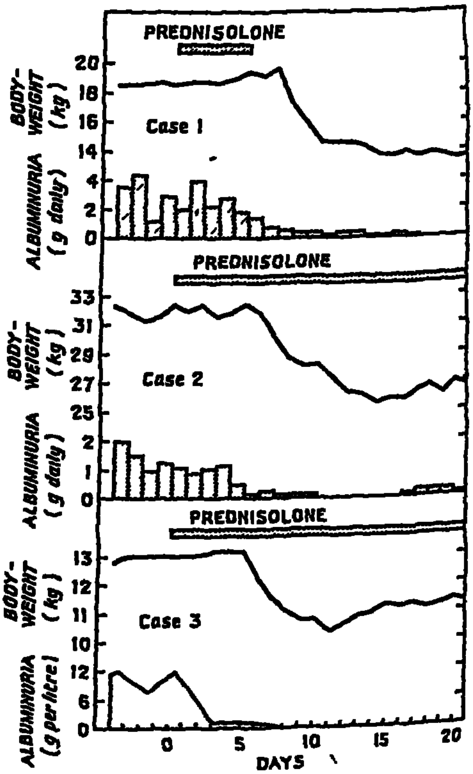


Fig 1—Relation of prednisolone treatment and albuminuria to loss of oedema and consequent loss of weight

PERFORATED ACUTE AND CHRONIC PEPTIC ULCER

CONSERVATIVE TREATMENT

HERMON TAYLOR
M A, M D, M Ch Camb, F R C S
SURGEON TO THE LONDON HOSPITAL AND KING GEORGE HOSPITAL, ILFORD

R P WARREN
M.B Lond, F R C S
LATE SURGICAL SENIOR REGISTRAR, LONDON HOSPITAL, AND KING GEORGE HOSPITAL, ILFORD

AFTER one of us reported 101 cases of perforated peptic ulcer treated conservatively at King George Hospital, Ilford (Hermon Taylor 1951), a further 99 patients (with 102 perforations) have been added to the total up to the end of 1954 We therefore had 200 cases in ten years, and the subsequent history of the majority of the survivors has been obtained

We review here the results, with special attention to the difference in behaviour between perforations of acute and of chronic ulcers, both immediately and with regard to the incidence of recurrent ulceration

Ten years ago the mortality of the aspiration method was lower than that of operative suture for which the figures at King George Hospital and elsewhere were rather unsatisfactory Since then the risk involved in surgical operations has become so small that the risk of death due to the operation itself, which the conservative method was designed to avoid, is no longer a factor in selecting treatment Indeed by 1951 the over all mortality of gastric aspiration in several hospitals was about equal to the best figures for operative suture (Hermon Taylor 1951)

The increasing safety of modern operations has led also to the practice of treating perforated ulcer cases by immediate partial gastrectomy This method averts not only the immediate complications of a sutured perforation but also the later ones from recurrence of the ulcer (Lowdon 1952, Noordijk 1953) But partial gastrectomy, though it has undoubted advantages in cases of chronic ulcers which have finally perforated, is an unnecessarily radical procedure for perforated acute ulcers, and these are generally still treated by simple suture

In our patients treated without operation, the distinction between acute and chronic ulcer at the time of admission has to be made entirely on the presence or absence of a history of dyspepsia On this criterion about a quarter of the perforations in our series have been of acute ulcers, and a clearcut difference has emerged between the results of treatment in the two groups In a word, *mortality, complications, and disability are confined almost entirely to the chronic ulcer group No patient with a perforated acute ulcer has died when treated by aspiration Only 1 has had a complication of any significance and nearly all have remained free of symptoms in the ten-year period of the trial*

Survey of Additional Cases

Errors

The serious consequences which theoretically might follow a mistaken diagnosis in a case of suspected perforated ulcer have been the focal point of opposition to the conservative method of treatment We have carefully collected all cases in which any error has been made, for however short a time

Errors have occurred in two directions (1) various other acute conditions have been diagnosed as perforations, and (2) perforations have been thought to be some other abdominal emergency

Under the first heading we have 2 cases of appendicitis and 2 cases of intestinal strangulation treated at the start by aspiration, but later by operation when the true diagnosis became clear the short delay did not prevent the full recovery of these patients 4 other patients were *not* operated on when the diagnosis was corrected Of these 4, 2 had biliary colic, 1 gastro enteritis, and 1 coronary thrombosis These patients may be said to have benefited from the conservative treatment of perforations adopted at the hospital In these 8 cases no harm has come to the patients The theoretical tragedies have not happened in practice

Under the second heading were 9 diagnoses—7 of acute appendicitis and 1 each of intestinal obstruction and perforated diverticulitis—in patients who actually had a perforated peptic ulcer They were all operated on because of the mistaken diagnosis, and 2 patients with widespread peritonitis died These 9 cases will not be included in the results tabulated here, which are those of conservative treatment only They are mentioned to complete the record of our fallibility

Mortality

93 patients were treated by gastric aspiration, with 11 deaths Of the 11 patients who died 7 were admitted moribund and could not be resuscitated, and the outcome was inevitable The 4 more debatable fatalities comprised 1 case of hæmatemesis followed by perforation 1 case *of severe bronchopneumonia with a per*foration and a small subphrenic abscess, 1 case of large subphrenic abscess, which perforated into the general peritoneal cavity, and 1 case of adrenal adenomata in a patient who was apparently convalescent but who collapsed after a simple operation to evacuate a collection of sterile fluid above the liver It is noteworthy that 10 of these 11 deaths were associated with chronic ulcers the 11th being a perforated carcinoma, none was a perforated acute ulcer The mortality is identical with that in the first 100 cases (Hermon Taylor 1951)

Complications During Treatment

Conservative treatment failed to seal the perforation in 5 cases and operation was undertaken for this reason, all 5 patients recovered Collections of peritoneal fluid were drained in 5 other cases, all during the second week after perforation This total of 10 intercurrent operations, compared with 12 such interventions in the first 100 cases, shows little change in this aspect of the treatment The important point is that in 21 of the 22 cases where operative interference was required, the perforations were of chronic ulcers An intercurrent operation was needed in only 1 case of perforated acute ulcer and that was for drainage of clear fluid from below the diaphragm on the twelfth day

Review of all Cases

In our cases, in the absence of any surgical exposure, the site of the ulcer is unknown at the time of perforation, but the history suggests whether it is acute or chronic Tables I and II, which have been drawn on this basis, show the results of treatment with regard to immediate mortality and to the incidence of recurrent ulceration in the survivors They do not include 4 cases of perforated carcinoma which occurred during the same period It will be seen (table I) that the mortality was nil in 47 patients who gave no history of previous dyspepsia

TABLE I—MORTALITY OF PEPTIC ULCER PERFORATIONS TREATED BY ASPIRATION OF STOMACH

—	Chronic ulcer	Acute ulcer
Total perforations *	143	47
Hospital deaths	20 (*14%*)	0
Survived	123 †	47

* Excluding (*a*) 4 perforations of carcinomas (2 deaths) (*b*) 9 cases treated by primary operation (3 deaths)

† 3 patients each had two perforations, patients in this group numbered 120

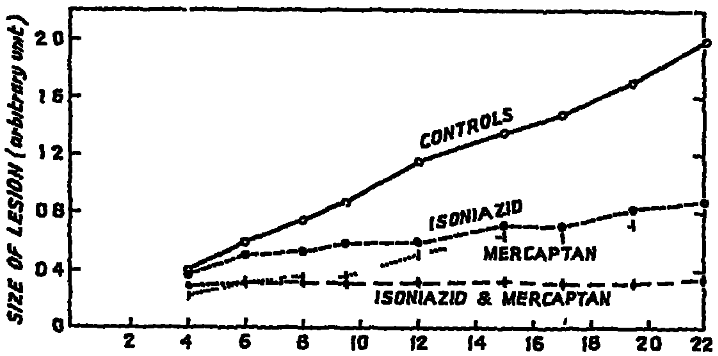


Fig 1—Development of corneal lesions in groups of mice under various types of treatment (experiment I)

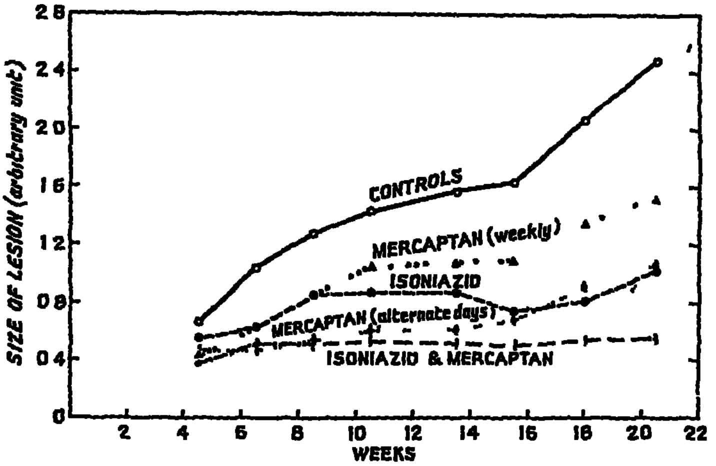


Fig 2—Development of corneal lesions in groups of mice under various types of treatment (experiment 2)

completely, because the true leprosy lesion became superimposed upon it after a latent period of 28–30 days Such a lesion first developed as a small dense focus in the area of the initial reaction, gradually progressed, became vascularised, and spread to involve more and more of the cornea Meanwhile its density further increased, and in 15 of 17 mice it spread to the sclera, which became thick and swollen

Treatment of the infected mice with the mercaptan, isoniazid, or a combination of the two resulted in lengthening of the latent period and slower development of the corneal lesions

The most striking effect was produced in experiment I *in the group of mice treated with isoniazid daily and the mercaptan every 2nd day* In this group no true lesions had developed in any of the mice up to 22 weeks after inoculation For this period only slight opacities equivalent to the initial reaction were seen in all the inoculated corneæ In the similarly treated group in experiment II, in which the mice received combined therapy of isoniazid daily and the mercaptan once a week, this complete suppression was *not* observed, yet the treatment was also strikingly effective Although true lesions developed in the cornea of all the mice and spread to the sclera in 7 of 8 mice they nevertheless remained small and progressed very slowly

In the two experiments 18 mice were treated with the mercaptan once every 2nd day In these mice there was significant delay in the development of the true lesions, which appeared after a latent period of $4^1/_2$–15 weeks They then progressed much more slowly than those of the controls, *but spread to the sclera in 15 of 17 surviving mice* (1 was killed for histology)

Administration of the drug once every week to 10 mice led to a short delay in the appearance of the true lesions, which progressed more rapidly (experiment II) than in the previous group and spread to the sclera in 9 mice

However, in comparing the activity of the mercaptan with that of isoniazid we found that the effect of isoniazid was similar to that of the mercaptan injected every 2nd day Although the lesions in the mice receiving the mercaptan every 2nd day progressed at first at a slower rate, at the 10th week in experiment I and the 14th week in experiment II they progressed more rapidly, and within about 2 weeks they were nearly as large as those in the isoniazid treated mice Since then there has been no difference in the progress of the lesions in the two groups The activity of the mercaptan injected once a week was less than that of isoniazid but still quite definite

Summary

The therapeutic effect of diethyldithiolisophthalate (compound 15688) alone and in combination with isoniazid on murine leprosy was studied in mice by the intracorneal technique

The most striking effect was obtained with the combined therapy of isoniazid daily and the mercaptan once every 2nd day, since no true lesions have developed up to the 22nd week after inoculation

Injection of the mercaptan alone once every 2nd day produced an effect similar to that obtained by the daily administration of isoniazid

We are greatly indebted to Dr G E Davies of Imperial Chemical Industries Ltd, for the supply of diethyldithiolisophthalate (compound 15688) used in this investigation, and to the Medical Research Council for defraying part of the expenses

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AFIBRINOGENÆMIA IN OBSTETRICS

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ASHTON, HYDE, AND GLOSSOP HOSPITAL GROUP

SERIOUS depletion of the blood *fibrinogen* was first described in this country as an obstetric complication by Barnett and Cussen (1954) and Barry et al (1955), and was discussed at the 14th British Congress of Obstetrics and Gynæcology (1955) This condition is therefore *sufficiently novel and imperfectly understood to justify* the publication of further cases

Case-reports

Case 1 —Gravida 4, aged 39, admitted as an emergency in December 1953, 36 weeks pregnant by dates, blood pressure 180 100 mm Hg, with a trace of albuminuria, uterus small for duration of pregnancy Four days after admission spontaneous labour produced, by normal delivery, a live baby weighing 3 lb 11 oz Shortly before this the patient had a rigor with a temperature of 102 F The placenta

placenta, when the risk of further hæmorrhage would be greatest fibrinogen should be given in relatively large dosage just before and after completion of the third stage In case 3 the view was taken that it might be better to give fibrinogen as soon as afibrinogenæmia was confirmed by laboratory examination, to forestall any further bleeding into the uterus or into the uterine muscle, which would lead to a "Couvelaire uterus", fibrinogen was also given at delivery

Serial estimations of plasma fibrinogen taken after the first injection of fibrinogen 0 3 g gave interesting evidence of the speed with which it takes effect (two minutes or less) and of the rate at which defibrinogenation took place (from a plasma fibrinogen level of 100 mg per 100 ml to one of 46 mg per 100 ml in about two hours)

Though case 2 lost only $1^1/_2$ pints of blood by concealed hæmorrhage, whereas case 3 lost 3 pints, case 2 very nearly died whereas case 3 never reached such a serious pass It would be unwise to link this to the timing of fibrinogen injection alone, since there was delay in induction of labour in case 2, and we agree with Barry et al (1955) that such delay is harmful

The adverse effect of dextran or other plasma substitutes, which has been emphasised by Scott (1955), was not a factor in these 2 cases, because the condition was present on admission before transfusion of any kind had been given

Conclusions

In afibrinogenæmia associated with accidental hæmorrhage Schneider's views of thromboplastin induced defibrinogenation of the blood seem acceptable, but the main site of deposition may be in the intra uterine clot

The advice of Barry et al (1955) to use double strength plasma in the milder cases and pure fibrinogen in the severe case, together with the need for delivery without avoidable delay, appears very sound Our experience resembles that of Barnett and Cussen (1954) in that the massive theoretical dosage of fibrinogen may not be necessary to control hæmorrhage It seems best to administer the fibrinogen in smaller divided doses, or by continuous drip, to keep pace with the defibrinogenation, and to supplement this with a further dose just before delivery

Summary

3 cases of afibrinogenæmia in obstetric patients are described

In case 1 the patient died, and necropsy showed wide spread hæmorrhages but no clear evidence of fibrin emboli

Cases 2 and 3 were associated with severe accidental hæmorrhage, both were treated with pure fibrinogen by different methods, the merits of which are discussed

In case 3 the effect of administering fibrinogen was assessed by serial estimations of plasma fibrinogen The intra-uterine blood clot contained 63 g of fibrin, and this high figure suggests that the bulk of the fibrin may be deposited in the uterus rather than in the vascular tree

We wish to thank Dr F Stratton, Director, Manchester Regional Blood Bank, for the provision of the fibrinogen used in these cases, and Dr John Kench, of the department of pathology in the University of Manchester, for much helpful information

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PREVALENCE OF CORONARY HEART-DISEASE IN ELDERLY COAL-WORKERS

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EVIDENCE is accumulating that coronary heart disease has become more prevalent in the past thirty years (Logan 1952, Ryle and Russell 1949) Some of the increase is more apparent than real, but the work of Morris (1951) leaves little doubt that the condition is commoner now than it was before the first world war The professional classes and sedentary workers are those mainly affected by the increase, and the prevalence is not generally thought to be high in miners

During the course of clinical studies of heart disease among miners and ex miners in East Glamorgan (Thomas 1956b) we have gained an impression, as have others before us (Cruickshank 1932, W E Hume cited by Cassidy 1946), that there is a high prevalence of coronary heart disease However, since the post mortem and clinical material on which such impressions have been gained may be biased by the method of selection, we have attempted to obtain a true estimate of prevalence by examining a representative sample of miners and ex-miners from a whole mining community of about 20,000 adults studied by Cochrane (1954)

We briefly describe the prevalence of coronary heart disease as shown by studies of hospital cases and necropsies, and, in greater detail, the results of the examination of a representative sample in the mining community

The phrase "coronary heart disease" is used to describe severe coronary artery disease of atherosclerotic origin, coronary thrombosis, myocardial infarction, and ischæmic heart disease due to chronic coronary insufficiency, when these conditions were of sufficient degree to produce heart disease detectable on clinical or post mortem examination

Prevalence in Hospital Cases and at Necropsy

In an analysis of 1000 necropsies on coal workers (James 1954) there were 244 cases of coronary heart disease Table I shows the age distribution of these cases

In at least two thirds of the cases (16%) the disease contributed to the cause of death

In 44 of an independent series of 134 cases of pneumoconiosis studied both clinically and at necropsy severe atheromatous lesions affecting a third or more of a major coronary vessel, myocardial infarction, or myocardial fibrosis were found at necropsy In 15 (11%) it contributed to the cause of death The condition was present in 37% of the 54 persons in the age group 55 64 and in 50% of the 26 persons aged 65 or more (table II)

Review of the clinical records suggested that an ante-mortem diagnosis was possible in 48% of these cases—i e, 16% of the total In the remaining 52% coronary heart disease was a silent condition (cf Boas and Boas 1949) This high prevalence of silent cases may have been due to the difficulty of diagnosing coronary heart disease in the presence of pulmonary disease Three factors—the character of chest pain, the presence of left ventricular enlargement without other cause, and the electrocardiographic findings—were therefore re examined with a view to improving the accuracy of diagnosis in these circumstances (Thomas 1956a) The findings suggested that

insufficient by themselves for the diagnosis of cardiac ischæmia in the presence of left ventricular hypertrophy *due to coexisting hypertension.* Left ventricular hypertrophy has been diagnosed by the criteria of Wilson et al. (1947) and of Sokolow and Lyon (1949).

Left ventricular enlargement and considerable left axis deviation, in the presence of massive pulmonary fibrosis calculated to produce a vertical heart with right preponderance, was ascribed to coronary heart disease where no other reason for enlargement of the left heart could be found.

RESULTS *

2 of the 55 men selected had died since the enumeration in the previous summer, one of pernicious anæmia and the other of heart failure and pneumoconiosis; they did not come to necropsy. 2 men had left the district, and 4 declined to participate; these 8 lapses had a mean age of 61·1 (range 56–64).

47 men, who form 85% of the original random sample (92% of those still living in the area), were examined (see table III).

Coronary Heart disease

18 cases of coronary heart disease were found, giving a prevalence of 38%. The mean age of these men (61·1), and the mean number of years they had worked underground (27, range 2–48) and at the coal face (12, range 0–37) did not differ significantly from those of the remaining men in the sample (60·6, 30, range 7–51 and 18, range 0–44, respectively).

Of the 18 men 10 considered themselves fit and were actively employed at the time of investigation. Of the remaining 8, 3 (nos. 3, 5, and 15) had taken up light jobs after episodes of heart failure or acute myocardial infarction, and 5 were out of work, of whom 2 (nos. 2 and 13) were in early heart failure, 2 (nos. 4 and 16) were convalescing from attacks of myocardial infarction, and 1 (no. 7) had lost an arm in an accident and was unemployed on this account. There was no material difference in mean age or mean systolic blood-pressure between the 7 men with and 11 men without disabling cardiac insufficiency. The disabled group was on average 14 lb. heavier, but the difference was not statistically significant (P≃0·3).

14 of the 18 cases of coronary heart disease were tentatively diagnosed as such by clinical and radiographic examination before recourse to electrocardiography. In 11 a provisional diagnosis was made.

4 of the 11 cases (nos. 4, 5, 15, and 16) gave a history indicating myocardial infarction; these and 4 others (nos. 1, 11, 13, and 14) gave a history of pain on effort typical of myocardial ischæmia. 1 man without pain (no. 2) had clinical heart block and left ventricular enlargement. 2 other men (nos. 17 and 18) *had radiographic evidence of left ventricular enlargement* for which no other cause could be found.

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* An appendix describing findings in the 24 cases referred to here by number may be had from the Pneumoconiosis Research Unit.

TABLE III—AGE, WEIGHT, BLOOD-PRESSURE, DIAGNOSIS, AND PHYSIOLOGICAL FINDINGS

No	Year of birth	Wt (lb.)	Clinical grade of dyspnœa	Blood-pressure (mm. Hg)		Disease of heart or circulation	Bronchitis	X-ray category of pneumoconiosis	Ballistocardiogram I–J deflection (arbitrary units)	M V V (indirect) (litres per min.)	Ventilation (litres per min.) B T P S		Blood lactic acid (mg. per 100 ml.)		Years at coal face	Years coal inde
				Systolic	Diastolic						Rest	Exercise	Rest	Exercise		
1	1891	182	1	180	85	C H D	No	1	25	99	8·1	22·8	8·7	10·8	19	19
2 S	1896	220	4	175	85	C H D	No	2		82					4	[illegible]
3 S	1895	120	3	170	100	C H D	No	P M F 3/C	8	13					37	[illegible]
4 S	1893	192	2	160	85	C H D	No	0	14	85					0	35
5 S	1892	220	1	165	90	C H D	No	0	10	120	10·7	25·0	13·6	26·0	5	9
6	1891	124	1	190	100	C H D	Yes	0	12	114	8·9	26·4	11·3	18·5	22	[illegible]
7 S	1896	161	1	225	110	C H D	No	0	10	71	10·7	25·0	11·8	22·2	14	13
8	1893	159	1	170	80	C H D	No	1	18	98	10·6	26·4	11·0	16·6	22	41
9 S	1892	189	1	158	100	C H D	Yes	0	13	91	16·8	27·4	13·9	13·7		[illegible]
10	1892	128	3	112	50	C H D A S	Yes	1	12	70	5·8	24·4	12·5	21·0	6	31
11	1897	138	2	130	85	C H D	No	P M F 3/C	11	82	6·9	19·7	11·7	26·5	26	46
12 S	1898	150	1	170	100	C H D	No	0	11	100	6·0	19·9	8·6	11·7	0	[illegible]
13	1890	121	3	250	125	C H D A S	Yes	3	30	40	11·2	*			11	36
14	1891	140	2	190	100	C H D	No	0	11	92	8·6	36·6	10·4	20·0		[illegible]
15	1891	154	3	125	75	C H D	No	0	17	70					6	[illegible]
16	1891	132	1	135	90	C H D A S	Yes	0	12	86						45
17	1896	126	2	130	75	C H D A S	No	0	4	100	10·3	41·3	11·5	23·8	21	43
18	1895	160	1	150	75	C H D	No	P M F 3/B	17	91	11·1	27·0	10·0	12·6	20	33
19	1901	129	3	170	90	A S	Yes	0	15	67	13·3	37·0	12·8	21·1		40
20	1893	165	3	150	90	A S	Yes	P M F 3/C	26	75	16·6	*			18	39
21	1892	121	1	210	95	A S	No	2	11	102	9·1	19·8	11·2	11·8	14	43
22	1893	124	4	110	70	I H D	No	P M F 3/D	19	30	6·5	31·1	17·7	41·0		47
23	1890	127	3	130	80	P H D	Yes	0	10	54	6·7	26·7	11·0	31·6	2	44
24 S	1893	102	4	150	80	I H D A S	Yes	0	10	28	8·0	32·1	8·9	20·4	15	[illegible]
25 S	1889	147	2	130	70		Yes	P M F 3/C	25	86	9·8	29·4	10·9	10·4	28	34
26	1896	140	4	125	75		Yes	P M F 2/D	29	73	22·1	*			6	16
27	1892	121	4	180	90		No	P M F 3/B	21	36	7·0	22·1	9·8	17·0	44	44
28	1897	132	2	145	90		No	2	26	76	12·9	26·8	13·4	12·7	16	31
29	1898	117	3	140	75		No	0	18	62	8·0	*			26	46
30	1889	164	3	130	90		No	2	8	67	14·2	29·3	13·3	14·1	19	51
31	1893	130	2	130	70		Yes	0	20	49	7·2	21·5	6·8	7·8		33
32	1889	126	2	130	80		No	P M F 2/B	12	65	8·4	25·6	12·4	10·8	13	43
33	1897	141	2	130	70		No	2	23	68	9·2	31·5	11·8	15·5	15	18
34	1891	138	1	120	70		No	2	11	65	10·2	26·0	12·1	16·5	26	33
35	1895	119	4	125	75		Yes	2	9	29	6·0	10·7†	11·7	13·4	14	45
36	1896	132	1				No	P M F 3/A	20	87	8·6	20·3	13·2	17·0	21	43
37	1891	105	2	160	110		No	0	10	74	9·2	22·0		20·8	7	7
38	1896	173	1	120	75		No	2	15	83	11·3	23·8	8·1	8·3	40	46
39	1892	157	1	150	90		No	1	13	111	11·0	25·0	10·4	20·9	16	16
40	1896	130	4	115	75		No	0	13	21	5·2	*			16	16
41 S	1895	114	1	150	90		Yes	1	16	77	10·4	28·6	10·0	15·7	20	30
42	1892	119	3	130	85		Yes	P M F 3/C	7	37	5·8	27·1	13·8	48·9	24	31
43	1891	112	2	170	90		No	2	8	75	4·3	21·5	11·6	18·2	28	33
44	1894	140	1	125	75		No	1	16	80	10·7	25·1	13·1	17·1	[illegible]	42
45	1895	112	2	110	75		Yes	0	11	41	17·0	28·3	11·2	15·3	10	39
46	1893	148	1	130	65		No	0	15	81	7·9	22·5	13·7	26·7	21	27
47	1894	159	1	120	70		No	2	27	84	11·6	11·6	12·2	35·1	11	12

* Gave up in 2nd minute of exercise.
† Gave up in 4th minute of exercise.

A S, generalised atherosclerosis.
B T P S, body temperature and pressure saturated.

C H D, coronary heart disease.
M V V, maximum ventilatory volume.
P H D, pulmonary heart disease.
P M F, progressive massive fibrosis of pneumoconiosis.
S, heavy smoker at some time (see text).

few weeks the diastolic pressure fell to 100–110 mm Hg, ut it rose later to 120 mm Hg

Nervous and tense patients have all experienced a ranquillising effect from serpasil, and in all cases the ulse-rate has decreased There seems to have been no ostural effect on the blood-pressure in patients taking erpasil only The interval between the start of treatment and significant improvement has been very varied—from two to twelve weeks—but it has usually been less than four weeks

We have been quite unable to forecast the probable effect on any patient before treatment was started, and are unable to correlate success or otherwise with ætiology, length of history, age, sex, or temperament Of the 17 patients who had good results with serpasil only, 3 had renal hypertension, and 1 had malignant essential hypertension Of the 9 who showed good results with serpasil added to pentolinium or hexamethonium, 1 had renal hypertension and 4 had malignant hypertension, 1 other had polyarteritis nodosa

Side effects were common, drowsiness and nasal stuffiness were experienced by over half the patients Diarrhœa occurred in 4 cases An unusual feature in 3 female patients was lactation

One is an unmarried woman, aged 29, who has never been pregnant Her breasts have enlarged and lactation has continued intermittently for six months, milk coming from both breasts at intervals of several days, unrelated to menstruation The quantity has not been recorded, but a 10 ml sample was obtained without difficulty, and was found to have the following composition total protein 2 8%, total fat 3 7%, lactose 6 5%, calcium 31 mg per 100 ml, phosphatase 11 5 King Armstrong units per 100 ml The protein content is higher than average but all figures are within accepted standards for normal human milk Microscopically the usual fat globules of various sizes were clearly visible This patient lives about 70 miles from Manchester and because of the difficulty of personally supervising her treatment she is not included in this series She has renal hypertension, the result of chronic type 1 nephritis, and her initial response to serpasil was excellent

The 2nd case is in a woman, aged 49, in whom swelling and tenderness of the breasts with secretion of small quantities of fluid occurred about a week before each of four menstrual periods The condition subsided and her periods ceased, presumably because of a natural menopause She has seven children

The 3rd case is in a woman, aged 38, who had continuous secretion for four weeks, unrelated to menstruation This ceased spontaneously although serpasil was continued She has one child, aged 10

We have had to stop treatment in 10 cases because of depression, one of these patients required admission for electroconvulsion therapy in a mental hospital, and one, we regret to report, committed suicide In nearly all these cases there was a history of previous instability One patient who was having injections of pentolinium and who was given serpasil developed moderately severe anginal pain at lunch time each day

We had had to reduce her dose of pentolinium gradually on account of hypotensive symptoms, and although she showed none of these symptoms at the time when angina developed, it was presumably caused by hypotension, as her blood pressure was found to drop from 190/130 mm Hg to 105/60 mm Hg on standing at midday Possibly she did not experience the usual symptoms of hypotension because she was seated on each occasion This patient's dosage of pentolinium had to be reduced by one third after the addition of serpasil

Illustrative cases —Figs 2 and 3 show the fall in blood-pressure in 2 successful cases, one patient receiving alternately serpasil and inert tablets, and the other patient having serpasil added to pentolinium treatment

Conclusions

As a result of this study of 54 patients treated with reserpine (serpasil), we conclude that the drug has a significant, and sometimes a profound, hypotensive effect in at least 40% of cases of severe hypertension, but it is obviously wasteful and useless to continue its administration in cases which do not respond

We have not been able to find any means by which the response may be foretold

In the most severe cases reserpine is probably better used in combination with other drugs

Reserpine is a dangerous drug The immediate side effects are not usually dramatic, but it may cause severe depression, and this led to suicide in one of our cases

Administration of reserpine to women occasionally results in lactation

We are grateful to Mr H Varley, biochemist to the Royal Infirmary, Manchester, for the milk analysis, to Mr J B Lloyd, chief pharmacist, and his staff for their coöperation in this investigation, and to Ciba Laboratories Ltd. for supplying inert tablets simulating 'Serpasil'

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PROGRESSIVE EXOPHTHALMOS TREATED BY ORBITAL DECOMPRESSION

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We describe here 30 cases of progressive exophthalmos treated by a type of orbital decompression not previously reported Other methods of treatment have lately been fully discussed elsewhere—notably by Naffziger (1954) and by Dobyns (1950)

Material

All 30 patients were treated in the department of neurological surgery of the General Hospital, Newcastle upon Tyne In 15 cases the disorder was unassociated with disease elsewhere in the body, and in the other 15 cases the patients had been treated for thyrotoxicosis

Progressive exophthalmos unassociated with disease elsewhere —The ages of the 15 patients (10 men, 5 women) in this group ranged from 28 to 71 years The disorder was unilateral in 12 cases and bilateral in 3 cases, and in each of these 3 cases bilateral decompression was carried out

Progressive exophthalmos associated with thyrotoxicosis —The ages of the 15 patients (7 men, 8 women) in this group ranged from 28 to 67 years In each of the 15 cases the disorder was bilateral, and in 9 bilateral decompression was carried out The disorder was related to previous treatment as follows first appeared after thyroidectomy, 3, increased after thyroidectomy, 6, first appeared after thiouracil, 1, increased after thiouracil, 3, improved after thiouracil, 1, increased after radioactive iodine, 1

All patients complained of pain in the orbit, this varied from a feeling of "grittiness" and irritation in the milder cases to very severe discomfort in the most severe In every case there was some ophthalmoplegia, but in 6 this was severe and was associated with diplopia. Corneal ulceration necessitated bilateral tarsorrhaphy in 2 cases and unilateral tarsorrhaphy in 3 cases

The Operation

After the scalp has been shaved and prepared the patient is placed on the operating table in the supine position The

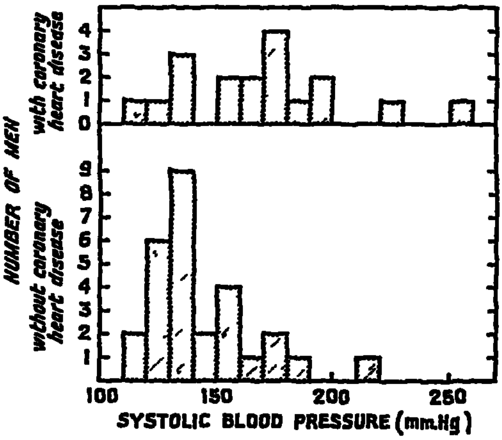

Fig 2—Distributions of systolic blood-pressure in men with and without coronary heart-disease

Of the 3 remaining men in whom coronary heart-disease was suspected on clinical or radiographic grounds 1 (no 9) had left ventricular enlargement and developed a paroxysm of auricular tachycardia on exercise, 1 (no 3) was in heart failure of recent origin and had radiographic evidence of left ventricular enlargement in the presence of massive pulmonary fibrosis, and 1 (no 1) had a moderate apical systolic murmur

4 men (nos 6, 7, 8, and 12) had no symptoms and no clinical signs of heart disease 1 of these men (no 6) did give a history of six months' illness two years previously, which may have been cardiac

Electrocardiograms proved, in our opinion, coronary heart disease in 17 men and strongly suggested it in 1 other (no 18), who had complicated pneumoconiosis with left ventricular enlargement but normal blood pressure

The commonest electrocardiographic pattern was that of left axis deviation with depression or deformity of the ST segment in leads I, II, VL, V_4, and V_6, with flat or inverted T waves in some of these leads

The electrocardiographic identification of possible coronary heart disease in the presence of gross signs of left ventricular hypertrophy presented a diagnostic problem in the case of 1 man (no 13) who had severe angina of effort Here a steep downward inclination of the ST segment in V_4 with no T wave was considered to clinch the diagnosis (cf Holzmann 1952)

In another case with pain on effort typical of cardiac ischæmia (no 10) some aortic stenosis was also present The blood pressure was 112/50 mm Hg, peripheral pulsation was good, and the electrocardiogram showed signs of cardiac ischæmia without left ventricular hypertrophy Coronary heart disease was considered the principal lesion This man died ten months after the survey, and necropsy revealed coronary thrombosis associated with severe atherosclerosis

The detailed electrocardiographic findings are shown in fig 1

Atherosclerosis

Generalised atherosclerosis of considerable degree was present in 4 of the 18 men who had coronary heart disease (nos 10, 13, 16, and 17) and in 4 other men who did not show electrocardiographic changes of myocardial ischæmia

In addition to greatly thickened and tortuous peripheral arteries, unfolded aorta, and irregular narrowing of the retinal arteries, 1 of these 4 men (no 19) had intermittent claudication and evidence of a previous cerebral thrombosis, 1 (no 20), who also had massive pulmonary fibrosis was orthopnœic had attacks of giddiness, and was in early congestive heart-failure, 1 (no 21) was hypertensive (blood-pressure 210/95 mm Hg) but had little subjective disability, and 1 (no 24) had pulmonary heart-disease

Coronary Heart disease, Blood pressure, and Body w

The mean blood-pressure recorded lying down w 150 0/84 1 mm Hg for all the men (average age 6 This agrees well with the values of 145/85 and 14 mm Hg reported for men of the same mean age b Hamilton et al (1954) and Miall and Oldham (195

The mean blood-pressure was 165 8/89 4 mm Hg f the 18 men with coronary heart disease and 139 mm Hg for the remainder The two groups were exactly comparable ages, and the 26 4 and 8 7 mm H mean differences in systolic and diastolic blood pressu are statistically significant (0 01>P>0 001 and 0 05> P>0 02 respectively) (fig 2)

The average body-weight of the men with corona heart-disease was 156 9 lb (range 120–220 lb) and f those without 133 8 lb (range 102–173 lb) The variatio in body-weight was significantly greater in the men with coronary heart disease (P<0 02) Thus the significan of the higher average is uncertain, though it appears reach the 5% level (fig 3) Coronary heart disease w present in 13 of the 22 men with systolic pressures 150 mm Hg or above, and in the 5 men whose bod weight exceeded 13 st, which was 40 lb more than mean weight for the whole group The systolic blo pressure ranged from 158 to 180 mm Hg in the men, but this is likely to be an overestimate of the t pressures because no allowance was made for arm g (cf Ragan and Bordley 1941)

Pulmonary Heart disease

Pulmonary heart disease was diagnosed on the elect cardiographic findings in 3 men 1 (no 22), who h worked underground for 28 years, had progressive m sive fibrosis and an unproductive winter cough with acute exacerbation The 2 others, neither of wh had pneumoconiosis, gave a history typical of chro bronchitis, one of these (no 24) had worked 11 ye as a collier and the other (no 23) 44 years as a repai underground

Ballistocardiography

The average amplitude of the I–J wave of the ballist cardiogram was obtained over the first 5–6 cardiac cycl after the start of breath-holding with the chest the inspiratory position Satisfactory measuremen were obtained in all except 1 man (no 2) with coron heart disease and heart-block, whose tracings were ve abnormal The mean value for the ballistic impulse w 13 5 (range 30–4) arbitrary units for the cases w coronary or pulmonary heart disease and 16 3 (ran 29–8) units for the remainder This difference is statistically significant (0 10<P<0 20) If, however, men with significant associated pulmonary disease excluded, the mean ballistic impulse of those remaini with coronary heart disease was 12 9 (range 4–25) un compared with 17 7 (range 8–29) units in those witho This difference, which is significant at the 5% level

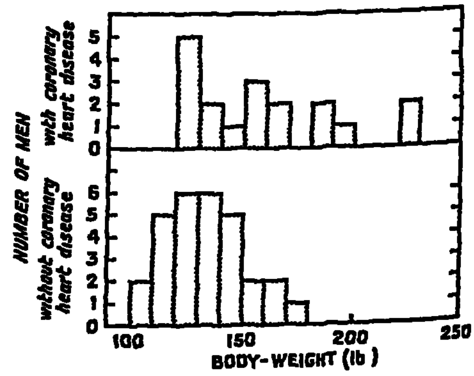

Fig 3—Distribution of body weight in men with and without coron heart-disease.

robably an increase in orbital fat, that the muscles are rge and infiltrated by lymphocytes, and that in the later tages in untreated cases the muscles may be replaced by brous tissue

Discussion

-Etiology

In some of our cases treatment of thyrotoxicosis had een followed by onset or exacerbation of exophthalmos The *general consensus of opinion* seems to be that an nterior-pituitary-gland hormone is responsible for the evelopment of the condition Experimentally this has een shown to be the case in many animals, Friedgood, or example, has demonstrated that in guineapigs nterior-pituitary extract will produce thyrotoxicosis and xophthalmos initially, and that after two to three weeks, lthough the thyrotoxicosis wanes, the exophthalmos continues to increase (Friedgood 1934) Dobyns and Wilson (1954) have demonstrated the presence of "exophthalmos-producing substance" in the serum of patients with progressive exophthalmos

-Treatment

All our cases were referred by physicians or ophthalmologists either because they felt that methods of treatment other than orbital decompression were unlikely to help or because other methods had been tried without success The condition is in many cases self-limiting and can be subject to remarkable remissions Our cases, however, were all truly "progressive"

The medical treatment of this disorder consists in measures to inhibit the secretion of thyrotrophic hormone by the pituitary gland Despite the theoretical basis for administration of thyroid gland, results seem to be poor Friedgood (1941) describes them as "notoriously unsatisfactory," and Dobyns (1950) has come to the same conclusion Russell Brain (1952), reviewing 150 cases, stated that 45% were unchanged by medical treatment and 15% were exacerbated Œstrogens and *p*-hydroxypropiophenone (H365) have also been tried (Okie et al 1952) The effects of cortisone and corticotrophin in the control of progressive exophthalmos appear to be disappointing (Medical Research Council 1955)

Radiotherapy applied to the pituitary gland is credited with some successes (Dobyns 1950), but in our opinion it is not justifiable to submit the pituitary gland and neighbouring structures, in particular the hypothalamus, to the effects of X-irradiation for this condition Orbital irradiation seems to be more successful in the non-thyrotoxic group (Jones 1951)

Laurent and Scopes (1955) have reported 1 case treated successfully by subconjunctival injection of hyaluronidase This method clearly needs further trial

The discovery of some reliable method of endocrine control may not be long delayed, but at present it seems that the only method of treatment that can be relied on to give consistently good results is adequate surgical decompression Most surgeons still use the operation described by Naffziger in 1931

Thus entails raising a coronal scalp flap and one or two frontal bone flaps, after elevation of the dura mater, the roof and lateral wall of the affected orbit or orbits are removed from above This operation has been extended by Poppen (1950) to include removal of the walls of the frontal and ethmoidal air sinuses

Dickson Wright (1948) has described a direct approach to the orbit, using an incision across the forehead and *temporal fossa*

We believe that the operation here described fulfils the need for adequate decompression while observing cosmetic considerations, furthermore, it is simple to perform

The indications for operation that we follow are severe exophthalmos unresponsive to medical treatment, threatened or actual corneal damage, pain, chemosis, papillœdema, and ophthalmoplegia causing diplopia

Because the results of decompression have proved so satisfactory, we enter a plea that patients should be referred before the cornea is damaged and before irreversible changes have taken place in the optic discs, extrinsic ocular muscles, or conjunctiva

Summary

An operation for orbital decompression in patients with progressive exophthalmos is described, and the results in 30 consecutive cases are reported The operation and pathological findings are analysed

We wish to thank our medical and ophthalmological colleagues for referring the patients to us, Mr J M L Howat for his help in the management of our patients, and Miss M E Bousfield for assistance

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INTERSTITIAL EMPHYSEMA, PNEUMOTHORAX, AND "AIR-BLOCK" IN THE NEWBORN

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INTERSTITIAL emphysema of the lung and mediastinum presents in the first few weeks of life in three fairly definite clinical categories

(1) The first group of cases appears to be the direct consequence of violent artificial respiration directly after birth Resuscitative emphysema occurs in asphyxiated infants and is often only a terminal event due to "heroic" attempts to maintain life Such infants are extremely ill from birth

(2) A second and well recognised group occurs in infants who have infection, often staphylococcal, of the respiratory tract In our experience these infants are all over the age of 6 days at the time of death and have various associated pulmonary conditions—e g, "bronchiectasis," pneumatoceles, and recurrent tension pneumothorax

(3) The third group is in several respects quite different from the others Interstitial air arises spontaneously without artificial respiration in infants that have been lusty at birth It occurs within a few hours or days after birth and is often rapidly fatal

This last group is the subject of this study The purpose of this paper is to demonstrate the incidence, the clinical features, and the apparent cause of this condition

Present Study

14 cases of interstitial emphysema of the lung and mediastinum, with death apparently due to air-block, were seen in the necropsies that I have done in the last five years Until 1954 the necropsies were almost entirely from a highly selected group of teaching hospital admissions, so the numbers gave little idea of the over-all prevalence of the disease Since 1954 the infants coming to necropsy have comprised the majority of deaths in Sheffield in this age group Thus the recent cases provide a guide to prevalence

Prevalence

Of the last 100 necropsies that I have done in 1954–55 in Sheffield on infants dying within 7 days of birth 48

STRESS FRACTURE OF RIBS IN PREGNANCY

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FRACTURE of a rib due to coughing was first described by Graves (1833) Since then 144 cases have been reported (Malgaine 1859, Gurlt 1862, Tunis 1890, Bähr 1894, Seilin 1917, Popischill 1921, Kleiner 1924, Halliwell 1929) Webb and Gilbert (1923), Palfrey (1924), and Swineford and McKinnon (1945) emphasised that these fractures might easily be missed and that they were far commoner than was generally supposed The great majority of reported cases were in patients with pulmonary tuberculosis (Oechsli 1936, Richardson 1936, Sakka 1938, Cohen 1949), but Mitchell (1951) reported that of 720 non tuberculous patients referred to him on account of chest symptoms 106 had pleural pain, and of these 14 had stress fractures of ribs

There are 13 recorded cases of stress fracture of the ribs in pregnancy In only 1 of these cases did the fracture occur in labour, and in this instance the fracture was due, not to the patient's expulsion efforts, but to a fit of coughing (Ahern 1894) In all cases the fracture occurred in the last months of pregnancy and in the present series all had fractures after the 36th week

In the 4 cases described by Paulley et al (1949) serum calcium and phosphorus levels were within normal limits

Case-reports

The 3 cases reported here attended Queen Charlotte's Maternity Hospital in the first two months of 1953

Case 14 —Multigravida (one previous normal pregnancy), aged 30 years At the 37th week of pregnancy the patient had an irritating, unproductive cough During a particul severe bout of coughing she felt a sudden snap in the low part of her left chest, and this pain persisted and was ag vated by coughing Radiographic examination revealed a transverse fracture of the shaft of the 11th rib at the junct of its middle and outer thirds

Case 15 —Primigravida, aged 33 years At the 42nd week of pregnancy the patient was sitting in a chair when she tur and coughed She felt a click in the right side of her ch and this was followed by a persistent pain Radiograph examination showed a transverse fracture of the shaft of th 11th rib at the junction of its middle and outer third

Case 16 —Primigravida, aged 30 years At the 36th week pregnancy a pain developed gradually in the left side of th patient's chest This was not initiated by coughing but wa aggravated by coughing and deep breathing The p gradually subsided in the following 3 weeks At the 3 week of pregnancy the patient felt a similar pain on the ri side, and again this was not initiated by coughing Rad graphic examination revealed a fracture of the shaft of 6th right rib, with minimal disalignment in the ant axillary line, and, immediately below it, a greenstick fract of the 7th right rib On the left side there were fracture *longer standing involving the left 6th and 7th ribs in* anterior axillary line, with slight callus formation

Discussion

More than a century ago Hilton (1852) taught th a rib fracture might give rise to pain indistinguishabl from that of pleurisy This erroneous diagnosi strengthened by the absence of displacement of fragments on physical or radiographic examinati

REPORTS OF STRESS FRACTURES OF RIBS IN PREGNANC

Source	Case no	Age (yr)	Parity	Duration of pregnancy	Site of fracture	Onset
Hérard (1855)	1	22		7th month	Lt 11	Cough fo months
Benoit (Bähr 1894)	2			9th month	Lt 9	Coughin chron br
Chonery (Bähr 1894)	3	23		?		Coughing
Dogadkin (1885)	4	27	Multip	9th month	Lt 8	Cough
Ahern (1894)	5			In labour	Lt 6	Coughing
Blanc (1908)	6			End of pregnancy	Multiple	Coughing
Paulley et al (1949)	7	21	Primip	36 weeks	Lt 10	Coughing chro bronch
	8	25	Multip	38 weeks	Lt 9 and 10	Coughi mildly
	9	36	Multip	40 weeks	Lt 11	Lifting coughi
	10	25	Primip	39 weeks	Lt 11	Coughi aft previ chokin
Evans (1949)	11	Late 20's	Multip	8th month	8 and 9	Coughing
Baar (1949)	12	26	Primip	37 weeks	Lt 11	Sharp
Marsh (1953)	13	31	Primip	34 weeks 36 weeks	Lt 8 Lt 10	Lifting *Lifting*
	,,	33	Multip (same case)	35 weeks	Lt 9	Sudden p on lifti
Present study	14	30	Multip	37 weeks	Lt 11	Severe b of cou ing snap
	15	33	Primip	42 weeks	Rt 11	Mild cou felt click
	16	30	Primip	36 weeks	Lt 6 and 7	No cou gradu onset
				38 weeks	Rt 6 and 7	No cou gradu onset

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coming from the nose. She called the midwife, who called he doctor, who ordered its immediate removal to hospital. The infant died in the ambulance aged about 14 hours.

Case 5.—The following is the letter that the family doctor sent with the child when the child was brought in for necropsy. "The child (a boy) was postmature and born at 4 P.M. The confinement was normal. There was a lot of meconium in the amniotic fluid. He recovered reasonably quickly and cried normally. Birth weight $8^1/_2$ lb. He appeared well at 10 A.M. today, but at 11 A.M. the midwife noticed that he was a little cyanosed. This cyanosis was when he cried. I was called to see him at noon, and again at 12.45 P.M., when arrangements were made to admit the child to the Children's Hospital." The infant died before it could be admitted, at about 1.20 P.M., aged $21^1/_2$ hours.

These histories illustrate the features of the whole series. All the infants were mature or postmature. In 7 there was a spontaneous remark on the presence of an abnormal amount of mucus or meconium on the face of the infant. Only 1 of the infants had "asphyxia" at birth. All cried spontaneously and did not require artificial respiration. 5 of the cases came to me by way of the coroner but many of the others could well have come the same way but for the enlightened outlook of the local coroner.

Pneumothorax was present in 11 of 13 in this series in whom the chest was opened under saline—on the left side in 10, and on both sides in 5.

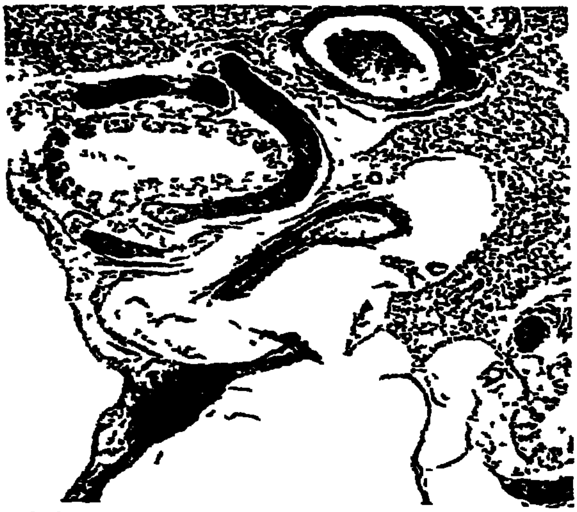


Fig 3—Low-power view of lung showing interstitial air compressing a vessel near a bronchus.

The ages of the infants at death were 4–49 hours. 2 had shown no abnormal symptoms and were simply found dead. The others had symptoms lasting from about half an hour to twenty-four hours consisting either of cyanosis or of a notable alteration in the character of respiration.

Pathology

The trachea and main bronchi in these cases did not appear to be obstructed.

The air vesicles in the interstitial tissue of the lung were larger as the hilum was approached, those at the hilum and junction of the lung and mediastinum often forming a sort of tense collar round the root of the lung (fig 1).

After fixation, the presence of air surrounding the vessels in their sheaths was usually obvious to the naked eye (fig 2) and more easily seen in sections (fig 3).

Microscopy revealed the presence of masses of mucus usually containing either whorled plugs of keratinised squames (fig 4) or small sheets of similar squames in the smaller bronchi and bronchioles. These keratinised non-nucleated squames are the cells found in vernix. Beyond many such masses of mucus small areas of dilated alveoli were often found (fig 5), and in some cases actual points of rupture of such acini into the connective tissue could be seen (fig 6).

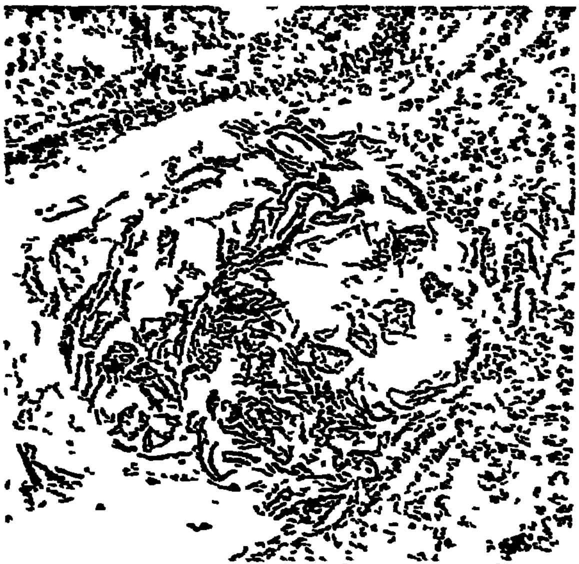


Fig 4—Bronchiole obstructed by non-nucleated keratinised squames—i.e., a mass of vernix.

No air-embolism was seen in this series of infants, and in no case was pneumonia or infection of the respiratory tract found.

None of these infants showed any developmental abnormality of the respiratory tract and mediastinum, and no pathological lesions were found outside the chest. The right hearts in the infants appeared to be unusually distended, but no significant enlargement of the liver was noted.

The immediate cause of death in all these infants was air in the pleural cavity and mediastinum with apparent compression of the vessels at the roots of the lungs, producing "air-block." The interstitial emphysema in all the cases appeared to be due to mucus, with amniotic debris and vernix, causing differing degrees of obstruction in the smaller air-passages of the lungs.

DISCUSSION

Prevalence

The recorded incidence of interstitial air in the chest in normal infants varies. Davis and Stevens (1930)

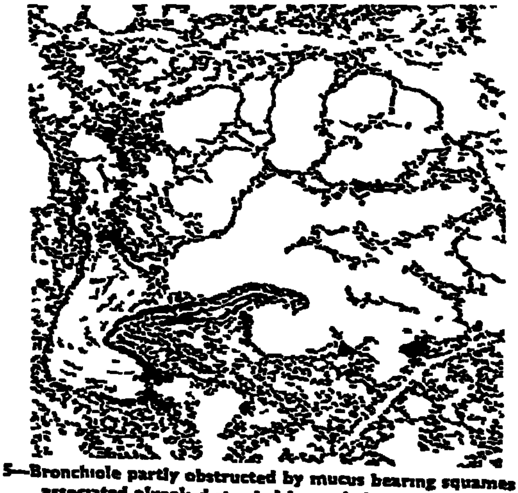
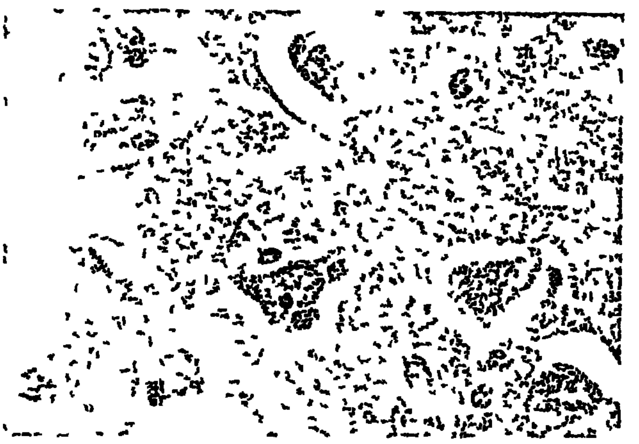


Fig 5—Bronchiole partly obstructed by mucus bearing squames, and associated alveoli distended beyond the obstruction.



Section of brain containing Negri bodies (×275)

for an hour or two He was seen again at 6 P M, when he was sitting up in bed eating an orange with some difficulty He complained of some tingling in the right arm for the last three or four days, and there was wasting of the interossei in the first and fourth spaces of the right hand Both arms appeared wasted compared to their condition a year ago, and the grip although equal, was not that expected in a man of his occupation Tuinal gr 3 was given for the night At 9 45 P M his father in law telephoned to say that the patient was as bad as ever, wandering in speech, restless, and frightening his wife

On re examination he was restless, with a tendency to dyspnœa He became calm when questioned, and admitted that he had been bitten by his dog while in Pakistan, where rabies is endemic It was only a scratch on his right forearm, and the dog died next day with fits His mates said it died of distemper Pressed to remember when he was bitten he said finally that it must have been at the end of February or the beginning of March Rabies was diagnosed and the patient was admitted to hospital that night

On admission there was slight weakness of his right arm, and the circumference of the right forearm was $^1/_2$ inch less than that of the left forearm His temperature was 100 2°F, pulse rate 120, and respirations 22 a minute He refused a glass of water vigorously but was not at all upset when the water taps were turned on Rabies was provisionally diagnosed, and intramuscular penicillin 500,000 units and phenobarbitone gr 3 were given

Investigations —On May 10 chest radiography showed that the lung fields were clear A blood count showed Hb 120%, white cells 22,100 per c mm (polymorphs 79%, lymphocytes 15%, monocytes 6%) No tubercle bacilli were seen in the sputum Lumbar puncture was not done

Treatment and Course —Intramuscular phenobarbitone gr 3 was given six-hourly The patient's general condition seemed a little improved, and the attacks of breathlessness, in which he threw back his head, jerked an arm, and complained that he could not breathe, decreased He stated that "belching wind" warded off attacks He refused fluids vigorously On May 11 he ate sections of orange, had one or two teaspoonfuls of tea, and was given a rectal saline drip Rhonchi and râles were present at both bases He was very loquacious A barium swallow was attempted, but he rejected the barium mixture His temperature was 99°F On May 12 he was mentally confused and still had spasms in which he complained that he could not breathe His temperature was 101°F At 5 P M he became more disoriented and restless He was given intramuscular paraldehyde 8 ml At 10 P M he became much more restless and was given another dose of intramuscular paraldehyde 8 ml His temperature had risen to 102°F At 1 20 A M on May 13 he became irrational, noisy, and abusive, and was given intramuscular paraldehyde 10 ml and intramuscular chlorpromazine 50 mg with effect The rectal drip was continued His general condition deteriorated, and he died at 5 A M

Necropsy Findings —Good physique, no scar on right forearm or elsewhere *Heart* myocardium pale and cloudy, a few petechial hæmorrhages beneath the visceral pericardium on the posterior aspect of the left ventricle *Larynx, trachea,* and *bronchi* contained much mucopus *Lungs* much co gestion *Mouth, pharynx,* and *œsophagus* normal L congested and swollen *Brain* congested, with scat petechial hæmorrhages *Spinal cord* not examined Portio of the right hippocampus and the right submaxillary g were fixed in formol saline solution, and other pieces w frozen in 50% glycerin The Group Laboratory report that sections of brain showed the perivascular lympho c collections of encephalitis with, in the hippocampus n the Negri bodies of rabies (see figure) The Central Pu Health Laboratory, Colindale, reported that sections of bra direct smear, Seller's stain, contained scanty Negri bodi The specimen fixed in formol saline solution appeared to b mainly white cortex, and sections of it showed no obvi abnormality The virus of rabies was isolated by inoculati of mice No Negri bodies were seen in the salivary gla but the rabies virus was isolated by inoculation of mice

Contacts

The case was notified to the Medical Officer of Heal the day after admission to hospital On his advice, a immediately the diagnosis was confirmed, the patient wife and child were given a light course of anti rab vaccine, because there is believed to be a slight risk infection by kissing The vaccine was supplied by th Lister Institute Daily injections of 2–4 ml into th abdominal wall were given for fifteen days, and n reaction was suffered by either patient Nine mont after contact both are well

One dog and three cats, pets in the household, we destroyed, two dogs were put into quarantine, and a now freed.

Discussion

Rabies is a disease of dogs, jackals, wolves, a vampire bats in Trinidad, transmitted to other mammal including man, by bites from infected animals T disease is ordinarily non existent in the United Kingdo having been eradicated originally by muzzling orders a subsequently by strict quarantine of dogs entering t country The cause is a neurotropic virus with a incubation period of from ten days to a year—usual not more than five months, and commonly from one t three months This variation is said to depend on bot the situation of the bite and the dose of virus inoculated A fresh abrasion licked by a rabid animal can b dangerous, and intact mucosa can transmit rabies

The virus spreads along the nerves from the site inoculation, hence bites on the face and hands, w rich in nerves and usually uncovered, are particula dangerous From the spinal cord the virus spreads bo distally and to the higher centres, hence all the nerv tissue in the body may be infected Infection reac the salivary glands along the nerves and not thro the blood-vessels

The necropsy findings are those of encephalitis, a the only typical laboratory findings are Negri bodies the nervous tissue on section and reproduction of t disease in animals by inoculation of infected tissue

The established disease falls into three phases

(1) The prodromal state, lasting from two to three da with malaise, fever, irritability, loss of appetite, and pa irritation at the site of the bite

(2) The stage of excitement, lasting from two to three da with difficulty in swallowing fluids, alternate rational a irrational periods, severe muscular spasm particularly affect the muscles of the pharynx and larynx, and an undue s ceptibility to stimuli—e g, noise and draughts Heavin on the chest, difficulty in breathing, and hydrophobia manifestations of the muscular spasm

(3) The paralytic stage, lasting about twenty four hour less, leads to death The patient commonly remains clea his mind until near the end

The paralytic type of disease ("dumb rabies") is ra There is no excitement, and the course is usually lon than that of the "furious" type follows infection of the lung in the newborn" Much misconception has been due to the attempt to consider immature, mature, and postmature infants as a single entity

DeCosta (1940) distinguished two types of pneumothorax in the newborn One, "pneumothorax abrupta," occurred at birth in debilitated infants and had a 42% mortality, and a second, "pneumothorax lenta," occurred hours or days after birth Of the 34 infants with the latter type of pneumothorax that he could find reported 2 had received artificial respiration Though he did consider that mucus, vernix, and coughing were important, he discussed also congenital deformity of the lung, trauma, and infection

Rothman (1937) described 2 cases in this country and considered that enlargement of the thymus, collapse of the epiglottis, and congenital pulmonary defects were of more importance than obstruction of the respiratory tract by inhaled material The reason for his inclusion of multiple defects appears to be that many cases of inspiratory obstruction accompanied by the most laboured inspiratory efforts do not produce emphysema or pneumothorax This view is based upon a misconception that interstitial emphysema is due to excessive inspiratory efforts, it not being generally realised that it is only by increased expiratory effort that air can be spontaneously expelled into the connective tissue

Prevention

The shortness of histories and the present poorly studied symptoms of the newborn suggest that interstitial emphysema will remain either a post mortem or radiological diagnosis for a little while Furthermore, the bronchi and bronchioles that are obstructed and responsible for the interstitial emphysema are, by the time the lesion has developed, too small to permit surgical aspiration Thus the clinical approach must be entirely towards prevention

Since amniotic debris and mucus were inhaled in all the cases, the clinical problem lies in dealing with a child showing meconium or excess mucus on the face and in the upper respiratory tract

There is a tendency to think that careful and complete removal of mucus is of major importance only in a weak immature infant, yet it seems that mucus can be, if anything, more dangerous in a mature child who cried lustily soon after birth It is possible that respiratory stimulation and enthusiastic methods to make a child give a "good yell" as soon as possible after birth are sometimes misplaced A mature child can probably withstand small areas of atelectasis better than it can interstitial emphysema

Summary

Clinical and pathological data are presented of 14 infants who died as a result of spontaneous interstitial emphysema of the lung and mediastinum within the first 6 days after birth

This condition appears to be due to excessive expiratory effort following inhalation of meconium or mucus

In a recent necropsy series this condition was apparently the commonest single cause of death in normally formed mature and postmature infants

It is a pleasure to acknowledge the coöperation of Dr T Colver Dr L P DeAbrew, Dr K F Garside, Dr R R Gordon, Prof R S Illingworth, Dr E Miller, Dr A J N Warrack, and Dr J D Young

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TREATMENT OF NEPHROSIS WITH PREDNISOLONE

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THE treatment of nephrosis is unsatisfactory Cation-exchange resins (McChesney et al 1951), artificial infection with malaria (Gairdner and Shute 1955), and hormones such as cortisone and corticotrophin (Arneil and Wilson 1952, 1953) have proved of limited value All these treatments can provoke diuresis on occasion but fail to reduce the albuminuria consistently The results of cortisone and corticotrophin treatment are confused by the retention of sodium during treatment and the loss of sodium when the treatment is stopped, since such electrolyte fluctuations materially alter the degree of œdema

With the advent of 'Deltacortril' (prednisolone) a synthetic hormone with a cortisone like action but little or no sodium-retaining property (Bunim et al 1955), it seemed possible that a potentially useful form of treatment was to hand Accordingly this substance was used to treat 4 œdematous patients with nephrosis at this hospital

Methods and Material

Albuminuria—The urine passed in every twenty four hours was collected and the absolute loss of albumin calculated by the Esbach method

Serum proteins—Total serum-proteins were estimated, and electrophoretic fractionation was done by a modification of the method described by Cremer and Tiselius (1950) Readings were made with a scanner of the 'EEL' type

Blood cholesterol Level—This was estimated by the method described by Dutton (1932)

Erythrocyte sedimentation Rate (E S R)—The standard Wintrobe method was used

Diet—The patients were allowed the normal ward diet but with the sodium content restricted to less than 2 g daily No additional potassium was given

Details of the 4 patients are given in table I The history, clinical findings and biochemistry (table II) were typical of nephrosis in each case

Results

Within six days of the start of treatment the albuminuria decreased strikingly in all 4 cases The daily loss of albumin decreased from 1–4 g to less than 0 25 g in each patient two weeks after the start of treatment Albuminuria disappeared completely in cases 1, 3, and 4 but reappeared (for a few days only) in case 3 six weeks after treatment had stopped The relationship of the alteration in albuminuria to the start of treatment and to the onset of diuresis for the 3 cases in which complete records were obtained is shown in fig 1 In all 4 patients diuresis began within eight days of the start of treatment and lasted from six to eight days During diuresis these nephrotics lost fluid amounting to 26–31% of their non-œdematous body-weight While œdematous they had seemed plump and well nourished, but this sudden fluid loss revealed the underlying wasting All 4 patients

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Recent work indicates that intestinal bacteria can affect the absorption of iron Stern et al [18,19] say that rabbits given oxytetracycline (terramycin) and penicillin absorbed no iron, but absorption was restored by adding *Escherichia coli* or enterococci to the diet Subrahmanyan et al [20] state that in man the extent to which phytates are broken down and their phosphorus is made available depends on a number of factors, the most important of which are intestinal bacteria and the calcium content of the diet

Megaloblastic anæmias in the tropics and subtropics are related to the diet [4,5] Some types of diet affect the ecological balance of the intestinal flora and upset the synthesis and absorption of essential factors, and the cure of these anæmias by penicillin is due to its destroying competitors for vitamin B_{12} and restoring the bacterial balance in the gut Similarly, imbalance of the intestinal flora caused by unsuitable diet, may be partly responsible for iron-deficiency anæmias

Loss of Iron

The view that the iron of the body is tenaciously held, and that it is mainly regulated by intestinal absorption through the ferritin-apoferritin/mucosal-block mechanism, is being modified Recent work shows that iron balance is maintained partly by controlling dietary iron absorption and partly through losses, and that the latter can contribute materially to the maintenance of iron balance Serum-iron levels are not necessarily an index of iron absorption [21–23]

The main routes by which iron is lost to the body are the bile (very small quantities), the urine (very small quantities), and the skin, saliva, and hair Mitchell and Hamilton [24] and Adams et al [25] estimated that the losses in cell rich sweat are high Stewart et al [26] concluded that they are insignificant, but their work was done on dogs, which have no eccrine sweat-glands and in which cell desquamation is low as in most fur bearing and hair-bearing animals Using radioactive ^{59}Fe, Dubach and her colleagues [27] found in man that the total quantities lost were between 0 5 and 1 0 mg per day Our own estimations have shown that losses by the dermal route (cell-rich plus cell-poor sweat) vary from 0 3 to 2 3 mg per day

The iron intake of the food is generally estimated in Britain and America as about 13–18 mg per day Of this the proportion absorbed is not more than 10% and probably nearer 8% Thus 15–18 mg in the diet would yield to the body not more than 1 5–2 0 mg daily

It will be evident that if (because the diet is unsatisfactory) absorption of iron from the gut is reduced, and (because the climate is hot and humid) loss of iron in the sweat is increased, the body may easily begin to lose more iron *than it gains* With a daily absorption of, say, 0 7–1 4 mg of iron, and a total loss at the lowest estimate of 1 0–1 5 mg (sweat, urine, fæces), an iron deficiency anæmia will sooner or later develop, even though the diet is adequate in iron

In the areas in which we worked malaria was not of much significance, and we did not regard it as an important cause of iron loss The iron liberated from the red cell by the malaria parasite is available for the resynthesis of hæmoglobin and the acute anæmia that sometimes occurs in severe malaria infection will generally respond to antimalarial drugs alone, no iron being required

TREATMENT

Our work in India showed that a large proportion of the microcytic anæmias respond simply to adequate doses of oral iron (20–35 grains of the ferrous salt daily)—even when the amount of iron in the diet is sufficient (It is known that checks to intestinal iron absorption can be overcome by greatly increasing the amount of dietary iron)

Some of these hypochromic microcytic iron deficiency anæmias failed to respond fully to oral iron alone In these cases we found that the total serum proteins were lower than normal, or the serum albumin was lower, or the marrow contained giant stab cells, indicating dyshæmopoiesis Cases with abnormally low serum proteins or serum albumin required protein in some form generally given as skimmed milk, before they made a full hæmatological response Those which failed to respond to iron and protein, and had giant stab cells in the marrow, made a normal recovery if given 5 mg of folic acid daily for one week, and/or 80 µg of vitamin B_{12} In some patients with normal serum-protein levels and no stab cells in the bone-marrow, iron treatment led to a fall in serum-protein level, reversal of the albumin/globulin ratio, and/or the appearance of stab cells

Many other workers have found low serum proteins and/or reversed albumin/globulin ratios in tropical anæmias Mitchell and Hamilton [24] state that dermal losses of nitrogen and even of amino acids can be considerable and that at high humid temperatures nitrogen loss is 5–7 times greater than at "comfortable" temperatures We have no information on this other than the failure of some of our Indian cases to make a complete hæmatological response unless given proteins It is possible that dermal losses of nitrogen may be affecting the synthesis of hæmoglobin

These tropical anæmias in many cases have multiple deficiencies which are not apparent while there is little blood regeneration The increased hæmopoiesis that follows iron treatment makes increased demands on the stores of protein, vitamin B_{12}, and folic acid, hence the fall in serum-proteins that frequently occurs during iron treatment, and/or the appearance of giant stab cells in *the marrow, or other signs of dyshæmopoiesis*

CONCLUSION

Microcytic anæmia is a very common and serious cause of ill health in most tropical and subtropical countries

It is seen in areas where the diet contains a *sufficiency* of iron

Our observations in India and Africa suggest that the two main causes of iron deficiency anæmias in such areas are (1) failure to absorb iron, because of the type of diet, and (2) excessive loss of iron

Even in normal adults on a normal diet, the maintenance of iron balance is more tenuous than has generally been supposed, on an unbalanced diet with excessive losses *the margin of safety* is even less

Iron is not the only substance needed for hæmoglobin synthesis The occurrence of abnormal serum-protein values the failure of some cases to respond to iron alone and the appearance of other deficiencies during iron treatment indicate the complexity *of the problem*

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Research Laboratories
and Ross Institute
of Tropical Hygiene

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protein levels in nephrosis It seemed likely that little progress would be made in treating nephrosis until some method of diminishing albuminuria could be found Prednisolone seems to have this property, if so, it should be used primarily to attack albuminuria High initial dosage could be used to eliminate albuminuria followed by such dosage as keeps the urine clear thereafter In this way the method of treating nephrosis with prednisolone would parallel the use of cortisone in suppressing the symptoms of disease, such as acute rheumatism Nor does it seem sensible to delay the start of treatment in the hope that the albuminuria will clear up spontaneously If the albuminuria of nephrosis were as painful as the arthritis of acute rheumatism, we would not stand idly by Yet the nephrotic albuminuria is a sign of much graver prognostic significance than the arthritis which obtains urgent admission and immediate treatment

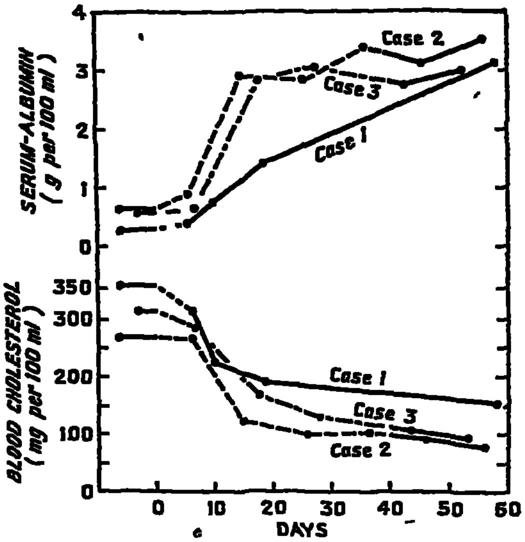

Fig 2—Blood-cholesterol and serum albumin levels in relation to prednisolone treatment.

Summary

Prednisolone treatment of 4 children with nephrosis led to reduction of albuminuria, considerable diuresis, a rise of serum-albumin and gamma globulin levels, a return to normal of the blood cholesterol level and the E S.R , and striking clinical improvement in all 4 cases In 3 patients albuminuria is no longer present, and in the other 1 it is greatly reduced

I wish to thank Prof Stanley Graham and Dr J H Hutchison for allowing me to treat patients in their wards, and Dr H Ellis C Wilson and staff for the biochemical investigations Messrs Pfizer Ltd provided generous supplies of 'Deltacortril'

ADDENDUM

A 5th successive case has now been treated A boy, aged $2^3/_4$ years, with a typical clinical and biochemical picture, began a course of prednisolone (as for cases 2 and 3) six days after the onset of signs Albuminuria lessened on the fourth day and was absent seven days later Diuresis occurred on the seventh day and no œdema has been detected since then Serum-proteins, blood cholesterol, and E S R all returned to normal within the treatment period of forty days

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THE ACTIVITY OF DIETHYLDITHIOLISOPHTHALATE ALONE AND COMBINED WITH ISONIAZID IN THE TREATMENT OF MURINE LEPROSY IN THE MOUSE CORNEA

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THE antituberculous activity of ethyl mercaptan and some of its derivatives was first described by Davies and Driver (1956), who found the most favourable compound to be diethyldithiolisophthalate (compound 15688) In view of the similarity between tubercle bacilli and leprosy bacilli and the fact that certain chemotherapeutic agents which have proved effective against tuberculosis are also of value against leprosy, it seemed possible that ethyl mercaptan compounds might produce a favourable effect on leprosy The present investigation was therefore undertaken to estimate the activity of compound 15688 alone and in combination with isoniazid, and the effect of isoniazid alone was also determined

Methods

The chemotherapeutic activity of the drug was investigated by the mouse corneal technique originally described by Rees and Robson (1950) in experimental tuberculosis and later applied to murine leprosy, details of the technique are given by Goulding et al (1953) and Naguib et al (1956)

The leprosy material for the present investigation was obtained from mice which, inoculated intracorneally with *Mycobacterium lepræmurium* (Douglas strain) from a rat leproma had developed generalised leprosy One mouse was killed 124 days, and the second 135 days, after inoculation, and their organs were used in preparing the suspension used in the two experiments as follows

The liver and spleen of each mouse were excised with sterile precautions and ground with a few ml of 0 05% 'Tween 80' in sterile physiological saline solution The suspension so obtained was first lightly centrifuged for 5 minutes at 500 r p m to precipitate the coarse material, and the supernatant fluid was centrifuged at 5500 r p m for 20 minutes to bring down the lepra bacilli with a very small amount of fine tissue debris This last precipitate was suspended in tween 80 saline solution and used for intracorneal inoculation

Diethyldithiolisophthalate, supplied as a transparent liquid, was used as a 50% solution in arachis oil in a dose of 5 mg per mouse every 2nd day or once a week Isoniazid was always given in a daily dose of 0 3 mg per mouse mixed with 5 g of M R C diet 41

Results

Two experiments were made on groups of 7–10 albino "C" mice In each experiment there was a control group, a group treated with isoniazid, and a group treated with the mercaptan once every 2nd day In addition to these three groups there was a group treated with isoniazid daily and the mercaptan every 2nd day in the first experiment, and in the second experiment there were two other groups one treated with the mercaptan once weekly, and the second receiving combined therapy with isoniazid daily and the mercaptan once a week The results of these experiments are shown in figs 1 and 2

In the control groups there was, soon after inoculation, an initial traumatic reaction consisting of an opaque corneal area equivalent to the site of inoculation This initial reaction faded gradually but never disappeared

The work described up to this point in the book includes Dr Wells's more important contributions to the understanding of airborne infection, and a clear account and interpretation would have been valuable Unfortunately much of the discussion is hard to follow and there are long and unnecessarily detailed descriptions of laboratory apparatus Most air bacteriologists in this country have found the slit sampler to be the most satisfactory instrument for sampling air Dr Wells apparently prefers the air centrifuge *in spite of its inferior performance with small particles*

Dr Wells then goes on to describe, in the second part of the book, his efforts to prevent airborne infections by means of "*sanitary ventilation*" *For this purpose he prefers* ultraviolet irradiation to ventilation in its generally accepted sense, and he records bacteriological and epidemiological experiments to support his claims for the efficacy of the method Some epidemiologists may not be satisfied with the statistical methods During one experiment infections occurring in an irradiated room were excluded from the results because the ultraviolet tubes had not been dusted

The chapter on dust borne infection is the best in the book Another useful feature is the comprehensive bibliography

In spite of these several criticisms, the book will be useful to the bacteriologist working on air hygiene because it provides, in one place, a record of Dr Wells's notable contributions to the subject

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Poliomyelitis (Philadelphia J B Lippincott London Pitman Medical Publishing Co 1956 Pp 567 60*s*)—The papers and discussions at the 3rd International Poliomyelitis Conference, held in Rome in 1954, have now been published The official delegates from the United Kingdom were Dr W H Bradley and Mr H J Seddon

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New Inventions

"STITCH-GUN" FOR SUTURING ATRIAL SEPTAL DEFECTS

OF the various closed methods of repairing atrial septal defects the most versatile is the atrial well, first described by Gross et al,[1] but placing sutures under blood by means of a needle-holder is difficult

I have devised an instrument to overcome this difficulty, it has been used in closing experimentally created atrial septal defects in animals, and suturing the margins has proved rapid and easy

The instrument consists of a head and a barrel housing a removable needle, mounted on a pistol grip (figs 1 and 2) At the pointed end of the needle is an open eye, at the other end is a thumb-plate and spring The spring prevents the needle from projecting beyond the barrel until the thumb-plate is pressed, and when the thumb-plate is released the needle automatically returns to the barrel On the pistol grip near the barrel are two spring catches to hold the thread

The suture is threaded into the grooves on the head (fig 3A), and the two long ends are secured in the spring catches The edge of the defect is palpated through the well with the left index finger, while the right hand holds the gun and places it so that the edge of the defect is in the U on the head of the gun (fig 4A) The thumb plate is then pressed and released, one end of the thread is held (fig 2), and the other *is allowed to slide through the spring catch The needle passes through the septum* at the margin of the defect, catches the thread in its eye and then pulls it back through the septal margin (figs 3B and C) With the left hand the needle is then pulled right out of the barrel, drawing with it the loose end of the thread, which now occupies the barrel (figs 4B and 3D) The fixed end of the thread is then released and the instrument removed from the heart

The stitch-gun may also be used for placing stitches elsewhere in the heart, or in other parts of the body where visibility or room to manœuvre are lacking

I should like to thank Mr A E Christmas who made the prototype for me The instrument has been made for me by Messrs Down Bros and Mayer & Phelps, 92, Borough High Street, London, S E 1

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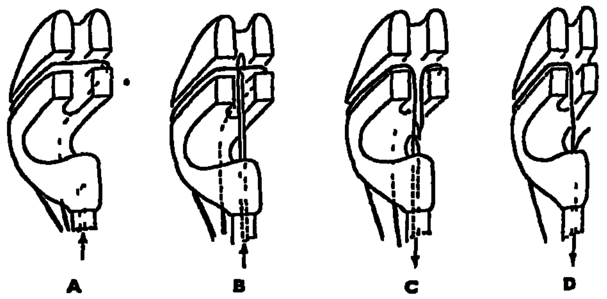

Fig 3—Action of needle on thread

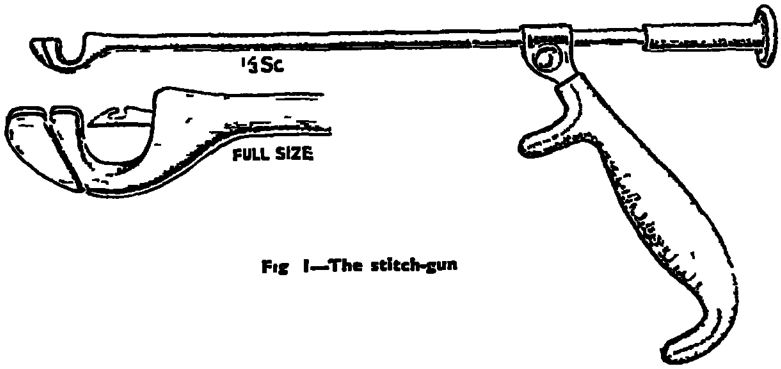

Fig 1—The stitch-gun

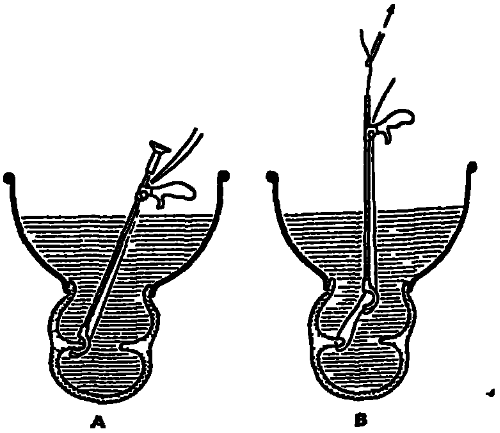

Fig 4—Stages in stitch

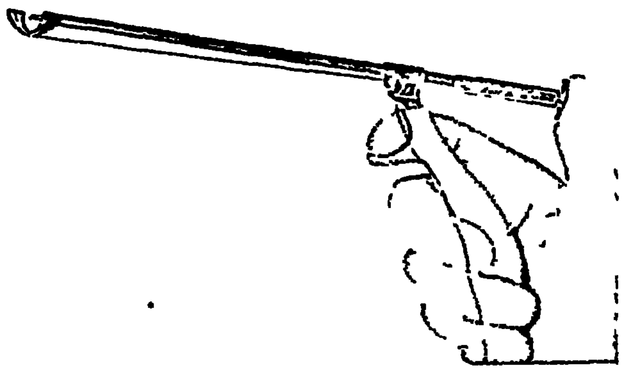
Fig 2—The stitch gun, with needle in position

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[1] Gross, R E, Watkins E, Pomeranz, A A, Goldsmith, E I *Surg Gynec Obstet* 1953 96 1

was easily expressed twelve minutes after the baby's birth but was incomplete; the patient then complained of nausea and upper abdominal pain, but her general condition was satisfactory. Some thirty minutes later there was a post-partum hæmorrhage of about 18 oz., and a succenturiate lobe was passed; the blood pressure decreased to 65/40 mm. Hg, and a dextran drip was set up, followed by blood and oxytocin in saline solution to counteract a tendency of the uterus to relax with continued slight hæmorrhage. The patient continued to deteriorate in spite of methylamphetamine hydrochloride, nikethamide, and continuous oxygen, and died three hours after delivery. The total estimated blood loss was 50 oz., and the blood did not clot.

Necropsy Findings.—Subarachnoid hæmorrhage, hepatic subcapsular hæmorrhage, pulmonary bronchial and alveolar hæmorrhages. The lungs showed numerous small infarcts with areas of collapse and emphysema. There was general congestion, with many pigment-laden phagocytes, but no evidence of fibrin emboli. Pancreas, kidneys, and adrenal glands were normal. An especially interesting feature was the failure of the blood to coagulate either before or after death; the fibrinogen content of the plasma taken before death was less than 100 mg. per 100 ml.

Case 2.—Gravida 2, aged 26, admitted as an emergency at 10 A.M. on July 9, 1955, with abdominal pain at the 35th week of gestation. The history was of swelling of the ankles and headache with the sudden onset of pain in the lower abdomen nine hours before admission. Her general condition was good, blood pressure 120/70 mm. Hg, pulse-rate 120; the uterus was larger than the dates suggested and was tense and tender; the fœtal heart was not heard. There was no vaginal bleeding; slight ankle œdema and heavy albuminuria were present. Blood taken for cross-matching did not clot; bleeding-time $3^{1}/_{2}$ minutes. At 8.30 P.M. no plasma fibrinogen could be found; labour was induced at this time, and a stillborn child was delivered at 3.20 A.M. next morning. The placenta was retained in spite of the administration of intravenous ergometrine, and a steady trickle of blood continued; the patient's general condition, which had begun to deteriorate even before delivery, now became serious in spite of the intravenous administration of 'Dextraven' and blood; by 5 A.M. improvement had taken place, and fibrinogen 0.75 g. was given intravenously, followed by manual removal of the placenta. About $1^{1}/_{2}$ pints of clot came away with the placenta, but bleeding continued, and the uterus was packed. Fibrinogen 0.75 g. was also given with the sixth pint of blood, and the patient began to improve slowly and had no further loss. Albuminuria was present in the puerperium, but there was no oliguria, and the fibrinogen level on the tenth day was 250 mg. per 100 ml. (i.e., normal). Bruising at the site of the intramuscular injections was observed up to the fourth day of the puerperium but not afterwards.

Case 3.—Gravida 3, aged 26, 36 weeks pregnant, admitted as an emergency on July 16, 1955. She had had slight backache on the previous night, since when she had felt no fœtal movements; at 9 A.M. before admission the backache recurred, followed by severe abdominal pain and vaginal bleeding. She was admitted at 4.30 P.M. with blood-pressure 130/80 mm. Hg, pulse-rate 92, typical signs of accidental hæmorrhage, fœtal heart sounds absent, and heavy albuminuria.

5.15 P.M.—Blood taken for cross-matching did not clot. No plasma fibrinogen was present.

7.5 P.M.—Artificial rupture of membranes.

9.4 P.M.—Fibrinogen 0.3 g. was given intravenously.

9.6 P.M.—Plasma fibrinogen 100 mg. per 100 ml. The blood clotted after ten minutes, but this was soft and began to disintegrate slowly though not completely.

10.7 P.M.—Plasma fibrinogen 80 mg. per 100 ml. Clot after ten minutes but soft, non-retractile, and partly redissolved.

11.15 P.M.—Plasma fibrinogen 46 mg. per 100 ml.; soft gelatinous clot, which completely dissolved in thirty minutes.

July 17, 12.15 A.M.—Oxytocin drip set up; contractions started within fifteen minutes.

2.5 A.M.—Precipitate delivery of stillborn infant; intravenous ergometrine given, and placenta expelled with about 2 pints of watery blood and 1 pint of clot. At the time of delivery fibrinogen 0.45 g. was given into the blood drip. The patient's condition remained good, without any post-partum hæmorrhage. The placenta showed a crater covering half the surface with adherent dark red clot.

Two days after delivery the plasma fibrinogen was 250 mg. per 100 ml. (normal), and Hb 50%; there was heavy albuminuria but no oliguria. By the fifth postpartum day there was only a trace of albuminuria, and Hb was 63% as a result of transfusion and intravenous iron. The patient was discharged later in good condition.

So far as possible the whole of the blood evacuated from the uterus at the delivery of the placenta was collected for estimation of its fibrin content; the extraordinarily large amount of 63 g. was found, which is very much greater than that normally present in the circulating blood at any time.

Pathology

The plasma fibrinogen levels were estimated by the micro-Kjeldahl method (King's modification). The amount of fibrin in the clot from the uterus in case 3 was estimated as follows:

The clot was washed with water, expressed, and dried as far as possible, and weighed. An aliquot portion was digested with 30% NaOH, and the protein was estimated by the biuret method; the result was expressed as grammes of fibrinogen.

The estimate is probably high but not more than +15%. The normal value for fibrinogen in the pregnant female is about 300 mg. per 100 ml. The blood volume of a healthy woman by the congo-red method is 70–100 ml. per kg. of body-weight, and a little higher in pregnancy. If the patient's blood volume was 6 litres, this amount would be equivalent to 18 g. of fibrinogen.

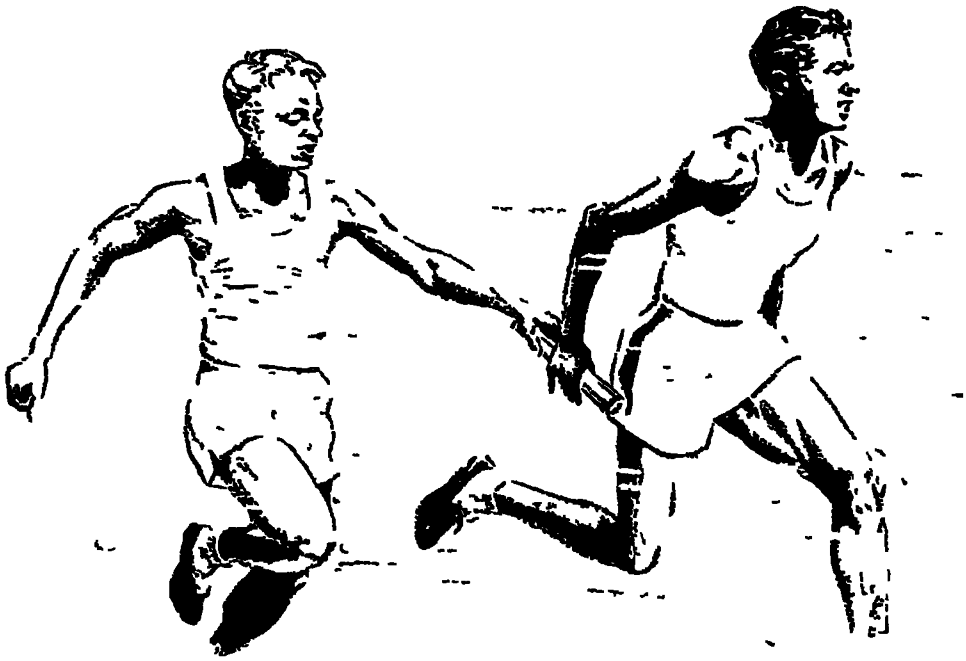
All fibrinogen is made in the liver (Tarver and Reinhardt 1947), and it is likely that there is a rapid turnover of the blood-proteins. Experiments on rabbits show that, when the fibrinogen is reduced as much as 90%, regeneration takes place in five or six hours (Drury and McMaster 1929). Greenberg (1951) estimates that there is a complete turnover of the blood-protein in from four to ten days. In case 3 about twenty-four hours elapsed between the original hæmorrhage and delivery, and at a rough estimate the patient may have replaced her fibrinogen at the rate of 1.5 g. an hour. If the mechanism for the production of fibrinogen was unimpaired, this would allow for the formation of an additional 36 g. of fibrinogen. With the 18 g. originally present this totals 54 g., which might have been serially deposited in the uterine clot. Our estimate from the clot was 63 g.

Discussion

These three cases present interesting contrasts and raise theoretical and practical problems. Cases 2 and 3 had partially concealed accidental hæmorrhage, which Schneider (1951) has shown to lead to the release of thromboplastin, causing the conversion of fibrinogen to fibrin. Case 1 had a retained succenturiate lobe and a postpartum hæmorrhage; she was toxæmic and pyrexial before delivery. We are therefore uncertain whether the cause was failure of fibrinogen formation owing to toxæmic or infective liver damage or to the liberation of thromboplastin from the uterus.

A second problem is the fate of the precipitated fibrin; Schneider (1951) suggests that it is deposited within the arterioles, especially of the lungs. Histological examination of the lungs in case 1 failed to show these "fibrin emboli," though the numerous small infarcts discovered might be connected with such a phenomenon. The amount of fibrin in the intra-uterine clot in case 3 suggests that, in some cases at least, the fibrin is deposited in the uterus more or less completely.

A third problem of great practical importance is the speed and duration of the defibrinogenation process; this is linked with the question of the best method of replacing fibrinogen. In case 2 it was argued that, since defibrinogenation continued at least until delivery of the



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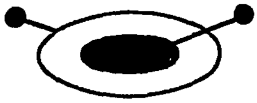

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TABLE I—AGE-DISTRIBUTION OF CORONARY HEART DISEASE IN 1000 NECROPSIES

Age (yr.)	No.	Coronary heart disease
<50	200	23 (11.5%)
50–59	297	66 (22.2%)
60 or more	503	155 (30.8%)

characteristic pain of cardiac ischæmia (Evans 1948) could usually be distinguished from the chest pain found in chronic pulmonary disease. The latter, though sometimes related to dyspnœa on exertion, was usually sharp and knife-like and of more variable onset, distribution, and duration in the same patient than the pain of cardiac origin.

Cardiac hypertrophy may be a feature of coronary heart disease (Boas 1951, Master 1954, Yater et al. 1948); in at least 37 of the 1000 necropsies the heart weighed more than 380 g. (range 380–880 g., mean 460 g.), but the kidney structure showed no evidence of hypertension, and no cause could be found other than coronary heart-disease. The increase in weight was largely due to left ventricular hypertrophy. By contrast, cardiac hypertrophy developing in pulmonary heart disease in the absence of coronary disease is mainly right ventricular in origin. Otherwise unexplained left ventricular enlargement in association with pulmonary disease, we think, is usually evidence of coronary heart-disease.

Study of the 134 cases which came to necropsy confirmed the diagnostic importance of the accepted criteria and of the lesser electrocardiographic signs described by Evans and McRae (1952) in the presence of massive fibrosis of pneumoconiosis, even in the absence of cardiac pain. ST–T changes with left ventricular preponderance in the presence of massive pulmonary fibrosis were found to be reliable evidence of coronary heart disease where other causes of left ventricular preponderance could be excluded.

TABLE II—AGE DISTRIBUTION OF CORONARY HEART DISEASE IN 134 CASES OF PNEUMOCONIOSIS STUDIED CLINICALLY AND AT NECROPSY

Age (yr.)	No.	Coronary heart disease
<55	54	11 (20.4%)
55–64	54	20 (37.0%)
65 or more	26	13 (50.0%)

These preliminary studies suggested a high prevalence of coronary heart disease in coalminers who came to necropsy. We recognised, however, that only limited conclusions should be drawn from such necropsy material (Mainland 1953) because no allowance could be made for the effects of differential mortality-rates and of case selection. The main study was therefore designed to find out if the observed 22–37% prevalence of coronary heart disease was typical of all miners and ex-miners in the older age group living in the area.

Prevalence in a Representative Sample of the Community

Method

55 names were selected at random from the Hollerith cards relating to the population of 1160 miners and ex-miners who were aged 55–64 on Jan. 1, 1954, and were living in the Rhondda Fach valley at the time of a private census conducted the previous summer (Cochrane 1954).

The men were visited in their homes and invited to attend as outpatients for an investigation of breathlessness. Transport was provided and loss of earnings made good. 4 men were seen on three afternoons in each week and subjected to clinical and electrocardiographic examination and assessment of respiratory function. A history of smoking habits was also taken. The method and findings of the physiological assessment are presented in detail elsewhere (Cotes et al. 1956).

Standard limb leads, unipolar limb leads, and chest leads V_1, V_4, and V_6 of the electrocardiogram were obtained at rest during quiet respiration and during full inspiration and expiration. The ballistocardiogram was recorded with a critically damped table having a flat frequency response curve and fitted with a mechanical oscillator to provide a dynamic calibration (Timbrell 1956). The standard electrocardiographic leads were recorded simultaneously.

Criteria for Diagnosis of Coronary Heart-disease

The criteria used for the diagnosis of coronary heart disease were those recognised in normal clinical practice but expanded and modified in the light of the preliminary studies described above.

A history of cardiac infarction and the diagnosis of it in retrospect were both accepted as evidence of coronary heart disease. It was recognised, in view of the high proportion of silent cases found in the preliminary study, that attacks of coronary occlusion might be atypical or silent in patients with pneumoconiosis (as in others) and would only be revealed by electrocardiography.

Left ventricular enlargement detected radiographically, in the absence of any other cause for its presence, was regarded as supporting evidence of coronary heart disease, particularly in the presence of pulmonary disease.

Electrocardiography

The electrocardiogram will show evidence of the effect of coronary insufficiency on the myocardium. The coronary insufficiency may be transient or prolonged, and the damage to the myocardium minimal or great, diffuse or localised. Changes indicating infarction of the heart are accepted as evidence of coronary heart disease. Signs of chronic or protracted ischæmia, with or without cardiac pain, may be present, in which part or whole of the insufficiency is due to coronary artery disease although there may be other disease—e.g., pulmonary disease—present at the same time. The presence of aortic-valve disease must also be detected and assessed.

Certain changes in the electrocardiogram are readily acceptable as evidence of this myocardial change resulting from ischæmia if other causes are excluded. These changes are often superimposed on an electrocardiogram showing left axis deviation, and this is important when pulmonary disease is also present.

The ST segment may be depressed in one or two standard leads and in one or more chest leads. There may be preterminal negativity of the T wave. These changes are seldom absent over some part of the left heart in coronary heart disease, and the peculiar shape of the tracing must be regarded as more important than the absolute degree of the depression of the ST segment (Holzmann 1952).

The presence of deep notching by a Q wave in lead I is abnormal. This does not apply to lead III, but the criteria for abnormality of the QIII or QSIII deflections, and their frequent association with coronary-artery disease, have been described (Ungerleider and Gubner 1947). The effect on lead III of deep held inspiration may also be of diagnostic value (Evans 1951); persistence of the Q wave for 0.04 sec. or more is considered abnormal.

Depression of a portion of the ST segment to form a trough, claw, or wing deformity, with low or blunted T waves in leads over the left ventricle, has been described in early myocardial injury associated with cardiac pain (Evans and McRae 1952). The significance of these signs in the diagnosis of coronary heart disease was confirmed in the preliminary study. These and other changes in the ST–T segments of the electrocardiogram are, however, tion of the Masters of the Supreme Court, and it would be a simple matter for the Master who examines the pleadings to order the reference of disputed medical matters to an independent expert The only real advantage of the informal pre-trial conference as used in the United States is its conscious search for the basis of a settlement out of court Even where settlement is impossible, the use of independent reports would help to remove at least the medical issues from the area of dispute Where the medical issues cannot be resolved before trial, an independent witness will be above any suspicion of partiality (suspicion of partiality by expert witnesses is probably not so great in this country as seems to be the case in New York, but it exists to some extent) But it is unavoidable in such cases that the expert should be called to give oral evidence and be liable to cross-examination, and that, in its turn, must give counsel the right to call other medical evidence That course may not be welcomed by those who feel that there is something discreditable about a clash of expert opinion in open court But English judges and lawyers are not likely to concede (any more than their colleagues in New York have done) that only one expert should be heard

There remains the question whether the British taxpayer would or should pay the bill for such a system of expert testimony The New York scheme was financed in its early stages by a grant of $20,000 each from the Alfred P Sloan Foundation and the Ford Motor Company Fund, but the cost is now borne by public funds If a similar arrangement was introduced here, it would hardly be feasible to limit it geographically, as has been done in America And the cost of a scheme applying to the whole country could probably be met only by the Exchequer The New York report suggests, however, that the cost of the project there was more than offset by savings in other ways The British reader may wish that the report had analysed this aspect more fully, but it does at least seem probable that a comparable plan in this country would be by no means as costly as it seems at first sight

Recurrent Dislocation of the Shoulder

Is recurrent dislocation of the shoulder largely preventable? It is surprising that we do not yet know the answer One school of thought holds that after reduction complete immobilisation with the forearm across the chest for 3-4 weeks is essential if recurrence is to be avoided, only thus, they say, will the torn structures in front of the shoulder-joint heal adequately The other school maintains that this immobilisation is an unnecessary imposition on the patient and that early movements are harmless In their view, recurrence or otherwise depends on the damage done by the original injury, if there is an avulsed glenoid labrum or a depressed fracture of the humeral head the patient is bound for later trouble, and immobilisation will not heal the one or restore the other to normal contours Neither side really knows, and one of them must be wrong it should not be hard to decide which Figures derived from series of patients treated at the time of original injury by one or other method are of very little value on this point the high proportion previously treated by early mobilisation is suggestive, but not significant unless we also know what proportion of *all* primary dislocations are treated by each method in that surgeon's particular "catchment area" In spite of the influential teaching of WATSON-JONES and others, it is probably true to say that most primary dislocations in this country still have less than one week's immobilisation and that often very incomplete McLAUGHLIN and CAVALLERO [1] recorded a high recurrence rate after early movement, but they included no adequate control group in which the joint was rigidly immobilised A definite answer would be given by a follow up study of a few hundred cases treated by each method Dislocation of the shoulder is common, recurrence when it comes, usually strikes within a year, and it is not so rare that a great many patients would have to be followed before getting at least a helpful indication

The primary treatment is, of course, not the only factor determining recurrence Age does not seem to be of much importance, and there is now less support for BANKART's view that the *mechanism of the original dislocation* in patients who have recurrences is always a fall backwards on to the shoulder or elbow so that the humeral head is driven directly forward Many workers, such as ADAMS [2] and DU TOIT and ROUX,[3] have reviewed this question and all the evidence indicates that there is no essential difference in the liability to recurrence, however the original dislocation was produced But there may well be anatomical abnormalities that predispose to recurrent dislocation, particularly variations in the attachment of the glenoid labrum and the size of the glenoid cavity, and it is significant that in GALLIE's series [4] of 200 cases there were three pairs of brothers and two pairs of twins Furthermore the condition is quite often bilateral, and this, for different reasons, is particularly so in epileptics There will always be some recurrent dislocations of the shoulder which start insidiously, or with trivial strains producing momentary subluxations, and then, with repetition, eventually progress to true recurrent dislocation

In the established case all the basic pathological changes have been known, though not always appreciated, since the 19th century, later workers have varied only in their opinion of the frequency and importance of the lesions from an ætiological standpoint There seems no doubt whatever that in most patients the vital factor is inadequate support for the humeral head at the anterior glenoid margin, whether due to *avulsion of the glenoid labrum* (BANKART's lesion), stripping of the capsule itself from the neck of the scapula, or even a stretched and lax capsule. BANKART's lesion is certainly not always present, in modern series its incidence varied from 65% to 100%, and it is interesting to note that in a recent review by DICKSON and DEVAS [5] of patients operated on by BANKART himself, or strictly according to his technique, only 32 of the 50 cases available for follow up had been found at operation to have the classical lesion With any lesion of this type there may be secondary atrophy and rounding off of the bony glenoid margin The second important site of abnormality is the posterolateral part of the humeral head, where a defect may be found which is apparently due

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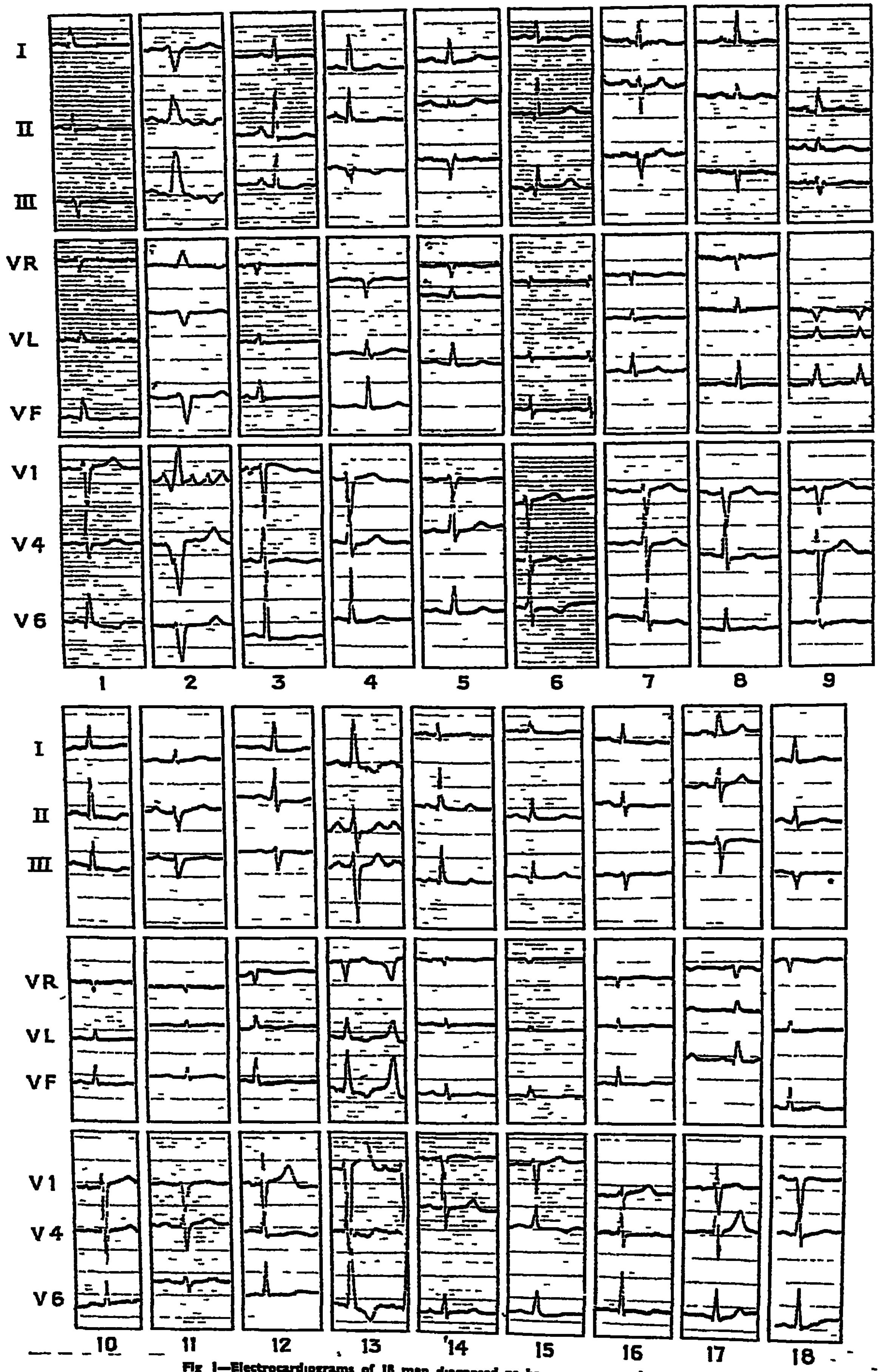

Fig 1—Electrocardiograms of 18 men diagnosed as having coronary heart disease

The ackee was studied again by HASSALL and REYLE,[8] and they isolated from extracts of its seeds two new polypeptides, hypoglycin A and B, which could produce fatal hypoglycæmia in laboratory animals This discovery not only was of importance to the possible rôle of the ackee in vomiting sickness, but suggested a new search for other plants of equal pharmacological interest ASPREY and THORNTON [9] made a valuable survey of medicinal plants of Jamaica, and their lists made it possible for the first time to identify accurately the scores of different local plants used regularly in bush teas by the Jamaican peasants HUGH-JONES [10] clinically tested the efficacy of some of these bush teas that were claimed to cure diabetes, but none was found to have a direct hypoglycæmic action like the extract of ackee seeds This ackee extract was not tested in man, partly because adequate quantities were not then available for clinical trial, but particularly because further animal work was judged to be necessary before the extract could be said to be safe for use in man The study of these hypoglycins may be as important to the fuller understanding of carbohydrate metabolism and diabetes mellitus as the investigation of the hypoglycæmic action of certain sulphonamides by JANBON and his associates,[11] to which we referred in a recent leading article [12]

Meanwhile the exact cause of vomiting sickness is still a mystery The circumstantial evidence against the ackee is high But ackees are a nutritious, cheap, and attractive food eaten with impunity by tens of thousands Rather than vainly attempt to ban the ackee, we must determine under what conditions hypoglycins appear in the arillus, whether preliminary starvation is necessary for the development of toxic hypoglycæmia, and whether other Jamaican plants ever contain these dangerous, but fascinating, substances

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Annotations

WOUNDS WITHOUT DRESSINGS

WHILE the major risks of surgery have steadily diminished over the past fifty years, many of its minor inconveniences have remained as irksome to the patient as ever Surgeons who have been subjected to surgery themselves must have been struck by the many trivial but painful procedures that follow the main performance in the operating-theatre Unlamented the bedpan is on its way out, and early ambulation seems to be on its way in Palumbo et al [1] have lately questioned once more the need for another uncomfortable feature of the postoperative routine—namely, the dressing of wounds

Earlier supporters of the "no dressing" school were Berkeley and Bonney [2] and several workers in America [3 4], but many surgeons remained unconvinced Palumbo et al have now treated 222 clean surgical wounds, in half of which the dressings were left in place for several days while in the other half they were removed after 6–24 hours The wounds included a wide variety of thoracotomy, laparotomy, and hernia incisions, and the investigators believe that complications were slightly less common in the group exposed to the air from the first day

It is perhaps a testimony to the profession's frequently unquestioning conservatism that there will be few to whom this will come as a surprise We have all learnt that cleanly incised wounds are sealed off by fibrin within a few hours of surgical closure, and that granulation tissue bridges the gap with astounding rapidity We have come to appreciate in the exposure treatment of burns that coolness, dryness, and light are bacteriostatic agents not to be despised, even in an era of antibiotics We know, or should at least suspect, that most wound infections are due not to stray staphylococci but to inadequate hæmostasis Thus, persistence with the ritual of prolonged wound dressing may spring more from deference to tradition than from scientific reasoning

Palumbo and his collaborators feel that "in these days of shortages in trained professional personnel, increasing living and hospital costs and need for economies it is necessary to develop and place in operation any method that will be beneficial to the patient, to the hospital, and to the trained personnel " Obviously much nursing time and effort can be saved More important, however, the patient can be spared changes of dressing—an unpleasant business even in the gentlest hands In the past such minor ordeals may have seemed trivial compared with the paralysing struggle under the anæsthetic mask or the nauseating discomfort of the immediate postoperative period Today, when even major operations leave but few unpleasant memories, they linger on in the mind—especially in the minds of children

The no-dressing method does, however, raise at least one problem which is mentioned and dismissed by Palumbo "There was no apparent opposition by the patients, relatives or visitors to seeing the incisions without dressings In fact, most patients were eager to watch their wounds during the healing process" This may be more true in America, where the layman is encouraged to take a much more active interest in his body's welfare than in this country

The method also invites comparison with the plastic 'Nobecutane,' an acrylic resin which, when dissolved in a mixture of acetic esters,[5] can be sprayed on wounds and forms over them a strong, thin, elastic, and transparent covering It can stay on until stitches are removed, and, being freely permeable to air and water (though not to bacteria), shares with the no-dressing technique the merit of allowing frequent inspection, a daily bath before the removal of stitches, and greater freedom for the patient to move about Over the no-dressing technique nobecutane has the advantage of making even an initial gauze and wool dressing unnecessary, of actually helping to hold the skin edges together, and (most important) of being applicable to a wide variety of outpatient and casualty procedures Rob and Eastcott,[6] who have used it to their satisfaction, do, however, mention some minor disadvantages The material is inflammable in the liquid form (though not after it has dried on the skin), the removal of stitches may be slightly painful because their ends catch on the plastic, its application is somewhat uncomfortable on an unanæsthetised raw surface, and, owing to the vasodilator properties of the solvent, it causes considerable oozing of blood As for this last disadvantage, Ellerker [7] feels that, though the accurate hæmostasis and skin apposition necessary to overcome it may be time consuming to the surgeon it is time well spent in the patient's interest probability, is in agreement with the observations that the ballistic impulse may be reduced below normal in coronary-artery disease (cf Scarborough et al 1952) The abnormalities in the form of the tracings were similar to those reported by these workers

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Smoking Habits

No significant relationship was obtained between the consumption of tobacco and coronary heart-disease when the consumption was expressed as the present intake or the average intake over life However, 7 of the 10 men who volunteered an intake or more than 25 g of tobacco daily for any period had coronary heart-disease

Discussion

Coronary heart-disease was diagnosed in 38% of the men in a sample drawn at random from the population of miners and ex-miners, aged 55–64, living in the community Half these men were known cases or presented with positive clinical findings, the other half had no symptoms attributable to coronary heart-disease, and this was only detected after a special search for its presence The total prevalence and the proportion of silent cases are similar to those found in the preliminary clinical and pathological investigation A higher prevalence might perhaps have been expected among these cases than in the random sample (cf Kilpatrick et al 1954, Mainland 1953) because coronary heart disease was a contributory cause of death in some instances

The sample of the population studied, and the men with and without coronary heart-disease, were typical of the whole as regards the prevalence of pneumoconiosis and chronic bronchitis, for which other estimates were available (Cotes et al 1956) Those with coronary disease had worked underground and at the coal-face for periods similar to those of the remaining men, and we found no evidence that the sample was in any way unrepresentative

The 38% prevalence of coronary heart disease might be compared with the 38% prevalence of all types of heart disease found in a group of men, aged 55–64, undergoing annual medical examinations in a United States industrial concern (Franco 1952) Not all of these men had coronary heart disease, however, and the method of selection in Franco's series may have increased the proportion of early cardiac cases while excluding those with much disability Gover (1948) obtained a 21% prevalence of clinical heart-disease in white men, aged 55–64, who formed part of the families of, or were, applicants for loans under a U.S farm rehabilitation programme All types of heart disease were included, but electrocardiograms were not recorded, and the number of men with a positive medical history is likely to have been underestimated Data comparable with our own on the total prevalence of coronary heart disease in a living population are not yet, but should soon become, available from studies in progress both in this country and in the U S—e g, Boas and Epstein (1954), Dawber et al (1951), Fales (1951), and Hilleboe et al (1954) Our findings on the relationships between coronary heart-disease and blood-pressure, body-weight, and consumption of tobacco are in agreement with the findings of other investigators—e g, Doll and Hill (1954), Hammond and Horn (1954), Keys (1954), and Parkinson and Bedford (1928)

The standardised mortality-rates in 1950 of deaths due to coronary heart disease in men aged 20–64 (Registrar General 1954) for coal hewers and getters (social class III) and other mine workers in coal (social class IV) were respectively 90 and 78, or 107 and 84 if deaths classified under myocardial degeneration are included These data suggest an average prevalence of coronary heart-disease among coal-workers In the absence of other figures for comparison the apparently high prevalence found in the present investigation is not necessarily remarkable, in view of the proportion of silent cases and the known high prevalence of coronary atheroma at this age A relatively low prevalence of disabling myocardial ischæmia might be anticipated in this population if the relationship between coronary heart-disease and physical activity which is found among workers in the Post Office and in London Transport (Morris et al. 1953) is also applicable in heavy industry Heavy work may, however, be in a class by itself in this respect (Rentoul 1951) In fact, at least 7 of the present 47 men had been in bed at some time through myocardial ischæmia, giving a 15% prevalence of active or latent coronary-artery disease sufficient to cause absence from work This figure may be compared with a 7% prevalence found in medical practitioners in the same age group (Morris et al 1952) This apparent difference is unrelated to pneumoconiosis or to "bronchitis" It is unlikely to be due to differences in smoking habits because miners are likely to consume relatively little tobacco This expectation has been confirmed in other studies in the Rhondda Fach (Higgins 1956)

The difference we have found could be explained on a survival basis if, as has been suggested—e g, Stocks (1954)—manual workers have a lower case fatality rate from cardiac infarction than those in other occupations, in these circumstances, even with the same attack-rate, a higher prevalence of coronary heart disease might be expected

Conclusions

A detailed clinical and physiological study was made of a sample drawn at random from a complete population of coal-workers aged 55–64

The 8% lapse rate for men living in the area at the time of survey was no higher than that for the preceding X-ray survey of the same population

The 38% prevalence of coronary heart-disease in this population of elderly coalminers and ex-miners is higher than that previously reported, and underlines the need for further investigations of this type

Summary

The prevalence of coronary heart disease was investigated in 47 of 55 men selected at random from a whole community of coalminers and ex-miners aged 55–64 Ballistocardiography was also done

38% of the men were found to have coronary heart-disease as defined, half of these (19%) had symptoms and the remainder (19%) were silent cases 15% of the men had at some time been in bed through myocardial ischæmia

The mean systolic and diastolic blood-pressures for the men with coronary disease (165 8/89 4 mm Hg) were higher ($P<0$ 05) than those for the remaining men in the sample (139 5/80 7 mm Hg)

The mean body-weights for the two groups were 156 9 lb and 133 8 lb respectively. The variation in body-weight was significantly greater in the men with coronary disease ($P<0$ 02), hence the significance of the higher average is uncertain, though it appears to reach the 5% level

We wish to thank Dr William Evans for his advice and criticisms, Dr Richard Doll for help in formulating the smoking questions, Dr W R L James for collaboration in the preliminary investigation, Dr J N Morris for reading the manuscript, our colleagues at the Pneumoconiosis Research Unit, especially Dr J C Gilson, director, Mr P D Oldham Dr T G Morris, and Mr R G Carpenter, for coöperation in the various stages of the survey, Mrs G M Budd and Mr G Jonathan for home visiting, and to Mrs J Newman and Mr A J Merrick for technical assistance

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operation in any individual depends mainly on his general condition and the type of arterial lesion , and the lesion is best analysed by arteriography, which has now become essential before any major surgical step is contemplated

PNEUMOCONIOSIS

IN a new Medical Research Council report[1] Dr J C Gilson and Dr P Hugh-Jones, of the council's Pneumoconiosis Research Unit in South Wales, describe the investigation they began in 1949 into the variations in lung function during particular stages of coalworkers' pneumoconiosis They are especially concerned with the cause of the disproportionate breathlessness associated with the condition, and the relation between the severity of the breathlessness and the *appearances of the chest* radiograph As we noted in a recent leading article,[2] Browne and his colleagues have lately cast doubt on the value of radiography in the assessment of pneumoconiosis , and these findings suggest that the existing compensation machinery for miners' pneumoconiosis should be reconsidered

From a review of work done in various countries Gilson and Hugh-Jones show that although much has been learned about lung-function tests neither the cause of the breathlessness nor the relation of its severity to the radiographic appearances has been properly established The report is concerned with the effects of prolonged inhalation of coal dust alone, which can cause a disabling form of pneumoconiosis different from silicosis The disease consists of two distinct pathological processes which may be distinguished radiographically "simple pneumoconiosis" due to the retention of coal dust, and progressing only if dust exposure continues , and "complicated pneumoconiosis" characterised by a superimposed infection with progressive massive fibrosis and advancing independently of any further dust exposure

Gilson and Hugh Jones studied 40 normal non-miners and 118 miners between the ages of 23 and 60 All the miners had had at least ten years at the coal face , and they were grouped into four different radiological stages of coalworkers' pneumoconiosis There was also a control group of normal working miners All the subjects were divided into age classes so that the effects of age and X-ray category could be separated The experiment was designed to determine the nature of the disturbance of lung function in pneumoconiosis, and to decide which combination of tests provided the best measure of disability The tests used were chosen for simplicity repeatability, discrimination (between normal and diseased states), and validity and they included besides clinical and electrocardiographic examinations, standard exercise ventilation and blood oxygen saturation, the total lung capacity *and its subdivisions diaphragm* movement, maximum voluntary ventilation, and intrapulmonary gas mixing and transpulmonary gas transfer by a new technique of recording the uptake of helium and carbon monoxide simultaneously

The exercise test was standardised for differences in weight, and age was taken into account , the exercise ventilation, taken as a percentage of the maximum voluntary ventilation (the "dyspnœic index") was the best index of breathlessness and compared well with independent clinical assessment The results show *that* breathlessness on exertion in coalworkers' pneumoconiosis is mainly caused by a reduction in the ventilatory capacity of the lungs The increasing air requirement associated with exercise accounts for only a small proportion of exertional dyspnœa it is the lung reserve which becomes severely limited with *increasing radiological abnormality* Gilson and Hugh Jones conclude that "in coalworkers' pneumoconiosis the excessive feeling of breathlessness on exertion results primarily from a diminution of the maximum ventilatory capacity of the lungs, and only to a relatively small extent from increase in the ventilation required for exercise"

But, especially in advanced disease, there is some increase in air requirement evidence of right heart strain shows that the pulmonary circulation is disturbed and, combined with ventilatory inequality between different parts of the lungs, as shown by helium mixing tests this suggests that the gas transfer deficit responsible for the increased ventilation is the result of changes in ventilation perfusion ratios The inequality of ventilation in the lungs increases with the degree of pneumoconiosis, the presence of massive shadows does not further increase the inequality until the latest stage of complicated pneumoconiosis, when it becomes much worse—although even then not *as severe as in advanced non industrial* emphysema A moderate degree of undersaturation of the blood with oxygen may often be found in complicated pneumoconiosis, but it is rarely severe , it is related to the inequality of ventilation, and in the latest stage to failure of the circulation also, with disturbed ventilation perfusion ratios Men in this stage have considerable functional emphysema, as measured objectively by a combination of several tests Those with simple pneumoconiosis have more evidence of emphysema than miners without the disease, but this functional change is severe only in the complicated form

As for the relation between the radiographic appearances *and breathlessness, in simple pneumoconiosis* it is age rather than the extent of the disease which is important in predicting the degree of disability In general, there is some breathlessness in simple pneumoconiosis, but this form of the disease causes only slightly more breathlessness than that which develops in *normal men* as they grow older In complicated pneumoconiosis on the other hand, breathlessness is nearly always severe, it increases with radiological abnormality , and it is augmented by increasing age

Gilson and Hugh Jones discuss the importance of the prevention of disability by periodic medical examination of miners In this respect *it is significant that* simple pneumoconiosis progresses only whilst exposure to dust continues, the extent *of* the disease being determined by the total dose of dust , and massive fibrosis arises only in the presence of considerable simple pneumoconiosis and then progresses in the absence of further dust inhalation Therefore, if dust suppression is adequate, and simple pneumoconiosis does not progress too far, little disability is caused , hence the necessity for periodic examination and removal *from* exposure to dust of those men who show signs of the disease

The report contains detailed accounts of the physio*logical function tests, together* with theoretical treatments of gas distribution and exchange in simple models and examinations of the basis of the methods used There is also a discussion of open and closed spirometry *tech*niques, and much else that is primarily of interest to the physiologist A factor analysis of the *results* shows to what extent supposedly different tests of lung function overlap The results of the various tests are finally represented most ingeniously on a three dimensional model so that partial correlations between tests may be readily seen, and those tests which measure practically the same thing are easily picked out On the usefulness *of tests, Gilson and Hugh Jones* declare "If an effort is made to find a combination of tests with minimum overlap, each one does not necessarily measure disability, since they may not be limiting factors It would appear that the best *combination* is likely to be some measure of maximum ventilatory capacity, possibly associated with tests to determine factors such as air flow resistance and lung viscance which limit the function together with a test of both non absorbed and absorbed gas uptake"

They are *to be* congratulated on the valuable contribution they have made *to the study of pneumoconiosis*

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① Gilson J C Hugh Jones P *Spec Rep Ser med Res Coun Lond* no 290 Lung Function in Coalworkers' Pneumoconiosis H M Stationery Office Pp 266 21s

[2] *Lancet* March 17 1956 p 326

Anterior oblique radiographs of the chest, repeated to show callus-formation, may reveal the fracture (Richardson 1936, Cramer 1943, Swineford and McKinnon 1945, Bodenheimer 1948, Douthwaite 1949, Mitchell 1951)

Case 15 fractured a rib when she turned in a chair and coughed simultaneously This association of asymmetrical posture with coughing was noticed by Seilin (1917), whose patient sustained a right sided rib fracture when she coughed with her right arm outstretched to close a window Atkinson (1898) reported a cough fracture in a patient who was hanging a heavy overcoat on a hook when an attack of coughing occurred

Case 16 is unusual in that there were bilateral multiple symmetrical fractures (the right ribs were fractured 3 weeks after the left) and in neither instance did the fractures follow a bout of coughing Mitchell (1951) declared that pain often came on gradually and many of his patients were surprised to learn that they had broken a rib

Site of Fracture

In the cases reported by Oechsli (1936) the fractures occurred "on a line extending from a point 4 cms from the costo chondral articulation of the 4th rib, obliquely caudally and laterally to the 9th rib in the mid-axillary line" This is the site of interdigitation of the external oblique and serratus anterior muscles Oechsli's series included no fracture below the 9th rib, and none of the patients were pregnant Richardson (1936) noted that the majority of fractures were at approximately the junction of the anterior and middle third of the rib

In the 4 cases in late pregnancy reported by Paulley et al (1949) the fractures involved the 9th–11th ribs and continued in a caudal direction the line described by Oechsli (1936)

In the 16 cases of stress fracture reported in pregnancy, the 6th–11th ribs have been involved, in 13 cases the fracture was on the left side, in 1 case on the right side (see accompanying table) and in 2 cases bilateral, in 2 cases the side is not recorded

Mechanism of Fracture

The earlier workers (Tunis 1890, Seilin 1917) suggested that the muscular pull of the diaphragm accounted for stress fractures of ribs This is clearly not so, since the fracture line lies well above its costal slips of origin

The line along which stress fractures occur corresponds to the interdigitation of the external oblique muscle inferiorly (ribs 6–12) and of the serratus anterior (ribs 1–8) and the costal slips of latissimus dorsi (ribs 9–12) superiorly Quiet expiration is normally passive, but in forced expiration additional expulsive effort is provided by the muscles of the abdominal wall and by the latissimus dorsi muscle, which contract suddenly and energetically.

In late pregnancy the costal margin is everted, owing to the enlarged uterus, and evidence that the lower ribs are then normally under stress is provided by the frequency of pain and tenderness of the interchondral joints between the 8th and 10th costal cartilages during the last 4 weeks of pregnancy An additional shearing stress brought about by the upward pull of the latissimus dorsi and serratus anterior (especially if the arm is abducted) and the downward and medial pull of the external oblique, on a rib already under strain, could provide conditions for stress fracture

Summary

13 reported cases of stress fractures of ribs in pregnancy are reviewed and 3 further cases are described Of these 3, 1 was unusual in that coughing was not responsible for the fracture

When a patient in late pregnancy suddenly has pleural pain, possibly initiated by coughing, with tenderness over the lower ribs, stress fracture should be considered and the patient should be examined radiographically

My thanks are due to Mr G F Gibberd, under whose care these patients were confined at Queen Charlotte's Maternity Hospital, for permission to publish

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A CASE OF RABIES IN SURREY

J Laughlin
M.A, M B Camb
GENERAL PRACTITIONER

D J C Ross
M.R C S

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Rabies is rare in this country, it is only seen in people who have become infected in countries where it is endemic and have travelled here during the incubation period In the past ten years two Servicemen have died of rabies in this country; the last civilian to die of rabies did so in 1911 Increased travel, particularly by air, may well raise the incidence of rabies here

Case-report

A man, aged 32, a bulldozer driver who had last been seen in March, 1954, with subdeltoid bursitis returned from Pakistan on April 27, 1955 He had been feverish on May 6 with a distaste for drink since May 7 He collapsed on May 9 and was behaving irrationally When seen at 3 15 P M he was sitting up in bed, was breathing rapidly, and sweating profusely He complained chiefly of a feeling of heaviness on his chest and inability to drink water or any other fluid for the past twenty four hours

On examination his temperature was 97°F, pulse rate 130, and respirations 60 a minute His tongue was coated and dry, and his throat red, with white viscid sputum round the fauces His pharynx and sclera were anæsthetic to touch When he was asked to breathe deeply, the tachypnœa ceased A few scattered rhonchi were found in his chest, and he had a loose cough He was given a capsule of 'Tuinal' gr 3, which he preferred to swallow dry Asked to drink some milk he became apprehensive, and his terror increased as the milk approached his mouth He took a mouthful and spat it out, his face and neck went into general spasm, the tachypnœa began again, and he complained of heaviness on the chest The tachypnœa ceased when he was told it was unnecessary He then remarked that he did not know before that he had such a vivid imagination He was left to rest -

TABLE I—AGUE COUNTY OF ESSEX, 1871–90
(REGISTRAR GENERAL 1918)

Deaths	Males	Females	Total
Number			
1871–80	38	24	62
1881–90	17	11	28
Rate per million			
1871–80	15 3	9 7	
1881–90	5 2	3 3	

saying in those parts that no young husband down on the marshes need despair if he fell too quickly out of love with his bride Provided she had come from some other part of the county, she was almost certain to die within the twelvemonth

The immunity of the indigenous male to one strain of the benign tertian parasite, the likely basis of this saying, was first demonstrated by the late Colonel S P James in 1924 He also showed that this resistance broke down when the individual was inoculated with another species or strain

There was a remarkable drop in the incidence of malaria during the last quarter of the 19th century, before the transmission cycle of malaria was understood, and therefore before any scientific attempts at malaria control could be made In Essex the number of deaths and death-rate from ague was more than halved between 1870 and 1890 (see table I) (Registrar-General 1918)

Her Majesty's Inspector of the School Board in 1874 described the Isle of Grain district in Kent as low-lying, aguish, and unhealthy, where no one would live if they could help it, and as many as 75% of the population of that area had attacks of ague in 1876 (Burnett 1906) The changing of the garrison at Tilbury fort every six months because of malaria was discontinued, about 1880, and Burnett said that by 1895 "the enemy [malaria] is subdued, for his victims are few, and there is not a more healthy place round the English coast, though what has induced the change it is not easy to determine" The answer is probably found in the history of a man called Henry Pye who became a farmer and took up residence on the Hoo peninsula in 1845 (Arnold 1947)

When he arrived, Hoo peninsula was a backward, poverty-stricken corner of an otherwise rich farming county Arnold describes Pye as "tough, enterprising, self opinionated, stubborn, progressive, outspoken, kindhearted, with a zest for work and sport" He owned one farm, but seems to have acted as manager for several He was a pioneer of mechanisation, owning and operating steam ploughs and steam thrashing tackle He drained the land he farmed, and cleaned the ditches and river outlets on the marsh He was known to keep a stock of quinine for his workers and their families When Pye died in 1909, malaria was rare in the Hoo community

These social economic advances, which Henry Pye symbolised were undoubtedly the main cause of the decline in malaria at that time (James 1929)

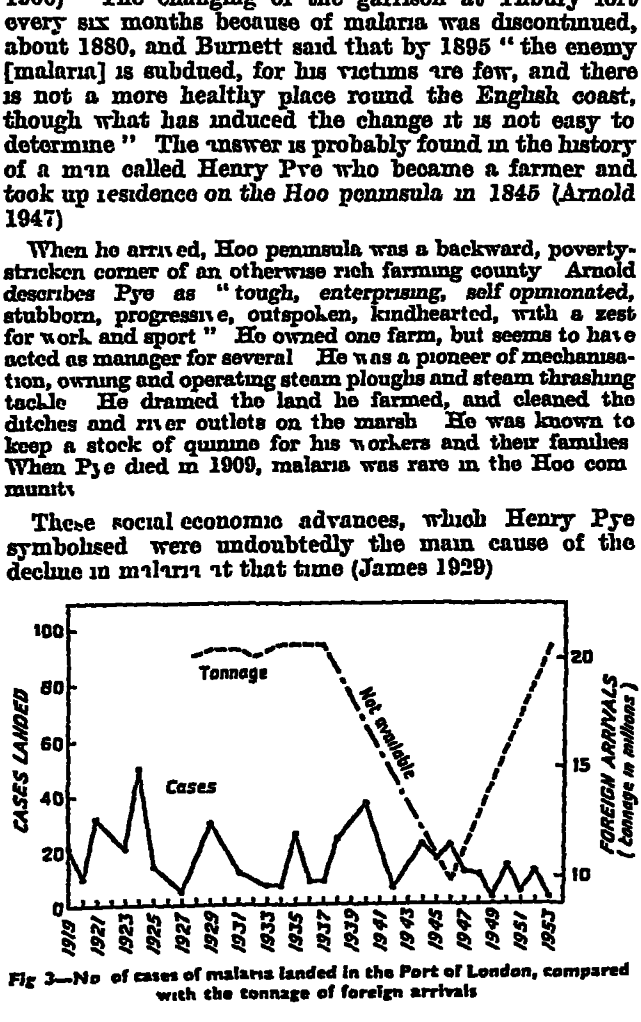

Fig 3—No of cases of malaria landed in the Port of London, compared with the tonnage of foreign arrivals

The causal parasite and the mode of transmission of malaria were first discovered at the very end of the 19th century Patrick Manson first demonstrated the life cycle of the *Filaria bancrofti* in the *Culex fatigans* mosquito in 1879, and this almost coincided with the microscopic recognition of the true parasite of malaria by Laveran, a French army surgeon stationed in Algiers In 1897 Ross, working under the inspiration and guidance of Manson, demonstrated the oöcysts on the stomach wall of *Anopheles stephensi*, and described the transmission cycle of malaria

Many years passed, and the 1914–18 war intervened before the results of these studies could be applied in effective mosquito control measures

World War I

There was an increase in the volume of shipping from tropical Africa because of the war, and many members of the crews of ships arriving at the Port of London from Dakar during the late summer of 1917 were found to be infected with the malignant tertian parasite The medical officer of health for the Port of London requested the local Government Board to take appropriate action in connection with the Port of Dakar, and he told all steamship companies how malaria can be controlled by quinine prophylactically and therapeutically (Willoughby 1918) In his annual report for 1919 there appear for the first time details of shipping arriving in London from malarial ports, together with local Government Board instructions that all passengers and crew who might be incubating malaria should remain under the observation of the medical officer of health at their destination Despite these precautions, the number of cases of malaria seen at the Port of London increased, and Dr Willoughby said in his report for 1923 "the opening out of trade with the West coast of Africa has resulted in malignant tertian malaria in epidemic form on ships" Fig 3 shows that the number of cases of malaria landed in the Port of London has gradually fallen since 1924 except for a slight peak in 1939–40, this decline was most noticeable after 1946, during a period of dramatic increase in the shipping tonnage arriving in the port The task Dr Willoughby started in 1917—the eradication of malaria as an occupational disease among ships' crews—has almost been achieved

TABLE II—CASES OF IMPORTED MALARIA NOTIFIED

Year	No	Year	No
1919	16 955	1944	0
1920	4168	1945	51[illegible]
1931	1644	1946	1054
1922	1356	1947	406
1923	853	1948	391
1924	1033	1949	246
1925	823	1950	263
1926	675	1951	177
1927		1952	108
		1953	5[illegible]9

The repatriation of Servicemen during the latter part of World War I was associated with an increase of imported malaria in the country as a whole (Ministry of Health 1919–53, and table II), but only in the Thames estuary did this have a significant effect on the incidence of indigenous malaria Large numbers of persistently relapsing cases were sent home following the severe epidemic of malaria among the troops in Salonika during the summer of 1916, and special camps were erected for them in various parts of the country One camp was situated in the Isle of Sheppey, and many of the men stationed there used to work at Grain Fort (fig 4) At that time there was an Air Force experimental station near Grain village, and many men stationed there mixed with the returned soldiers Many of the infected troops had relapses while in the camps, and as the anopheline density in this area was high it was not surprising that by the summer of 1917 cases of malaria occurred among the civilian population, as well as among men in nearby

The differential diagnosis is from hysteria, tetanus, atropine poisoning, Landry's paralysis, and encephalitis In the present case the condition was immediately recognised as out of the ordinary run of illness, and an intrathoracic disease, psychosis, and hysteria were first considered After the second visit the disease was recognised to be an organic condition, probably of the central nervous system Acquaintance with the patient in health, appreciation that he had insight into his mental state, and the discovery of signs of organic nervous disease helped in reaching this conclusion It was the recognition of the difficulty in swallowing fluids as hydrophobia, and the knowledge that rabies was endemic in Pakistan, which made the correct diagnosis possible

After admission to hospital hysteria was considered a possibility owing to anæsthesia of the pharynx and sclera and the patient's bizarre behaviour This diagnosis was excluded by the continued pyrexia, the leucocytosis, the rapid deterioration of his condition and early death, which was certified as due to encephalitis pending confirmation of the clinical diagnosis of rabies by laboratory investigation

Conclusion and Summary

A case of rabies, which developed in a man ten days after his return to this country from Pakistan and about two months after the bite, which left no scar, is described

The diagnosis of established rabies is entirely clinical Laboratory tests are only useful in the examination of necropsy material from either the suspected dog or the patient Established rabies is always fatal

Having witnessed the course of this illness, we have no sympathy for those misguided sentimentalists who wish to reduce the quarantine period for dogs entering this country

We wish to thank Dr H A Leggett, physician superintendent, and Dr T N Gledhill, pathologist, of Redhill County Hospital, and Colonel H R Bensted and Dr L A Hatch (who isolated the rabies virus), of the Central Public Health Laboratory, for clinical and pathological data, Dr Cyrus Ive, medical officer of health, for information on the preventive measures to be taken, Mr J S Sheppard, photographer, of the Royal Free Hospital, for the photomicrograph, and Dr Neville Southwell for advice and encouragement in the preparation of the paper

Preliminary Communication

NUTRITIONAL AND INTESTINAL FACTORS AND IRON LOSSES IN THE GENESIS OF TROPICAL ANÆMIAS

ALTHOUGH the nutritional megaloblastic anæmias[1-8] are common in the tropics and subtropics, they are not nearly so common as the hypochromic microcytic iron-deficiency anæmias Especially in the coastal, riverine, and lacustrine areas of Africa, India, and other damp hot regions these hypochromic anæmias are a grave cause of chronic ill health.

The blood shows a mean corpuscular volume (M C V) of 45–65 c µ, with a mean corpuscular hæmoglobin (M C H) of 13–20 µg and a mean corpuscular hæmoglobin content (M C.H C) of 20–28%[3, 9] The bone marrow is erythronormoblastic, and vitamin B_{12} levels in the serum are normal During treatment with iron these anæmias become macrocytic, the M C V rising to 110–150 c µ in about ten to fifteen days, but they do not become megaloblastic

ÆTIOLOGY

These severe microcytic anæmias often occur in areas where the diet contains an adequate amount of iron For this there are at least three possible explanations (1) loss of blood from the gut, caused by intestinal parasites, (2) failure to absorb iron from the gut, and (3) loss of iron in fæces, urine, or sweat

Loss of Blood from the Gut

Although hookworm may play a part in the genesis of the tropical microcytic anæmias, this is probably not a paramount one In Mysore State, which has a very high hookworm prevalence, many people have loads up to 9000 (Dr Patwardhan, Dr Work, Dr Anderson personal communication), but the hæmoglobin level in this State, and in those individuals who have heavy loads, is not significantly different from the level in States which have a lesser incidence or in people who have lighter infestations or none In different places in India we found infestation-rates as low as 8% or as high as 85%, but the prevalence of anæmia, and the average hæmoglobin, were not significantly different

In one centre where the infestation rate was 52%, among 300 adults and children the mean hæmoglobin was 9 4 g per 100 ml in another area, where the infestation rate was 12%, the mean hæmoglobin was 9 0 g Taking only cases that had mean hæmoglobins below 6 0 g, the average hæmoglobin in the worm infested cases was 4 8 g, while in the non infested cases it was 4 9 g

Failure in Absorption of Iron from the Gut

A number of factors affect the absorption of dietary iron—e g, gastric acidity, the presence of reducing substances such as ascorbic acid, soluble phytates in the diet, abnormal calcium/phosphorus ratios, and the solid content of cereal foods[10-14] Variations in iron absorption occur that are independent of anæmia and are closely related to the type of diet

In India and Ceylon the main article of diet is rice, which even when polished has a high phytic phosphorus content[15] Rice is further extremely deficient in calcium, and one of the serious deficiencies in the rice eater's diet is calcium[16] A rough estimate of the daily calcium, phosphorus, and iron intake of the average Indian and Ceylon peasant diet would give about the following calcium 106–200 mg, phosphorus 600–1000 mg, iron 14–28 mg With such a diet 5% or less of the iron would be absorbed, yielding about 0 7–1 4 mg of iron daily In addition, in the riverine, lacustrine, and coastal areas fish is eaten and adds to the phosphorus content of the diet

A common practice among the poorer classes of India and Ceylon is the chewing of betel nut leaves with added lime This yields about the calcium equivalent of 10 oz of milk daily, and the habit may account for the lesser prevalence of anæmia found by Stewart[17] among the beggar samples of his group in Pakistan

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to estimate the degree of protection from malarial infection which the presence of domestic animals has given to the human community

World War II

The application during World War II of this knowledge of the *A maculipennis atroparvus* enabled precautions to be taken to avoid a repetition of the 1917–19 epidemic A map was prepared by the Ministry of Health showing the areas where malaria was most likely to be contracted and where the disease was most likely to spread (fig 5) This map contained three areas, and the percentage of cases of indigenous malaria from each area after the 1914–18 war was area A 69, area B, 23, area C, 5, and outside these areas, 3 From these figures it was deduced that, should a malaria problem arise, it would most probably be in area A, and to a lesser extent in area B Copies of this map were sent in 1942 to the directors of hygiene of each of the three fighting Services, and the request was made that, as far as possible, potentially relapsing cases of malaria should not be congregated in areas A or B

Prompt action was taken over every notified indigenous case of malaria during and since World War II the patient's house was visited and a mosquito survey made Patients were usually treated with mepacrine, and the rooms and staircase of the house were sprayed with dicophane (D D T), as were any animal houses which were found to be harbouring large numbers of adult mosquitoes

These precautions were particularly vigorous in Kent or Essex, and the striking absence of a major outbreak of malaria after the late war seems to have justified the measures taken (table III and fig 6)

Recent Industrial Developments

The construction of the Kent Oil Refinery was started in 1950 at Grain, on the very site of the last malaria epidemic in this country The peak construction force of 8000 was the largest ever assembled in this country on any one site, and 2000 of this force were accommodated in a labour camp adjacent to the site A certain proportion of this force were ex-Servicemen or coloured immigrants who had recently been in parts of the world where malaria is endemic, and who might therefore exhibit a relapse parasitæmia This produced a nightly concentration of man power, contrary to the Ministry's war-time recommendations.

A meeting of representatives of the Ministry of Health and local authorities was held in the summer of 1952 on the Isle of Grain to examine the potential risk of an outbreak of malaria which this concentration of men might have created Mr P G Shute (representing the Ministry) demonstrated a large number of *A maculipennis atroparvus* in the camp sleeping quarters, and the meeting recommended that immediate steps should be taken to eliminate the high concentration of mosquitoes in the area of the camp These steps were taken and although we took blood slides from all persons on the site who reported sick with a fever of unknown origin, to my knowledge no malarial parasitæmia was ever found

Floods considerably damaged the sea wall around Grain in 1953, and reconstruction work resulted in many burrow pits and other small collections of brackish water being left inside the wall Larvæ of *A maculipennis atroparvus* were still being found in gravel pits near Grain village early in the summer of that year, and some anxiety was felt because these potential mosquito breeding grounds were close to the jetties at which many tankers from the Middle East arrived Frequent complaints by refinery personnel of being bitten at night warned us that mosquitoes were about in no small numbers

This uncertain presence of a malarial hazard made me request a second meeting in September, 1954, attended by representatives of local authorities, Service medical representatives, and other specialists, including Prof G Macdonald of the London School of Hygiene and Tropical Medicine The following recommendation received unanimous approval "The meeting, after having considered the history of the incidence of anopheline and culicine mosquito infestation locally, and elsewhere in the United Kingdom, is satisfied that there still exists a heavy incidence of mosquitoes in the Isle of Grain. This infestation, in addition to creating a serious nuisance, makes possible the transmission of malaria in changed circumstances now existing The meeting, therefore, strongly recommends that adequate measures should be undertaken to control the breeding of mosquitoes in the Isle of Grain, and is satisfied that this could be achieved at a reasonable cost" And while we attempt to implement these recommendations, we are a little relieved by the fact that no case of indigenous malaria has been reported.

Conclusion

Perhaps the ghost of malaria in the Thames area has been finally laid Malaria has fought a losing battle, first with the social and economic advances of the late 19th century, and later with scientific attacks against its lines of communication It is unlikely that imported *malaria will ever again succeed in reproducing the 1917* epidemic, and all that remains is the nuisance of mosquito bites

I wish to thank Mr R J Marsh and Mr E N Moore, the librarians of Rochester and Gravesend, for their assistance and also Mr P G Shute, assistant director of the Malaria Reference Laboratory, Epsom, for his technical advice I would like to acknowledge the ready assistance given me by many medical officers of health and general practitioners in Kent and Essex I also thank Dr J Greenwood Wilson medical officer of health for the Port of London, and Dr S D McClean, chief medical officer of the British Petroleum Company Ltd, for reading this paper, and Mr C S Cleverly, general manager of Kent Oil Refinery Ltd, for permitting me to publish it

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Statistics for England and Wales

Provisional death-rates from cancer, tuberculosis, and maternal mortality in England and Wales in 1955 have been announced by the Registrar-General[1]

Cancer —The death rate for all forms of cancer was 2252 per million population for men, and 1873 for women, the 1954 figures were 2223 and 1861 The rate for cancer of the lung and bronchus increased in men from 657 per million in 1954 to 693 in 1955, and in women from 102 per million in 1954 to 106 in 1955 Of the deaths from cancer in males 31% were certified as due to cancer of the lung and bronchus, of the deaths from cancer in women only 6% were so certified

Tuberculosis —The provisional death rate from respiratory tuberculosis in 1955 was 131 per million—a decrease of 18% compared with the previous year The death rate from other forms of tuberculosis was 15 per million, compared with 19 in 1954

Maternal causes —The provisional rate for maternal mortality (including abortion) was 0 64 per 1000 live and still births —the lowest ever recorded

The Registrar-General estimates,[2] on certain stated assumptions, that the total population of England and Wales will increase from 44 023,000 as at mid 1955 to 45,580,000 in 1965, 46,304,000 in 1975, and 46,690,000 in 1985, declining to 46,328,000 in 1995

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[1] Registrar General's weekly return no 13 1956 H M Stationery Office Pp 20 1s 3d

[2] Registrar General's return for the quarter ended Dec 31 1955 H.M Stationery Office Pp 23 1s 6d

Reviews of Books

Essentials of Forensic Medicine

C J POLSON, F R C P, professor of forensic medicine, University of Leeds London English Universities Press 1955 Pp 561 30*s*

TEXTBOOKS on the specialties of medicine fall into two categories, the "shorter" and the "much longer" The former guide the student and refresh the practitioner, the latter are books of reference for the expert—and, in legal medicine, for those who want to test the expert's knowledge To expect both in one volume is asking too much, and Professor Polson has plainly set out to enjoy writing at length on a subject he evidently revels in, exploring the literature and collecting what Montaigne would have called *un amas de fleurs etrangeres* It is superbly done, for he writes well, lucidly, and sanely, weaving the vivid and the more mundane chapters of forensic medicine, medical ethics, law and insanity into a comprehensive whole that is both informative and readable The book is no short guide to the subject for the student, but it will delight the specialist who cannot summon Professor Polson's enthusiasm for research into the literature The absence of pictures is a break with tradition, made deliberately, so as to "focus attention on the text" A toxicology on similar lines is to follow

The Clinical Approach in Medical Practice

G E BEAUMONT, D M F R C P, honorary consultant physician, Middlesex Hospital London J & A Churchill 1956 Pp 469 45*s*

THIS is a sequel to Dr Beaumont's *Applied Medicine*, and it follows similar lines The emphasis throughout is on practical clinical matters, and both this book and its predecessor show clearly how a skilled and intelligent physician's mind works when he is faced with a difficult diagnostic problem

In one section he describes some interesting cases he has met, and in another he and a group of pupils discuss, by the method of question and answer, the differential diagnosis of other cases In the case descriptions Dr Beaumont amply proves how repaying is care in history-taking and bedside examination In the question and answer demonstrations he explodes with wit and erudition (some of his pupils are remarkably well informed, too) and the joint result is both instructive and diverting There are two new features a section describing in detail the psychological reactions of some tuberculous patients to their disease, and a short philosophic excursion into the ethics of prolonging life in advanced heart-disease Dr Beaumont seems less at home with such emotional matters, and this part of the book is rather dull, but the rest is more entertaining than many a novel

Splenin A in Rheumatic Fever

The testing of splenin A as an anti-inflammatory agent ALVIN F COBURN, M D, LUCILE V MOORE, M D, JUDITH WOOD, M D, MARY ROBERTS, R N, Rheumatic Fever Research Institute, Northwestern University Medical School, Chicago, Ill Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 86 27*s* 6*d*

IN the modern therapeutic arena a favourite battle with the crowd involves Allergy, and particularly the chimera Rheumatic Allergy Here comes a dark horse in the trampled wake of the giants Corticotrophin and Cortisone, challenging perhaps the most elusive champion of all, Rheumatic Fever Is Splenin A a worthy opponent? On its form it will do As Ungar described it, splenin A is a product of the spleen which decreases capillary permeability, increases capillary resistance, and shortens bleeding-time Like corticotrophin and cortisone it increases the antifibrinolytic activity of guineapig serum, but unlike these hormones has a similar action in splenectomised animals Moreover, it inhibits anaphylactic arthritis in the guineapig—and is not hypersensitivity its opponents' Achilles heel?

How will the issue be judged? Not by therapeutic trial, the challenger, unfortunately, is as yet too meagre of substance By clinical impression then, and a consensus of opinion about anti-inflammatory effect The skirmishing begins, the contestants are hidden in clouds of dust The challenger sometimes seems to be on top, but alas! when the air clears, the champion looks the fitter of the two, and the laurels are still firmly on his brow What does the crowd think? It has been offered poor material for judgment, so it very sensibly keeps its thumb in its fist, and refuses to consider its verdict

A Hundred Years of Nursing

SIR ZACHARY COPE London Heinemann Medical Books 1955 Pp 144 10*s* 6*d*

THE main part of Sir Zachary Cope's interesting book describes the history of nursing at St Mary's Hospital, Paddington, since it was opened in 1851, but in a first chapter he gives a short account of the general history of nursing during the same period, which shows the striking changes which have taken place

In 1860 the matron asked if a gratuity might be given to a sister who was leaving after seven years' service The board recommended that she be given £3 to pay her travelling expenses The matron herself was dealt with rather shabbily Her salary remained at £50 per annum for twelve years, after which an increase of £10 a year was granted And out of her meagre salary £12 had to be spent on washing

James Parkinson 1755-1824

Editor MACDONALD CRITCHLEY, M D, F R C P London Macmillan 1955 Pp 268 15*s*

To mark the bicentenary of Parkinson's birth four papers dealing with Parkinson's disease have been attractively published The book includes the original Essay on the Shaking Palsy There is also an introduction by the editor, a biographical essay by Dr W H McMenemey, an account of the pathology of Parkinson's disease by Dr J G Greenfield, and a clinical analysis of the paralysis-agitans syndrome by Sir Francis Walshe

Parkinson led an exciting life He was something of a political revolutionary but escaped the fate of transportation and imprisonment which befell several of his associates Two of his tracts were entitled Revolution without Bloodshed or Reformation preferable to Revolt (1794), and Whilst the Honest Poor are Wanting Bread (1795) His papers on medical subjects included Hints for the Improvement of Trusses (1802), Some Accounts of the Effects of Lightning (1789), and one of the earliest descriptions of a Case of Diseased Appendix Vermiformis (1816) He emerges as a competent and keenly observant surburban practitioner, and an eccentric But for all that he was an engaging and likeable character, modest, unassuming, and warm hearted His famous essay is a great rarity, but it is very profitable reading How effective are the words with which Parkinson opened "Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported, with a propensity to bend the trunk forwards, and to pass from a walking to a running pace, the senses and intellects being uninjured"

The editor and his collaborators have done well in republishing and adorning this classical piece of medical writing

Airborne Contagion and Air Hygiene

WILLIAM FIRTH WELLS, PH D, laboratory for the study of airborne infection, University of Pennsylvania School of Medicine Cambridge Mass Harvard University Press London Oxford University Press 1955 Pp 423 48*s*

FOR more than twenty years Dr Wells has been engaged on the problems of airborne infection Much of his published work has been highly technical, and it was therefore encouraging to read in the preface to this book that "much of the original work had . to be revalued, and significance, only implicit in published papers, made explicit in the book." But he has not entirely succeeded in this last purpose

In the first part, Dr Wells describes, in physical and mathematical terms, the formation and behaviour of respiratory droplets He examines the merits of various devices used for the bacteriological analysis of air and describes the influence of ventilation and ultraviolet irradiation on airborne organisms The first part of the book ends with a consideration of the factors influencing penetration of infected particles into the lung clinical staff of the teaching hospital in collaboration with preclinical teachers

The college also wishes to point out that the very necessary integration between preclinical and clinical studies cannot be achieved unless the character of the examinations which separate them is altered

Clinical Studies

During this period a thorough training in clinical methods and clinical thought has to be combined with increasing acquisition of knowledge of disease and the care of the sick The student must learn how to use clinical techniques, he must learn how to interpret signs and symptoms of disease in terms of disordered structure and function, and he must gain a working knowledge not only of the causes and effects of disease but also of the requirements of physical and mental health All the time, factual information has to be kept in balance with clinical facility

Such studies fall naturally into three stages (1) a period devoted largely to methods of examination, both clinical and ancillary, (2) a period in which clinical practice is associated with the more academic study of disease processes (clinical pathology, morbid anatomy, and environmental pathology), and (3) a period of practice with increasing responsibility but still under supervision During this last stage much may be gained by arranging for the student to spend some months wholly or mainly in any department chosen by himself, for both his interest and his understanding will be stimulated by working in an atmosphere of progress and research In addition, teaching authorities will no doubt wish their curricula to be sufficiently variable to allow students of unusual aptitude and ability to avail themselves of opportunities for special experience

Throughout the clinical period, the fundamental unity of medicine should be emphasised, and the barriers between departments must not be such as to prevent the student from moving from one to another—either in person or in thought

As to how the time of the clinical curriculum should be divided between different branches of medicine and its specialties, the college hopes that the General Medical Council will make no formal recommendation, since it is preferable that each school should work out the kind of curriculum best suited to its own character and capacities In general, however, it may be stated that, though clinical principles can be learnt in any clinical department if the teacher has skill in teaching them, the early training in method is ordinarily best given in departments of general medicine and general surgery, and then strengthened in selected special departments

Provisional-registration Year

A year of responsible practice under supervision will normally complete the doctor's basic education by fitting him to take full responsibility for the care of patients, even though at first he is unlikely to practise independently Teaching authorities will note, however, that this year following qualification provides them with an opportunity to assess every student's clinical ability more satisfactorily than has hitherto been possible Like the learner driver of a motor vehicle, the student is called upon to display his trustworthiness, and, if he fails to do so, a further period of work under supervision ought to be prescribed Senior members of the medical profession accepting responsibility for this final stage of basic medical education should recognise its importance both to the young doctor and to the public, and should not regard their final certificate as a formality to be fulfilled even if their pupil's performance has been below the standard they expect

Length of Curriculum

The scope and possibilities of medicine have so much enlarged that its efficient practice is in many respects becoming harder The period at present assigned to the preclinical and clinical studies preceding qualification is a minimum of five years, and this minimum cannot be reduced until the council are satisfied, by observation, that a basic medical education need not last so long A comprehensive vocational training would clearly have to last much longer

Because of the importance of preserving the student's freshness of mind during this protracted period, care must be taken to give him sufficient holidays

Reconsideration of Curricula

The difficulty of judging the relative merits of different educational methods makes it desirable to permit, and even promote, experiments in medical education By their diversity (which the General Medical Council have always striven to maintain), and also by their stability, medical schools in this country are well fitted to explore fresh possibilities for the teaching of the future doctor In refraining from detailed recommendations, the council would give much-needed encouragement to teaching authorities to reconsider their curricula as a whole, in the knowledge that, within wide limits, variation will be permissible Equal freedom to differ on method could perhaps be accorded to separate medical schools governed by a single teaching authority

A curriculum must be largely an expression of the particular features and facilities of each medical school and in the final analysis its success will depend not on regulations but on the teachers' attitude of mind and the facilities at their disposal The subjects will often matter less than the circumstances in which they are taught

In each school there must be enough teachers able to give the time required for the realisation of their concept of teaching, and it is the responsibility of the school to build a teaching team capable of carrying into effect its particular scheme of education In such arrangements it should be borne in mind that full use of the valuable clinical teachers who work both in teaching hospitals and in regional hospitals is impossible unless they are enabled to spend some sessions at the teaching hospital additional to those arranged for the care of the patients in their charge

Specialisation and the advent of the National Health Service have substantially altered the clinical facilities offered to students by the teaching hospitals Already different patterns of teaching hospital have emerged and, though the relative merits of these patterns cannot yet be evaluated, a duty rests on each board of governors to see that the clinical facilities for its students are as good as it can make them

To this end some teaching hospitals and universities may feel it necessary to request alterations in the arrangement of the hospital service, and in such cases the council should be willing to offer advice and, where appropriate, support Students in their clinical period could profit by experience of medical practice outside hospital, under conditions within the immediate control of their medical school * and the creation of facilities of this kind—e g, university health centres—exemplifies not only the need for medical schools to break new ground but also the problems they will face in so doing The college hopes that in the solution of such problems the council will wish to help

Just as the imposition of a single curriculum would stifle the initiative of the medical schools, so uniformity of the curriculum in any one medical school can stifle the initiative and ignore the particular requirements of particular students To subject all students to a common course in which knowledge is acquired passively, from instruction, is a partial confession of failure Instead

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* A brief period as observer in a general practice may also be useful in showing the student what sort of work general practitioners do But in the college's view such observation is supplementary to basic medical education and not an essential part of it

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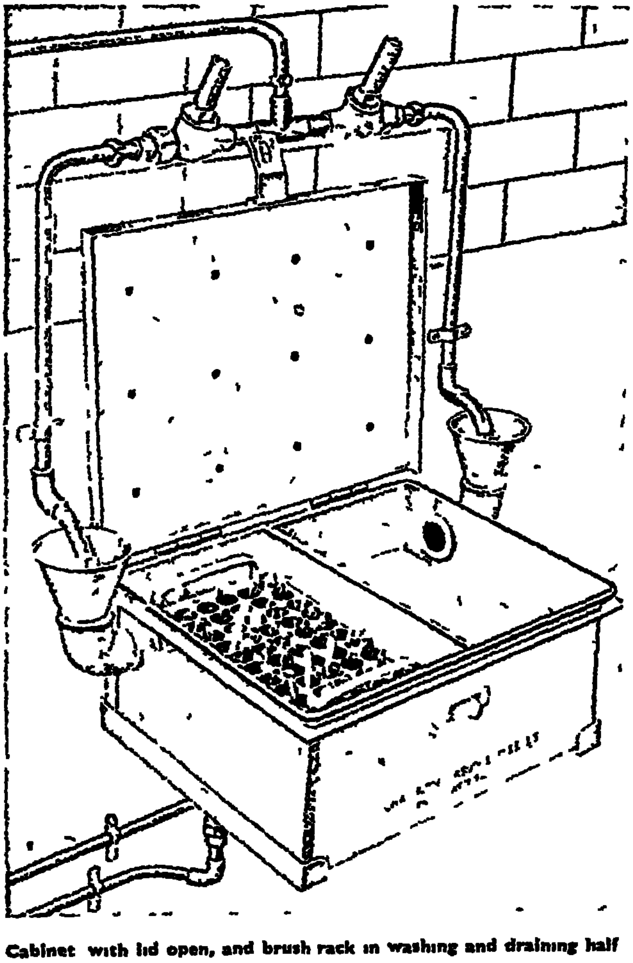
cabinet can be locked Both halves of the tank can be drained and are connected to inlet water-pipes To prevent contamination of the inlet water pipes, these are not connected directly with the water mains The inlet pipe on the half of the tank occupied by the sterilising solution allows this half to be well rinsed when the solution is changed, there is sometimes a slight deposit at the end of two or three days The taps for the inlet and drainage pipes are operated by a removable key, which is in the possession of the charge nurse

The brushes are collected from the patients and placed in a stainless steel rack similar to a test tube stand, which has two horizontal plates perforated with 60 holes The rack and brushes are then thoroughly rinsed with tap water to remove debris and placed in the half of the tank containing the 1 in 200 solution of monochlorisothymol for two hours, after which they are placed in the half of the tank containing tap water After one hour, the water is drained off and the brushes left to dry until required



Cabinet with lid open, and brush rack in washing and draining half

The solution of monochlorisothymol has been found to be effective in the cabinet for three days, after which time there was slight contamination Because the substance is comparatively cheap, a fresh supply of solution is issued on Mondays, Thursdays, and Saturdays

CONCLUSION

It is highly desirable that oral hygiene should be observed in all hospitals, and this method of sterilising and storing toothbrushes is simple, clean, and effective, as well as being economical in cost and labour.

I wish to thank Dr A H Wilson, medical superintendent of Meanwood Park Hospital, for his help in the preparation of this article

In England Now

A Running Commentary by Peripatetic Correspondents

In Renaissance Italy physicians and artists shared the shelter of the same guild, and the great medical teachers studied anatomy alongside the Leonardos of the day The past centuries—economic evolution, if you wish—have dissolved this intimate and happy association The doctor has drifted from art to the sterner shores of science, and the artist has abandoned the study of Nature and succumbed to his own surrealistic vision Yet even now doctors turn to art for release from what Osler called "the malign influence of the routine" The members of the Medical Art Society[1] do not form a "school," but they do share one quality—the holiday spirit They are happy (sometimes happy-go-lucky), warm, spontaneous, often exuberant They are escapists, though their escape may be not years in Tahiti but a fortnight in Provence, or an hour at a window looking down on Regent's Park

Even R A Beaver's beautifully quiet *Queen Anne Street* is a Sunday townscape H Elliott-Blake's *Las Aldea de Miel* is inspired, like all good landscapes, by familiarity, not by strangeness, the houses, the chalky soil, the gray, windy sky have the intimacy of experience that made Corot and Constable so evocative W G Scott Brown's cool, delicate tones are closer to the late French impressionists, but it is his own power to create air and light, not the muffled footsteps in the sand of Degas and Berthe Morisot, that makes his *On the Beach* one of the most memorable pictures of the exhibition P. Tuttnauer's *The Beach* is a brave effort at *pointillisme*—which miraculously succeeds, it is not as monumental as Seurat but quite as sparkling B U Coffey's *Crucifixion* is Blakeian in vision (but he should expurgate Salvador Dali), and R T Payne's three pictures are lone representatives of the truly contemporary school *Phoenix* is his best

Water colours have many attractions for the amateur—they are clean, orderly (as those things go), cheap, and, it seems, so absurdly simple No wonder that many a beginner who recklessly takes the plunge, gets swirled about in a pool of transparent washes, tints, and shadings and emerges spluttering—or reaching for oils with which he can start, stop, scrape, and cover over at his heart's and eye's delight But happy are those who survive, and remain restfully afloat in the medium and twice happy those who, like B A Brooke, learn to command it His *House of Usher* is water colour at its most romantic and its most brilliant the challenge of Poe gallantly met But in a quieter vein there are many admirable water colours here G H Rose uses the damp rawness of the paper to make his *Miller's Lane* hauntingly bleak, in a lucky moment T Holmes Sellors catches the breaking clouds of a summer storm, and Mary Wiles the fading radiance and silvery grace of what can only be Bruges Henry Wilson's *Harvest Time near Ely*, K Shirley Smith's *A Corner in the Meadow*, Constance Appleton's *Ullapool*, and Sir Philip Manson Bahr's *A Sussex Lane* are a random selection of others which pleased Liverpool and the North are well represented by a handful of pictures T N A Jeffcoate's luminous *Spring* and C Wells's *Treaddur Bay* are most attractive

The portraits are few but excellent Josephine Roth's drawings are character studies of rare distinction and W G Sears's *Heather* is expressive Of the sculptures G Konstam's *Boy with a Parrot* is delightful and technically accomplished J Rostowski's squinting terracotta boy has infinite charm, but his *Split Personality* and *Obsession* suggest that schizophrenics are no more suited to sculpture than unknown political prisoners

This is not to say that medical subjects are unsuited to art—do not our nurses outshine the dancers of the Paris Opera? But for the moment Art remains on the periphery, a whim in the holiday mood, while Science jealously guards the gates

* * *

The paraplegic in our ward needed a new self-propelling chair and, to set the wheels in motion, the official request form was properly signed, countersigned, sealed, and sent off with the blessings of even the hospital secretary In the good old days, when a spade was a spade, a chair was also a chair, but such simple considerations are no longer

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[1] Their exhibition is at Walker's Galleries, 118, New Bond Street London W 1, till April 21

THE LANCET

LONDON SATURDAY, APRIL 14, 1956

Medical Evidence

How can the Law best obtain expert medical evidence? The normal method both in this country and the United States is for the opposing parties in a dispute to call their own medical witnesses these witnesses are then cross-examined and, if they disagree, it is for the judge or jury to decide what evidence to accept There are some exceptions occasionally in this country the parties may put in an agreed medical report, in nullity cases the court may ask (though it does not compel) either party to submit to medical examination by an impartial doctor, and in cases under the National Insurance Acts, the claimant may also be required to undergo impartial medical examination All these however, may be regarded as the exceptions which prove the rule

Many people feel that the usual methods of giving medical evidence could be improved[1], and those who seek reform will welcome a report[2] by a special committee of the New York Bar Association on a proposal to use impartial medical testimony in cases of personal injury As some 80% of the cases in the United States trial courts are concerned with injury and involve medical evidence there seem to be good grounds for the claim that "the project is directed at the very core of court operations" The idea was conceived by the judges of the Supreme Court of New York and was put to the test experimentally, first in New York County and later in Bronx County as well, with the cooperation of the local bar associations and medical societies The results were so satisfactory that impartial medical testimony is now a regular part of the operations of the Supreme Court of New York State Under the new arrangement, the judge may, before the trial, order the examination of an injured person by an impartial medical expert Before doing so, he consults counsel for the two sides, but their consent is not necessary In fact, during the two years covered by the report no lawyer registered any sharp objection, indeed, in some cases, the lawyers themselves asked for an impartial expert This step is facilitated and even encouraged by a feature of the American legal system which does not exist in Britain—namely, the pre-trial conference This conference enables the judge and the lawyers for both sides to explore the issues in the case and the possibilities of a settlement, the discussions being held in an informal atmosphere, usually some months before trial If the judge orders an examination by an impartial expert, the pre-trial conference is adjourned In making his order, the judge indicates the nature of the medical dispute and the type of specialist who should carry out the examination, occasionally, of course, more than one specialist is needed The actual selection of medical experts is made by a specially constituted "medical record office" from panels drawn up by the local medical societies In due course, the pre-trial conference is resumed when the case will again be discussed in the light of the expert findings

From the incomplete statistics available it seems that well over a quarter of the cases referred in this way to impartial experts were settled at or before the resumed pre trial conference of the remainder, a substantial number were settled after the resumed conference but before trial In all, over half the cases seem to have been settled before trial In considering these statistics, it must be borne in mind that the possibilities of a settlement do not always depend on the medical evidence Even if the medical evidence is accepted by both parties, there may be other issues for trial—for example, the alleged negligence of the defendant and contributory negligence on the part of the plaintiff Moreover, even where there is agreement on the nature of the injuries there remains the question of damages But, of course, there will always be cases in which there is an honest difference of opinion between the medical experts If the cas goes to trial, the impartial expert may be called t give evidence at the request either of counsel or judge. If so called, he will be subject to cross-exan nation and either party may call their own exper But the effective scope of cross-examination and tone in which it is conducted are different impartial expert will have been chosen from a panel drawn up by the medical societies and he will be a recognised specialist in his field His impartiality is emphasised by the fact that he is paid out of special funds and not by the contesting parties Indeed, such a standing has been achieved by the impartial expert that a few American judges and lawyers are beginning to fear that his importance is over-emphasised and that his word is too readily treated as gospel

Some other results of the New York project are worth noting Often plaintiffs have been persuaded to abandon inflated claims for damages, but in other cases the independent medical report has convinced the defendant that the plaintiff's case was well founded Occasionally, examination by a specialist of high standing has strengthened the plaintiff's case by drawing attention to points overlooked by his own doctor The new method of taking evidence once again demonstrated that many doctors were slow to use radiological and other diagnostic techniques, and the New York Bar Association think that the result may be an improvement in the diagnosis of injuries " it is likely that the project will not only help in informing judges and juries of what doctors know (thus improving the process of legal fact-finding), but will go one step further and help the doctors themselves in discovering the truth (thus improving the basic process of medical fact-finding)"

The success of the project immediately raises the question whether a similar scheme could usefully be introduced in this country There can be little doubt that it would be of great value in the pre-trial stages Although many actions arising out of physical injury are already settled before trial, the use of independent medical reports would provide a more satisfactory basis for settlements The American lawyers, worked out their plan with the pre-trial conference in mind, but the fact that British law does not provide for this conference need not preclude the introduction of a similar scheme here Our courts have a highly developed system of pre-trial instructions, operating through the jurisdicgrowing tyranny of the large organisation which claims the exclusive right to speak for a particular group or calling, and to control the actions of its members It is therefore vital that the Royal Colleges and Corporations should remain free to express independent views, and to act or withhold action in any field of medicine including its relations with the State

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[1] e *Lancet* 1951 ii 483

[2] mpartial Medical Testimony a Report by a Special Committee of the Association of the Bar of th City of New York New York and London Macmillan P 6d

But I know that many members of the B M.A fully recognise this, and realise that any attempt by the Association to dominate rather than collaborate would not only fail, but seriously injure the status of medicine in this country Indeed the B M A Council in its report states that it "is satisfied that the decision to establish the Joint Committee was a right and wise one The committee has worked harmoniously and effectively" For that very reason many will share my regret at this attack upon the Royal College of Physicians, which must make it more difficult to maintain that cooperation in the Joint Committee and between the Joint Committee and the General Medical Services Committee, which some of us have worked hard to achieve

The Royal College of Physicians,
London, S W 1

W RUSSELL BRAIN

DEHYDRATION FROM TUBE-FEEDING

SIR,—Prolonged tube feeding requires a liquid diet of adequate calorie and protein content, some of the formulæ even provide what would appear to be an excess of protein (140 g or more daily) The production of osmotically active substances from one such preparation ('Complan') can be calculated as at least 1100 milliosmols per day, and the amount of water given with it, following the makers' instructions, may be as little as 1900 ml It seemed to us that this might require an osmotic performance beyond the capacity of the kidneys of some patients

In order to define the necessary osmolarity, we have given complan as a 20% solution to two healthy subjects Although neither subject became thirsty, and in neither did the plasma-sodium level rise, the urine osmolarity, calculated as 2 $(Na + K + NH_4)$ + urea, rose to 940 and 1120 milliosmols per litre, *this level might not be attained in patients* with impaired renal function Moreover the blood urea level rose in one subject from 33 to 63 mg per 100 ml in four days, and in the other from 28 to 61 mg per 100 ml in three days Both subjects became constipated on the low-residue diet

We do not of course, believe that blood urea levels of this order do any harm, but we record this finding to prevent such levels under similar circumstances being ascribed to renal insufficiency (the urea clearance in both subjects was normal) We would also question the need for so high a protein intake, and suggest that such regimes are potentially dehydrating Water depletion on high-protein diets has been reported by Engel and Jaeger,[1] and we have ourselves seen a patient whose plasma sodium level rose to 160 m eq per litre on this type of regime

We would question the need for régimes so high in protein content for tube feeding, especially for comatose patients who cannot complain of thirst and so draw attention to their dehydration As a practical measure, we would recommend giving smaller amounts of these feeds, making up the caloric deficit with glucose, and giving an ample allowance of water—sufficient to prevent thirst in the conscious patient

Department of Medicine
University of Manchester

OLIVER WRONG
D A K BLACK

FRESH MILK OR TABLETS ?

SIR —You mention (Feb 25) two difficulties in the supply of school milk—that of supplying remote schools with fresh milk, and the reluctance of milk suppliers to allow discount or to agree to competitive tenders

The opposition by the milk trade to competitive ten and the *formation of price rings* are regrettable, parti in towns where discount could be given without detr the trader's profit The supply of milk to village scho often less profitable to the trader, who has to supply a number of one third pint bottles and transport them l distances by a certain time each morning The probl greatest if the local authority stands out for a paste supply, which often means inducing a trader from a town undertake a long country round If traders tender for schools at the normal retail price of milk, the authority be receiving fair treatment, indeed some traders have helpful in supplying remote schools at little profit bec they recognise the importance of school milk to the comm and it would be unfortunate if they felt themselves to b included in the criticisms made by the Committee on Pu Accounts, who appear, as is so often the case with bod *reviewing administrative arrangements*, to be thinking ma in terms of towns

It would be even more unfortunate if anything we done to make supplies of pasteurised milk to rural scho more difficult to obtain than they already are I can believe that tablets, however alluring the fruit flavo are an entirely satisfactory substitute

County Hall,
Trowbridge Wiltshire

C D L LACEY

AFTER MENINGITIS

SIR,—*In your annotation of March 24* you expr concern at the tragic sequelæ of meningitis in childre and quote Desmit,[1] who, in the Hague, had a mortalit of 7%, and a failure rate (died or left with gross defect *of 22% in 114 cases*

It must come as a surprise to learn that, in this countr the over all mortality from meningococcal meningitis is 20 rising to 25% in the 0–4 age group[2] In the first year of l alone 550 deaths were attributed to meningococcal meningi in the years 1946–54 The fatality rate during this time h remained persistently high Judging from Desmit's experien it is not unreasonable to suggest that, with a mortality of 20 more than half the cases of meningitis in this countr eith die or are left with gross defects

With the present number of powerful antibiotic treatment should be satisfactory Early and accura diagnosis is essential It is possible that antibiotic a a double edged weapon A sequence of events no uncommon is for a practitioner to be called to see a chi in the early stages of a meningococcal infection, when th symptoms typically suggest an infection of the upp respiratory tract Oral penicillin is prescribed It absorption is irregular, and its passage through the bloo brain barrier in adequate amounts is doubtful Th infection is not killed, but smoulders on By the time th child reaches hospital permanent cerebral damage ma have occurred The classical picture of meningitis ma no longer be apparent, and further delay may occ before a diagnosis is made and adequate treatment give *It is customary for a lumbar puncture to be* carried ou only if there is a definite indication It should be a golde rule for a lumbar puncture to be done on all urge pædiatric admissions, *unless there is a definite* indicatio *against* (i e , if some other diagnosis is obvious) If th was done, unsuspected cases of meningitis would come t light, and delay be avoided

It is also essential that suspected cases of meningit should be admitted only to units which have a twent four hour pathological service, and where the cerebr spinal fluid can be examined, the organism identifie and the appropriate treatment carried out witho delay Meningitis is just as much an *emergency* as acu appendicitis, and a pathological laboratory is as essenti to the one as an operating theatre to the other No o would consider admitting a patient with acute appendici to a hospital without a theatre, yet there must be ma to a crush fracture caused by impaction against the glenoid margin at the moment of dislocation, or possibly to secondary flattening from repeated episodes In some series as few as 20% of cases showed this defect, in others they all had it This variation depended to some extent on the care with which the defect was looked for In abduction and external rotation this defect engages with the glenoid, and the joint may lose its stability and become dislocated

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[1] Engel F L, Jaeger C *Amer J Med* 1954 17, 196

[1] Desmit E M *Arch Dis Childh* 1955 30 415

[2] Report of the Ministry of Health 1954 part II p 18

Recurrent dislocation has for many years attracted he inventors of new operations Bearing in mind the asic abnormalities, it is not surprising that the only perations that have stood the test of time are those which produce some sort of buttress at the anterior glenoid margin It does not seem to matter much whether this is achieved by reattachment of the avulsed glenoid labrum or capsule or by the use of the tendon of subscapularis (the PUTTI-PLATT operation[6]), fascia lata (GALLIE), bone blocks from free grafts or a displaced coracoid process, or scar tissue (HIPPOCRATES used the cautery for this purpose) Simply to use the anterior approach ensures the formation of some scar tissue just where it is needed Those who believe in the importance of the humeral defect insist hat some loss of external rotation must be accepted o as to prevent the defect reaching the glenoid, and hat without this disability the patient is still in danger of recurrence While many patients regain a full range of movement after these operations, most are left with slight loss of abduction and considerable loss of external rotation DU TOIT and ROUX do not believe that this loss is necessary, they fix the avulsed labrum to the glenoid margin with the staples originally introduced by FOUCHE and proceed to remobilise the shoulder immediately after operation They claim that in this way full movement is rapidly regained, the period of postoperative disability is much shortened, and there is no danger of recurrence The use of staples is not without danger, they can pull out, and more than one has had to be removed as a loose body in the shoulder-joint It is however, a simple method which may appeal to those who have found that the suture work involved in any repair at the margin of the glenoid is not quite so easy as some advocates of this operation maintain It will still be some years before we can judge whether some restriction of movement must really be endured in order to guard against recurrence But however the repair work is done, most recurrences are due either to major violence that might well dislocate a normal joint or to technical faults that only greater care and experience will eradicate

Vomiting Sickness in Jamaica

FOR more than fifty years an often rapidly fatal illness called 'vomiting sickness' has been known in Jamaica Most of its victims are children between the ages of two and ten years, and they are always from the poorly nourished peasant class The onset is said to be abrupt, usually but not always with vomiting. and there is invariably a feeling of intense weakness Prostration soon follows, but there is no fever and no diarrhœa Recovery may be complete in a few hours, but often, after periods of semi-coma, the child lapses into deep coma, with twitching convulsions, and death

As long ago as 1916, SIR HAROLD SCOTT[1] suggested that the illness was caused by eating the fruit of the ackee tree (*Blighia sapida*) and it has often been called "ackee poisoning" Ackees are a favourite food in Jamaica, but are rarely eaten elsewhere The ackee tree bears handsome bright-red pear-like fruits which split when they are ripe, into three segments Within are three hard seeds, looking like black shiny acorns, each on top of a yellow fleshy arillus about an inch long It is this arillus which is cooked and eaten, it tastes like a fatty variety of roast chestnut, but it is even more appetising But while ackees are freely eaten everywhere in Jamaica, vomiting sickness is confined to a few peasants, mostly children Moreover, vomiting sickness may be sporadic, it may affect a particular family, or it may occasionally be epidemic but then only in the winter months December to March, and in certain localised areas Yet the distribution of ackees is island-wide and crops are eaten in other months Doubt was thus expressed that the ackee was the cause of vomiting sickness, though EVANS and ARNOLD[2] had prepared extracts from it which were toxic to animals Many other plants taken as "bush teas" were incriminated instead BARNETT[3] the Jamaican government's chemist, blamed certain yams which he found to contain, when immature, a toxic glucoside

Some observers even raised doubts about the existence of vomiting sickness as a separate disease they thought the term merely included a wide variety of conditions wrongly diagnosed, and after 1944 the Registrar-General of Jamaica ceased to record it as a cause of death In 1951 however there was an outbreak in the parish of St James (with a population of about 75 000) in which 151 people were affected and 32 died This revived alarm about the condition, and the Jamaican government voted a substantial sum of money for the investigation of the illness by the island's medical department, in collaboration with the University College of the West Indies, the work to be organised by DR CICELY WILLIAMS[4] It was soon apparent that most isolated cases of vomiting sickness had been wrongly diagnosed Then 4 out of 5 children of a family who had apparently been well and active were seen at the new University College Hospital they had had the characteristic abrupt onset of weakness and drowsiness with vomiting, and 2 were dead within a day STUART et al[5] found extreme hypoglycæmia (blood-sugar levels as low as 22 mg per 100 ml were recorded) in each of these 4 children and in 5 others who had the same typical illness This observation established the condition as a true clinical entity and laid the foundation for its logical treatment by prompt and large doses of glucose Biopsy and necropsy[6,7] showed fatty changes in the liver with almost complete absence of glycogen, and glycogen was replaced after successful glucose therapy Since the disease was thought to be due to an unknown ingested toxin which produced temporary enzyme block, probably inhibiting gluconeogenesis, the name "acute toxic hypoglycæmia" was proposed.

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[6] Osmond Clarke H J *Bone Jt Surg* 1948 30B 19

[1] Scott H H *Ann trop Med Parasit* 1916 10 1

[2] Evans K I Arnold L E *Trans R Soc trop Med Hyg* 1938 32 355

[3] Barnett W L Reports of Government Chemist, Jamaica 1943 and 1948

[4] Williams C D *Med Wom Fed J* April, 1954

[5] Stuart K L Jelliffe D B Hill K R *J trop Pediat* 1955 1 69

[6] Patrick S J Jelliffe D B Stuart K L *Ibid* p 88

[7] Hill K R, Bras, G Clearkin K P *W Indian med J* 1955 4 91

On the very important question of "settling down" you seem to suggest that this is largely unnecessary, because modern methods of treatment have shortened the period of hospital treatment I am quite aware of the difficulties of reintegrating the patient mentally or otherwise into the family after a lengthy stay, but I would like to emphasise what appears to be self-evident, though it does not seem so to all psychiatrists—that mental disorders, though sometimes treatable by physical means, are mental They can rarely be overcome in a rush, and certainly no problems of life can be solved by physical treatment

I think it is time that in psychiatry the rôle of the asylum and retreat were acknowledged For some time at least, the best treatment is the retreat, with or without spiritual help from the doctor or priest

West Hallam,
Derbyshire

D J SALFIELD

TEA IN THE OFFICE

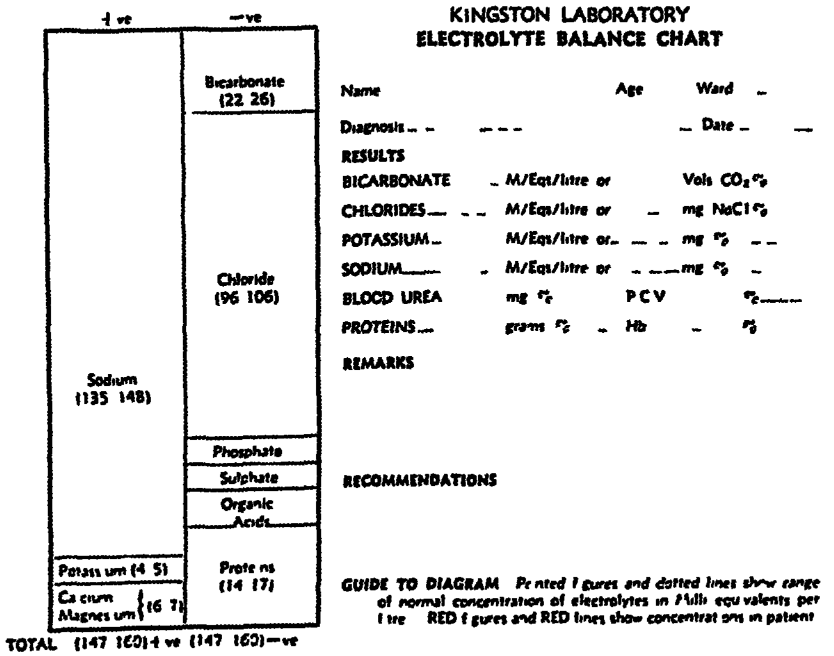
SIR,—Your issue of March 3 has been brought to our attention, with particular reference to "In England Now" and the tea-making equipment to be seen in a hospital general typist's office You may consider that we are oversensitive about this, but when one appreciates the totally inadequate canteen facilities for clerical staff in so many hospitals, the extra time these girls willingly work without recompense, and the lack of limelight which comes their way as compared with that shining on other hospital workers, the remarks printed can only be considered as an abuse of the restricted space accorded to you by the discontented typographers that week

Plymouth and District
Health Service Branch,
National and Local Government
Officers Association

ROBERT BEUL
J DAVIDSON

CONTROL OF WATER AND ELECTROLYTE DISORDERS

SIR,—The form presented by Dr Preedy and Mr Richardson (Feb 4) is designed for the use of house officers "who do not have time to understand or maintain complicated charts" It would, therefore, be a good practice for the laboratory to present all the facts of analysis in the most helpful way, and in an attempt to do this we have devised an electrolyte balance chart and diagram (according to Gamble) (see figure)


+ve
−ve
Bicarbonate (22 26)
Chloride (96 106)
Sodium (135 148)
Phosphate
Sulphate
Organic Acids
Potassium (4 5)
Proteins (14 17)
Calcium
Magnesium
(6 7)

TOTAL (147 160)+ve (147 160)−ve

KINGSTON LABORATORY
ELECTROLYTE BALANCE CHART

Name Age Ward

Diagnosis Date

RESULTS

BICARBONATE M/Eqs/litre or Vols CO$_2$%

CHLORIDES M/Eqs/litre or mg NaCl%

POTASSIUM M/Eqs/litre or mg %

SODIUM M/Eqs/litre or mg %

BLOOD UREA mg % P C V %

PROTEINS grams % Hb %

REMARKS

RECOMMENDATIONS

GUIDE TO DIAGRAM Printed figures and dotted lines show range of normal concentration of electrolytes in Milli equivalents per litre RED figures and RED lines show concentrations in patient

The alterations from normal of each ionic compartment is indicated, and in the space for recommendations the site and amount of fluids required for treatment may be indicated Although this is combined with a visit to the bedside by the pathologist, it is our experience that in many cases it is only after the chart has been completed that the clinical and biochemical pictures tend to fall together and the further treatment becomes clearer Our list of normal values may not entirely coincide with all those in other hospitals but we have given figures most nearly fitting 95% of the normals, found by the methods we use

Pathological Laboratory,
Kingston Hospital, Surrey

P DIGNALL

SPONTANEOUS HYPOPARATHYROIDISM WITH MEGALOBLASTIC ANÆMIA

SIR,—The case reported by Dr Hurwitz (Feb 4) would appear to be the second example of this extremely rare combination and not the first as Dr Hurwitz believes An identical case was reported by Reisner and Ellsworth [1] in America

The American case has many features in common with that reported by Hurwitz The age at onset and the sex were the same, and in both girls the physical build was suggestive of pseudohypoparathyroidism although this was proved not to be the correct diagnosis

The American case sheds further light on the nature of the megaloblastic anæmia Unlike the patient of Dr Hurwitz this girl had at no time received any anticonvulsant drugs so phenytoin sodium can be completely excluded as a possible cause Reisner and Ellsworth showed that the anæmia in their patient was unaffected by *oral* vitamin B_{12}, but that the addition of intrinsic factor to the vitamin B_{12} given orally produced a reticulocyte peak of 23 7% after eight days treatment This is presumptive evidence that the patient was lacking in intrinsic factor and was in fact suffering from pernicious anæmia

Manchester

S SHUBERT

UTERINE DYSFUNCTION DURING LABOUR

SIR,—I should like to comment on Dr Cramond's use of an inventory as described in his letter (Jan 28)

The "lie" scale from the Minnesota multiphasic personality inventory was incorporated with 65 other items (whose source was unspecified) and was scored as it is in the M M P I This procedure is of very doubtful validity It is impossible to know in advance the effect of lifting a scale from the context within which it was standardised, the effect might be to distort the scale so that the original scoring standards become inappropriate It seems, then, that Dr Cramond should either regard his inventory as a new test and standardise it anew, or else use the whole M M P I and score the "lie" scale according to Hathaway and McKinley's tables

There is a danger in the latter method, however Hathaway and McKinley standardised the test on Americans Dr Cramond has tested Scottish women, and it is impossible to say whether a test standardised in one country will be valid in another Dr Cramond's results suggest that in this case it is not In two separate investigations a third of his patients had significantly high "lie" scores This is a very high proportion, and one must ask why In view of the large numbers tested, chance can be ruled out as a determining factor This leaves two alternatives first, that Dr Cramond's group was not a normal one but contained a large proportion of women who were mentally ill, and second that the American scoring of the "lie" scale is not applicable to the answers given by Scottish women The second explanation seems the more probable

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[1] Reisner D J, Ellsworth R M Ann intern Med 1955 43, 1116

CARDIAC MANIFESTATIONS OF POLIOMYELITIS

CARDIOVASCULAR collapse is a serious complication of bulbar poliomyelitis Hildes et al[1] point out that it usually develops within forty-eight hours of the onset of bulbar paralysis High pyrexia and tachycardia are common Most patients have a normal blood-pressure until shock begins, when the pressure may fall precipitously or over a period of some hours On the other hand, there may be transient hypertension before the stage of shock Pulmonary œdema is usually a notable feature, the onset of which commonly precedes death by a few hours Hypertension is not confined to acute collapse, Weinstein and Shelokov[2] noted prolonged elevation of the blood-pressure in 7% of all their patients, most of whom had bulbospinal involvement

Electrocardiographic changes have been recorded in poliomyelitis in from 13 to 77% of patients Fox et al[3] described changes in 32% of 189 cases, they believe that E C G abnormalities are as likely to appear in patients with spinal lesions only as in those with bulbar involvement They found ST depression and/or T-wave changes in 90% of patients with E C G abnormalities—a figure comparable with that of most observers Changes in conduction, whether supraventricular or ventricular were unusual

It was not realised until 1942 that the heart could be directly affected by poliomyelitis, Saphir and Wile[4] then demonstrated lesions in the myocardium in 6 out of 7 fatal cases They found extensive perivascular foci of lymphocytes and polymorphs throughout the myocardium and in the subendocardial tissue Monocytes were sometimes present and there was multiplication of adventitial cells Occasionally inflammatory cells invaded the interstitial tissue diffusely, although degenerative changes in the muscle fibres were always mild These features have since been confirmed by others, and it is now generally recognised that myocarditis does develop in some epidemics of poliomyelitis Weinstein and Shelokov[2] believe that the milder form of myocarditis is due to hypoxia, while the more severe kind may be the result of actual invasion of the heart by the virus, but there is little evidence to support such a distinction

The significance of myocarditis as a cause of clinical signs or of death is hard to assess Hildes et al[1] report the necropsy findings in 20 cases of cardiovascular collapse, in all of which there were medullary lesions varying from mild damage to diffuse involvement with focal destruction Although Baker and his colleagues[5] believed that destruction of the anteromedial reticular substance of the medulla was responsible for the onset of circulatory failure, Hildes et al found that the vasomotor centre was often involved in patients dying of causes other than poliomyelitis The invariable presence of medullary damage and the occasional finding of transient hypertension in both fatal and non fatal cases led them to suggest that severe vasoconstriction, arising as a result of the medullary lesion, leads to cardiovascular failure and pulmonary œdema Since myocarditis was present in only 14 of their 20 patients, they do not think it is likely to be the basis of the condition, although its presence would undoubtedly aggravate it The myocarditis is unaccompanied by suggestive clinical signs, it gives rise to no characteristic E C G abnormalities, and only a few cases with E C G changes are subsequently shown to have cardiac lesions

Our knowledge of these features of poliomyelitis and the assessment of their significance is far from complete Hypertension and cardiovascular collapse are probably due to involvement of the vasomotor centre, and myocarditis is probably incidental and not a basic factor in the clinical picture The E C G changes are non-specific and of the same type as those found in other diseases with systemic overtones they do not indicate the presence of myocarditis

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[1] Hildes J A, Schaberg A, Alcock, A J W *Circulation* 1955, 12 986

[2] Weinstein, L Shelokov, A *New Engl J Med* 1951 244, 281

[3] Fox, M J Sennett L, Kuzma, J F *Lancet* 1953 ii 353

[4] Saphir O Wile S A *Amer J med Sci* 1942 203 781

[5] Baker, A B, Matzke, H A, Brown J R *Arch Neurol Psychiat* 1950, 63, 257

ATHEROSCLEROSIS IN THE LOWER LIMB

THE occluding mass in the lumen of an atherosclerotic artery is part atheroma, part thrombosis, and the thrombosis may develop in several layers until obstruction is finally complete It has been known for some time that the common site for the initial block in the arteries of the leg is Hunter's canal, particularly at its lower end near the opening in adductor magnus Why this should be so is not certain although Lindbom[1] suggests that it is intimal hæmorrhage which precipitates the eventual thrombosis and that this is more likely at places where the artery is tethered and immobile so that angulation or traction strains from joint and muscle movement can "fracture" the intima From the area of primary occlusion a secondary thrombosis spreads proximally, and its extent is determined by the calibre of the branches leaving the artery thus the profunda femoris becomes of great importance and its muscle branches often provide the main collateral supply It usually remains patent and remarkably free from disease Less often the popliteal artery is the site of initial thrombosis, which may spread in either direction to the femoral or tibial arteries

The degree of ischæmia caused by occlusion of a large artery depends on the volume and pressure of the collateral flow When this is efficient, as in many lesions involving only a short segment, the patient may have very few symptoms and the flow through the main artery beyond the block is almost normal Often, however, the blood-supply to the feet is inadequate and the clinical picture of acute ischæmia results There are several possible causes general atherosclerosis may make the collateral vessels stiff and unyielding so that they can no longer enlarge, big collateral arteries—for example the profunda femoris or the geniculate anastomoses—may be involved in the clot, or the smaller vessels distal to the main occlusion may be blocked, thus adding a second and disastrous barrier to the peripheral flow

Arteriography has few complications and it has enabled surgeons to follow the anatomical variations of atherosclerosis with considerable accuracy Much of this important information has been reviewed by Mavor,[2] who found the femoral artery to be the site of occlusion in 104 of his 142 patients with atherosclerosis and calf claudication This precise knowledge of the spread of the disease has more than an academic interest since the success of surgery largely depends on the site and extent of the thrombosis In many of Mavor's patients direct surgery was contra-indicated either by the extent of the arterial lesion or because of the patient's general health There is little point in eliminating claudication in a man who has angina after walking 100 yards Mavor claims, however, that local palliative surgery would have been justified in 59% of his patients There are many direct and indirect procedures available which will increase peripheral blood flow When the small distal vessels below the knee are grossly involved a lumbar sympathectomy improves the skin circulation and nutrition but will not improve exercise tolerance Occlusions in the superficial femoral artery are probably best treated by the by-pass operation[3] which is designed to leave the already established collateral circulation unimpaired Thrombosed large-bore arteries, such as the aorta or iliacs, are best resected and the arterial pathway reconstituted with a synthetic or a homologous artery graft The choice of the great majority, who do so voluntarily, be paid cut price rates?

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[1] Lindbom A *Acta radiol Stockh* 1950 suppl 80, 1

[2] Mavor, G E *Brit J Surg* 1956, 43, 352

[3] See *Lancet*, Jan 14, 1956, p 93

Another fact, well known to the Ministry, is that only a few whole time specialists in general medicine and geriatrics will average more than 30–40 visits a year, if that The whole time specialist who does 33 a year, for which he receives 4 guineas, is actually in pocket, after paying tax and superannuation, £2 3s at the bottom of the S H M O salary scale and £1 8s at the top of the consultant This works out at the princely sum of from 1s 3d to 10d a visit!

The cost of running a car without adequate mileage allowances and income tax relief is fast becoming prohibitive Purchase tax on small cars is up by £30–40 and cost of insurance, tyres, repairs, and so on has risen or is rising steeply Telephone charges are also up

The specialist who is on call for emergency visits must travel everywhere by car and keep his telephone constantly attended These visits, too, are frequently wanted at inconvenient times, and encroach on the specialist's scant leisure Under the new agreement, he must do a considerable number (or none at all) before he even ceases to be heavily out of pocket on each Few general practitioners will feel like calling him out under these circumstances

So in specialties like pathology, radiology, chest diseases, and psychiatry, where the majority of specialists are whole time, patients will be deprived of a specialist's opinion in their homes, and continue to be needlessly admitted to hospital beds, costing 20 guineas or so a week

It has long been evident (and the agreement just mentioned bears out the point) that the manner in which the negotiations about terms and conditions of service are at present carried on in Whitley B Medical Committee is greatly to the disadvantage of whole time specialists

Firstly, there is only 1 whole time regional specialist against 15 part time and a professor from the teaching hospitals, on the staff side, which allows the management side to play off part time interests against whole time In fact when part time specialists' mileage allowances were raised in 1952 regional boards were empowered to cut those of whole timers

Secondly, the grave defect of the Whitley machinery is that the staff side cannot take any claim, however just, to arbitration without the consent of the management side—a right denied to no other grade of health service employee Although the management side has openly acknowledged the injustice done to whole time specialists, it has consistently refused, during four years of negotiations, to either remedy the injustice or allow their claims to go to arbitration

At present the whole time S H M O is earning the equivalent of the lowest paid group of general practitioners pre war, who (according to the Spens report) could not give of their best to their patients because they were harassed by financial worries

The whole time consultant is now paid at the same rate as specialists in second and third rate municipal hospitals pre-war, and critics of whole time service never weary of telling us what conditions were like in those institutions

Whole time specialists do well over a third of the consultant work in the N H S, and if their status continues to be down graded the standard of their work will deteriorate *pari passu*—no political chicanery can disguise or alter the fact

Even Mr Macleod grudgingly admitted, in reply to questions in the House that whole time specialists are unfairly treated, but added that this was a matter for the appropriate Whitley Council' As that excuse has had its day, is his successor prepared to allow the whole time specialists' claims to go to arbitration? What would he have to fear from such a step, if he believed that these claims were being fairly dealt with at present? Now that the claims of whole time specialists have been endorsed by the Guillebaud Committee (Report para 404 "We are also of opinion that it is undesirable that the financial arrangements relating to the consultant service should be such as to provide financial inducement to a consultant to apply for a part time rather than a whole time appointment") the Minister of Health cannot any show of justice, refuse either to meet them or to al them to go to arbitration

It has been suggested by my colleagues and m that the formation of a whole time specialists g comprising S H M O s and consultants, under the of the B M A, would enable us to press our claims vigorously, and letters in support of this view h poured in from all over the country

Farnborough Hospital,
Kent

LEO GILCHRIST

PULMONARY EMBOLISM AND 5-HYDROXYTRYPTAMINE

SIR,—Your annotation (Feb 4) comments on an experiments showing that the vascular effects of hydroxytryptamine are antagonised by the "a adrenaline" drug, 'Dibenamine' You suggest that t drug might possibly be of therapeutic use, but that still in an experimental stage

This compound was the first member of the β haloalk amines found to have "anti adrenaline" activity, and action has been very thoroughly investigated It antagonis the excitor effects of adrenaline, noradrenaline, and ma other sympathomimetic amines[1] Replacing one benz group by a phenoxyisopropyl group results in a benzyl chlorethylamine hydrochloride, 'Dibenyline' ('Dibenzyl or 688A in America), which is well tolerated and is ora active and has been subjected to more extensive clin investigation It has been found useful in the treatment peripheral vascular disease and allied conditions, and is n available for clinical use

Further clinical investigations have been suggested in various other vascular conditions, in hypertensive stat including eclampsia, in migraine, and in chilblains, in wh some of the following factors are thought to be implicated (1) increased sympathetic activity, (2) increase in circulat pressor substances, (3) increased vascular sensitivity t pressor substances, (4) conditions in which increased bl flow might result from reduction in normal sympathetic to Some of these investigations are being undertaken currently

Smith Kline & French,
123 Coldharbour Lane,
London, S E 5

KENNETH CARTER
Medical director

MESTINON IN CEREBRAL PALSY

SIR,—From time to time it has been claimed th cholinergic substances benefit some cases of cerebral palsy Neostigmine has been used with varying succ it has the disadvantage that it may produce gastro intestinal side effects necessitating the concomitant u of atropine A new compound 'Mestinon' (the dimeth carbamic ester of 1-methyl-3-hydroxy pyridinium bromide) is claimed to be longer acting and to have few visceral side effects than neostigmine I found that in children with cerebral palsy mestinon, given by mouth half an hour before a physiotherapy session, seemed to enhance the value of that treatment for those who main disability was spasticity, and to a lesser extent for those having athetosis with tension Those with ataxia derived no benefit

A controlled trial was then carried out over a peri of three months

It was decided to test the drug only in "spastics," and 32 children were paired as closely as possible on the bas of age, type of disability, and severity Some of the children were in a special residential unit and others attended as outpatients One child of each pair received 20 mg of mestinon twice daily, and the other received an inert tab of identical size The identity of the active tablet was n revealed by the manufacturers until the end of the trial The impressions of the physiotherapist were recorded at each attendance, as were the impressions of the parent of the day cases and the school teachers of the residential gr

Of those receiving mestinon, 9 were considered to ha improved more quickly than they would have without tab

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[1] Goodman L S Gilman A Pharmacological Basis of Th peutics New York 1955

Public Health

MALARIA AND THE THAMES *

W D L SMITH
M.B St And, D.P.H., D.T.M & H.
REFINERY MEDICAL OFFICER KENT OIL REFINERY LTD, ASSISTANT PORT MEDICAL OFFICER, PORT OF LONDON HEALTH AUTHORITY

THE early history of endemic malaria in this country can be traced in the writings of kings dictators, essayists, doctors and poets The Venerable Bede, in his Ecclesiastical History written in Latin and boldly translated into Anglo Saxon by King Alfred draws attention to a prevalent long-continued fever, which he calls "lencten adl" ("spring ill") The habit of the parasites to lie dormant during the winter and become active in the spring was therefore familiar to the early Anglo Saxons This high spring incidence was, of course, characteristic of benign tertian malaria, the parasite undergoing the pre-erythrocytic cycle in the liver of the affected person during the latent period That the cause was not a large number of fresh infections in the spring can be shown by comparing the monthly figures for malaria in man with the density of infected anopheles The latter reaches a peak in the late autumn many months after the incidence of malaria passes its maximum James (1929)

It is very difficult to estimate the extent of malaria during early times because the term "ague" was applied indiscriminately to many fevers Historians warn us against assuming that the hot agues the new agues, and the epidemic agues of the 17th century necessarily refer to malaria (Creighton 1894) The Oxford English Dictionary pays little heed to this warning, and without reservation interprets Chaucer's ague as malaria Shakespeare uses the word ague both medically and metaphorically, and occasionally mistakenly When Macbeth says of the force encamped before his castle—'here let them lie till famine and ague eat them up'—he undoubtedly referred to that scourge of armies typhus or spotted ague and not malaria Similarly the ague which paralysed Cromwell's army in Ireland was no doubt typhus However, the essayist Butler, in Stuart times, is correct in his reference to malaria When the lady in *Hudibras* rejects the advances of the Puritan knight, telling him that love is fickle, first hot but soon turning cold she says 'Tis but an Ague that's reverst, Whose hot fit takes the patient first" Butler could use this metaphor in full confidence that its point would be appreciated by his readers, so familiar was everyone with the successive stages of an attack of malaria in those days Today a footnote would be necessary to explain its significance to the ordinary English reader

When Sir Walter Raleigh lay in the Tower of London awaiting execution, relapses of malaria troubled him sorely, and just before the grim procession set out for the place of execution he prayed fervently that he might not be seized with an ague fit on the scaffold lest his enemies should say that he had met his death shivering with fear By a strange twist of fate, King James I, who was responsible for Raleigh's execution, died in a fit of ague Sydenham well known for the accuracy of his observations described malaria or intermittent fever as he called it, in epidemic form between 1661 and 1664 This epidemic was probably precipitated by the extraordinarily hot summer weather of 1661, which lasted through the autumn and winter into the new year, and to which Samuel Pepys refers in his Diary

During the 18th century the Lambeth and Westminster marshes were notoriously associated with malaria but not all the malaria which developed in London was contracted there Malaria had long been accepted almost as an occupational disease among the nomadic hop-pickers of Kent, many of whom returned to London at the end of the season Malaria was described by Daniel Defoe when he referred to the London gentry who went shooting in the Essex marshes and often returned with an Essex ague on their backs which they found a heavier load than the fowls they had shot The first person known to have used the word malaria meaning 'bad air' was Horace Walpole While staying in Rome in 1840 he wrote to Thomas Grey in London describing the local disease as "a horrid thing called the mal'aria, which comes to Rome every summer, and kills one"

The last of the extensive epidemics in this country occurred between 1857 and 1859 coinciding with two very hot summers That malaria was common in Westminster may be gathered from the records of patients treated in St Thomas's Hospital between 1850 and 1860 These show that 1 in 20 patients had malaria In Gravesend Hospital at that time 30% of the patients were diagnosed as having malarial fever The Registrar of Strood wrote in 1857 'an unusually hot summer has operated still more to make the marshes and adjacent districts intensely unhealthy Many deaths have been registered from intermittent fever directly or indirectly (McArthur 1951)

Incidence and Distribution in England

The first accurate assessment of the incidence and distribution of malaria in England became available in Whitley's report as medical officer of the Privy Council in 1863. Whitley's list of places where malaria was known to be endemic corresponds closely to that for the ten years ended 1926 (James 1929 and figs 1 and 2) In other words, the areas which were potentially malarious had changed little in seventy years and in terms of mosquito bionomics, only in those parts of England could the transmitting anopheles thrive The Thames estuary, and particularly the north coast of Kent, have probably been the most important focus of endemic malaria for the past century There was a cynical

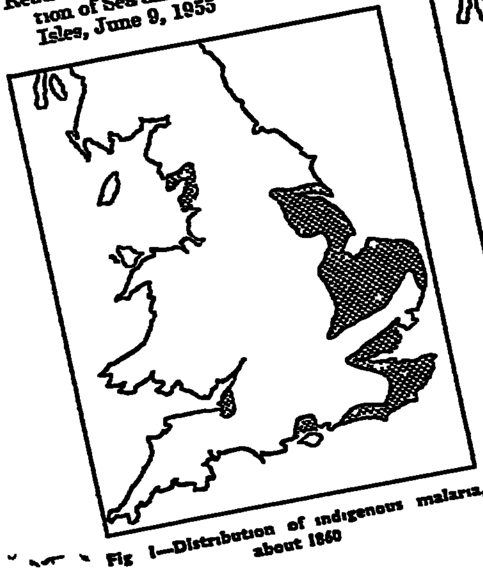

Fig 1—Distribution of indigenous malaria, about 1860

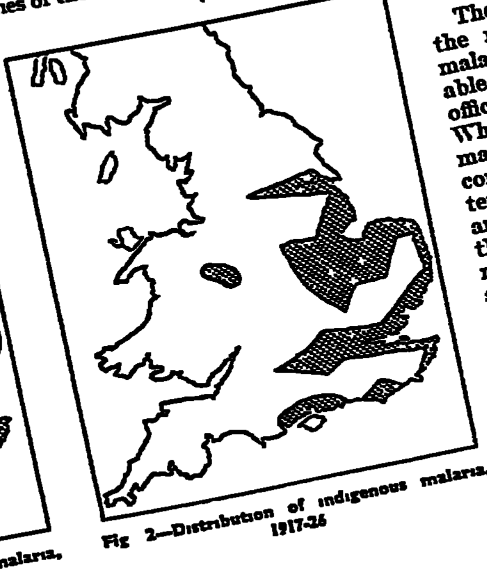

Fig 2—Distribution of indigenous malaria, 1917-26

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* Read at the annual meeting and conference of the Association of Sea and Air Port Health Authorities of the British Isles, June 9, 1955

Recently I examined the body of a man, aged 77, who had been treated with stilbœstrol for prostatic cancer The coronary arteries showed minimal atherosclerosis, in the aorta, though still atherosclerotic and calcified, many of the atherosclerotic ulcers were overgrown by a thin layer of endothelium, presumably the first stage towards healing

Dietetic studies have shown that atherosclerosis is associated with excess fat in the diet[4] Prolonged treatment with anticoagulants recanalises thrombosed arteries[5] which become functionally active[6] It may be possible to "pre select" candidates for coronary disease[7], often premonitory signs are noticed[8] These observations suggest that for these patients as well as those with coronary disease a strict fat-free diet, prolonged anti coagulation, and stilbœstrol therapy are worth considera tion not only as treatment but also as a preventive measure in the "pre selected" and in those who have had premonitory symptoms The possible side effects of stilbœstrol must of course be borne in mind

Pathology Department,
Worthing Hospital

R AIDIN

AN UNUSUAL CASE OF SHINGLES

SIR,—Dr Jackson described last year[9] a case illustrating the long time which may elapse between the onset of herpetic pain and of the eruption, and the diagnostic confusion that may arise in the interval In the following case the site of the lesion was unusual, and the neurological features were more prominent than the dermatological

A businessman and churchwarden, aged 61, was seen on a Saturday evening, complaining of a symptom he said he had never had before—constipation—which had lasted for four days From the Tuesday to the Thursday he had passed no urine Despite this he had experienced no pain, but had noticed tightness and distension of the lower abdomen, which had caused him surprisingly little alarm On the Friday, micturition had gradually become re established, but his anxiety remained on account of his failure to defæcate On examination there was a small area of crusted herpetic lesions, measuring 2 in by 2 in, over the sacrum in the *dermatome supplied by segments S2 and S3*

The inference was that an attack of herpes zoster involving the lumbosacral posterior nerve root ganglia had interrupted the sacral reflex arc, resulting in acute retention of urine and constipation due to the unopposed action of the lumbar sympathetic fibres In addition, interruption of the afferent fibres had disturbed the sensory component of the reflex, as in tabes dorsalis, so that the patient had been unaware of the degree of distension of the bladder, and had had no pain Following explanation and reassurance, function returned to normal in the next two days

London S E 25

M KEITH THOMPSON

ERYTHEMA MULTIFORME EXUDATIVUM

SIR,—Erythema multiforme exudativum crops up only a few times in the experience of those working in general medicine The extensive and severe type which involves at once the skin, conjunctivæ, buccal mucosa, genitalia, and urethra is rare even in skin and infectious disease wards In the following case, in which all those sites were affected, there was good reason to believe that the renal parenchyma and the gastric mucosa were also involved

A married woman aged 73 who had been taking no drugs began on Dec 1, 1954 to have back pain malaise, and anorexia The symptoms continued, and on Dec 8 her throat and eyes became painful The mouth gums vulva and inner surfaces of the eyelids were ulcerated and produced a seropur exudate On Dec 10 she was admitted to this hospital u the care of Dr Emyr Jones, after the onset of pain hæmaturia, and what was thought to be a purpuric r in its early stages The epigastrium, right hypochond and right loin were tender There had been no pre abdominal pain The next day the rash was typical o bullous erythema multiforme The frank hæmaturia cea but albumin and many red cells and granular casts per in the urine The abdominal pain was relieved by milk a alkalis, although it was painful to swallow even fluids D comfort was maximal for about four days, before the ra and mucosal lesions began to improve on palliative treatm only The urine became normal, but the abdominal sympto continued longer A barium meal and radiograph on Jan 1955, showed a small gastric ulcer on the lesser curve A intravenous pyelogram on Jan 13 showed good bilate excretion of dye Before discharge the patient had abdominal symptoms *The barium meal was repeated o* July 22, when no ulcer could be seen

Caernarvon and Anglesey
General Hospital Bangor

C F HINGSTON

HÆMATEMESIS

SIR,—Mr Brandon's article last week is most interest ing, but there are no controls, and no actual evidence that the patients were benefited by the drugs give Would simple washing out of the stomach be equally effective?

Crichton Royal, Dumfries

J G BANCROFT

SIR,—In his article last week, Mr Brandon revive the adrenaline washing of the stomach, previously out lined in Hamilton Bailey's *Emergency Surgery* He i the first, however, to stress the importance of using a adrenaline 'Stypven' mixture as a diagnostic therapeut test

His paper is a milestone in the treatment of hæmatem esis The reason for my saying so is that I know that t method works Only limitation of opportunity, and du and pensionable ears, have prevented me from carryin out an investigation on a larger scale

The duty surgeon faced with hæmatemesis in a fre hly admitted case has to consider whether the blood come from (*a*) chronic gastroduodenal ulcers, (*b*) acute gastric erosions, or (*c*) œsophageal varices Adrenaline 1 200,000 lavage of the stomach will control bleedin from gastric erosions, because the blood is coming fro capillaries To set up a series of five test tubes and empty into them successive half hourly washings i a satisfying and dramatic demonstration of the efficacy of this treatment in cases of capillary hæmorrhage I have not myself used stypven, but I can see no contra indica tion to its use Unlike Mr Brandon, I would empha e that hæmorrhage from a *gastrojejunal anastomosi can* be controlled by this method Its success depends on the size of the bleeding vessel

If successive washings become less and less blood stained, conservative treatment is strongly indicated An operation may do no good The vast number of negative laparotomies for bleeding ulcers could be avoided by the knowledge derived from preliminary adrenaline lavage Equally, persistent bleeding after adrenaline lavage is a definite indication for surgery, *because th* bleeding must be from a sizable vessel This test ma well be more valuable than routine gastroscopy, becau a final and definite decision for or against operation ma be obtained within two to three hours of admission

In addition to this routine test for hæmatemesis I would suggest the regular passage of a balloon into th stomach The mild pressure exerted when it is pulled up against the cardia will help to control œsophageal hæmorrhage, and thus help to differentiate betwee bleeding of gastric and œsophageal origin Many a Miller Abbott tube lying fallow in the drawers of surgical wards could usefully be shortened *to a length of 3 fe* and used to control hæmorrhage, and transmit adrenaline camps who had not served overseas By the end of 1918 50% of the local population of Grain had contracted malaria, and in many of the old wooden houses particularly near the sea, it was common in a family with 5 or 6 children to have 3 or 4 cases of malaria A feature of this epidemic, which confirmed the local and domestic habits of the insect vector, was that in towns where outbreaks occurred patients were often found to be neighbours Many of the infections among children were not diagnosed for many days or even weeks, and this was one of the most important contributory factors in the large number of cases in Kent in 1917 and 1918 Of the 481 confirmed indigenous cases during this period, 82% occurred in Kent (Shute 1949 and table III)

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[4] *Lancet* 1953 ii 1121
[5] Wright H P Kubik M M Hayden M *Brit med J* 1953 i 1021
[6] Snow P J D Morgan Jones A Daber K S *Brit Heart J* 1955 17 503
[7] Gertler M M Garn S M White P D *J Amer med Ass* 1951 147 621
[8] Harris K *Brit med J* 1955 ii 874
[9] Jackson R S *Lancet* 1955 i 52

Malaria became compulsorily notifiable under the Public Health, Pneumonia, Malaria, and Dysentery regulations which were introduced in 1919 and amended in 1926

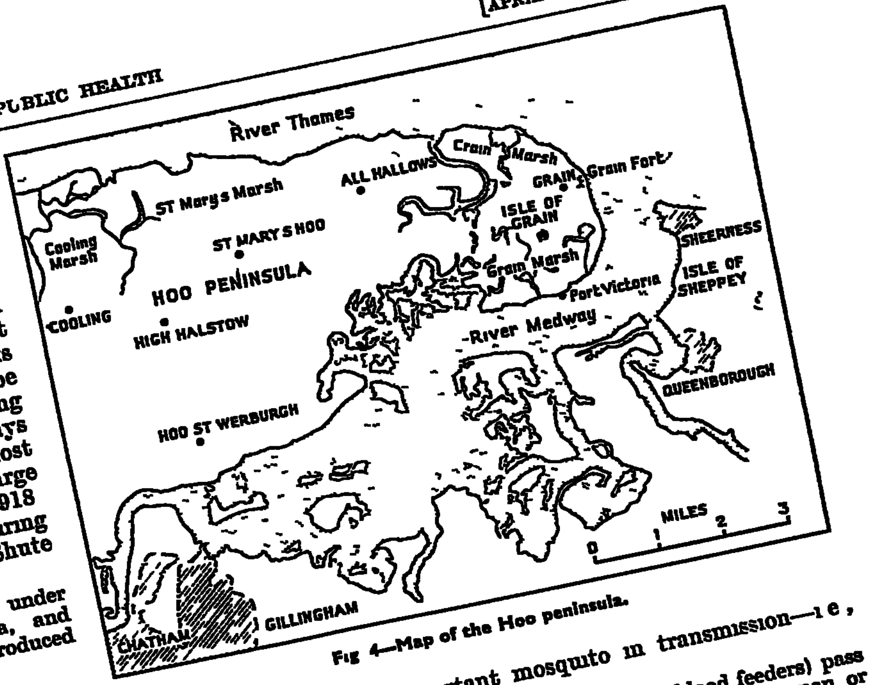

Fig 4—Map of the Hoo peninsula.

The Parasite and the Mosquito

Between the first and second world wars great advances were made in our knowledge of the transmitting anopheline mosquitoes in this country and of the causal parasites, and I will briefly review that knowledge against the background of the Thames

The characteristics of each of the 4 species of parasite show why all the indigenous malaria in this country is due to *Plasmodium vivax*

The tropical strains of *Plasmodium falciparum* are not capable of being transmitted by the English anopheles, and, although the European strain can be transmitted under artificial conditions, the temperature requirements for their development in the mosquito are rarely fulfilled in this country Infections due to *Plasmodium ovale* are comparatively rare, and when they occur they are always self limiting and seldom relapse Although relapses are most persistent in quartan infection caused by *Plasmodium malariæ*, there are few gametocytes in the blood and transmission is infrequent, except when mosquito density is extremely high Lastly, and most important, relapses occur in 50% of cases of benign tertian malaria caused by *Plasmodium vivax* (Shute 1945), and the parasite develops in the mosquito at temperatures as low as 60°F It would appear therefore that only in benign tertian malaria is there a parasite with all the qualities necessary to survive in England

TABLE III—CASES OF INDIGENOUS MALARIA NOTIFIED

County	1917	1918	1919	1920	1921	1944	1945	1946	1947	1948
Kent	198	72	89	25	10		3	3	1	2
Essex	6	6	5				1			
Surrey	2					4		1	1	1
Suffolk	3	4		1		3			1	
Hampshire	6	4	2	1			2			
Sussex		1								

It is possible that in olden days several species of mosquito transmitted malaria, *A plumbeus* breeds largely in holes in tree-trunks or large branches, and may have been a vector when large parts of Kent and Essex were covered with forest There were 2 cases in 1953 of indigenous benign tertian malaria in Lambeth which were thought to have been transmitted by this species of mosquito (Shute 1954) However, in recent years, since the mode of transmission of malaria has been known, there would appear to be only one important mosquito in transmission—i e , *maculipennis atroparvus*

The adult females (which are the only blood feeders) pass the greater part of their lives indoors, either in human or animal houses Once fertilised, the female mosquito remains so for the rest of her life and can begin the next spring's generation of mosquitoes quite independently of the male (Shute 1945) The female requires a blood meal to allow her ovaries to mature (which takes two to six days) and she prefers animal to human blood When her ovaries mature, she leaves the house and lays her eggs in water—preferably brackish water The coastal marshes of the Thames estuary, with their scatter of farms and dwellings are ideal breeding-grounds for the anopheles, and the age old practice in rural Kent and Essex of keeping one or more pigs in dark, warm, poorly ventilated buildings provided ample food and shelter The mosquitoes' preference for animal blood was appreciated by the owners of small holdings, who often used to arrange their pig sties in circles round their houses If there are no animal houses to provide the necessary food and shelter, the mosquito will seek them elsewhere, and a bedroom offers a suitable alternative, especially if overcrowded These feeding habits probably explain the increased incidence of malaria among small children in the Kent epidemic of 1917–19 The female mosquito tends to remain indoors in the late summer, when she has become sexually liberated and has no need to lay eggs, it is then that the danger of several human infections in one house is maximal It is impossible

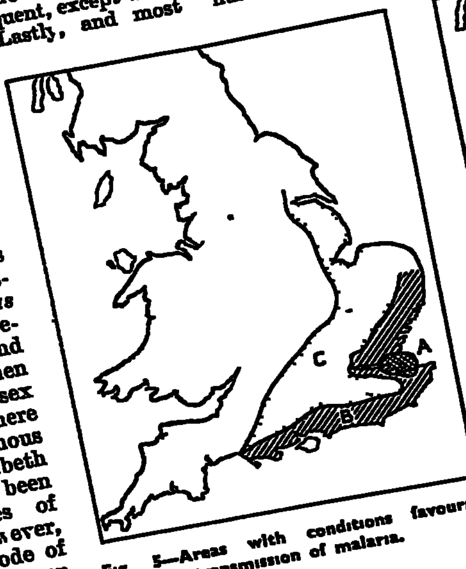

Fig 5—Areas with conditions favouring transmission of malaria.

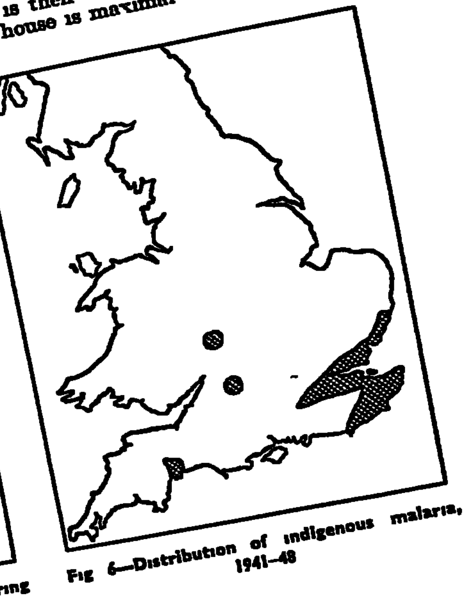

Fig 6—Distribution of indigenous malaria, 1941–48

At first sight the table seems to confirm Dr MacIver's assumption, especially if we consider the first year of life But the difference between the vaccinated and unvaccinated group is not statistically significant, and so we cannot assert that smallpox vaccination protects in any degree against paralytic poliomyelitis We believe that Dr MacIver's observations do not allow any conclusions as long as his material is not statistically proved

These findings are to be published in detail in the *Wiener medizinische Wochenschrift*

Bundesstaatliche
Impfstoffgewinnungsanstalt
Vienna

K BERGER
F PUNTIGAM

STREPTONIVICIN

SIR,—As Mr Lees has remarked (March 17), albomycin and streptonivicin ('Albamycin,' Upjohn) are entirely different compounds Detailed information on streptonivicin can be found in a series of publications from the Upjohn Company[1] By agreement between the co discoverers, the Upjohn Company and Merck and Company, the generic name streptonivicin has been abandoned in favour of novobiocin

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U S A

CHARLES G SMITH

PLASMA FIBRINOLYTIC ACTIVITY IN CIRRHOSIS OF THE LIVER

SIR,—I would like to congratulate Dr Kwaan and his colleagues on their extremely interesting papers (Jan 21) It seems opportune to mention the results obtained eighteen months ago from an investigation for abnormal fibrinolytic activity in 6 patients with hepatic cirrhosis under the care of Dr Sheila Sherlock at the Postgraduate Medical School of London

Firstly, however, I am a little disappointed to find that Dr Kwaan and his colleagues make no mention of using a low temperature technique between obtaining blood and setting up their tests, especially in the case of their healthy controls

The investigation of spontaneous fibrinolysis has been bedevilled by the lability of the factor responsible, which lability was first reported by us in 1952[2] and was confirmed in 1953[3] *Until then fibrinolytic activity had not been found* in the blood of healthy people at rest, but had been noted only after severe stress[4] Once we had discovered that the fibrinolytic factor is temperature labile in unclotted blood and plasma, we demonstrated considerable fibrinolytic activity in blood taken from healthy people at rest[5] Later we showed that adrenaline and exercise probably only enhance what is normally present[6] In fact, with our method the activity in the resting subject was as great or greater than that found by Macfarlane after adrenaline injection, and our figures with the latter were correspondingly much greater

The relevance of these observations is that if blood or plasma to which an anticoagulant has been added is allowed *to stand at room temperature, its fibrinolytic activity is rather rapidly reduced* The labile fibrinolytic component is stabilised when clotting occurs, presumably by adsorption on the fibrin net work, and can in fact be adsorbed on to pre formed clots from fibrinolytic plasma[7] (This, I would suggest, happened when Dr Kwaan and his colleagues immersed their fibrin webs in fibrinolytic plasma) The fibrinolytic component, according to our observations, is temperature labile whether the blood is obtained from subjects at rest or after stress, or from cirrhotic patients We have, however, some evidence *that when fibrinolytic activity is massive its lability may* be diminished It follows, therefore, that unless the investigator of spontaneous fibrinolysis cools the blood samples immediately and uses a low-temperature technique, or at least makes his clots at a standard *time after* venepuncture, he is in danger of obtaining discordant and confusing results Now that fibrinolysis is giving rise to more general interest the importance of recognising the lability of the fibrinolytic factor in unclotted blood and plasma cannot be too strongly emphasised

This criticism is not intended to cast doubt on the general conclusions reached by Dr Kwaan and his colleagues, since they were dealing with massive fibrinolytic activity, with perhaps a consequent reduction of lability , and if, as one supposes, *their tests* were set up *shortly* after the blood samples were obtained, the results are acceptable , although the criticism does apply to the data obtained with healthy controls *One would, however, be grateful for information* about how quickly the tests were set up

Concerning my own results with cirrhotic patients, the object was to *determine* whether such patients have enough fibrinolytic activity in their blood to jeopardise the stability of blood clots formed in hæmorrhage from œsophageal varices Some of these patients bleed uncontrollably, and if massive fibrinolytic activity were present it might account for recurrent hæmorrhage leading to death A number of investigations were carried out, but only the relevant ones are mentioned here

It was *argued that* if fibrinolysis *in vivo* were responsible for recurring hæmorrhage the most rewarding measurement would be the lysis time of a whole blood clot in vitro We have found, however, that unless a whole blood clot lyses within about twenty four hours of incubation it is unlikely to lyse at all, being adversely affected in vitro by cellular breakdown which is manifested by deep brown discoloration within twenty four to thirty six hours This is not so with whole-plasma clots or buffered-plasma clots[6] The results of the several investigations on 6 patients with cirrhosis are, therefore, given as the lysis times of whole plasma clots with the lysis times of the whole blood clots in parentheses where relevant (the method has been described[6])

Case no	*Sex*	*Lysis times (hours)*
1	F	8½ (11), 55, 5 (6½)
2	F	13 (18), 57
3	F	32, 76, 108
4	F	128 46, 94
5	M	15½ (17), 23 (27)
6	M	3½ (3½) 10 (13½) 97, 77, 10 (14), 92, 13 (18½) 47, 93, 96, 104

Prolonged incubation of citrated plasma, diluted and undiluted, from these patients gave no reduction of fibrinogen content even when fibrinolytic activity was great, which agrees exactly with the results obtained by Dr Kwaan and his colleagues I would question, however, *the authors' statement* about the lack of inhibition obtained with serum plasmin inhibitor They may be correct but they do not make it clear *whether whole serum or a fraction was used* Certainly I found serum itself to be inhibitory

In three experiments in which the patient's serum and my serum were added in increasing amounts to a 1 10 dilution of the patient's fibrinolytic plasma, there was a linear increase in lysis time, my serum being slightly *more* inhibitory than that of any of the 3 patients The results accorded with the observations of Lackner and myself,[8] about the linear relation between dilution and lysis time in our study of normal fibrinolytic activity

None of these patients *had operations* or were given corticotrophin during the period of observation I concluded that on occasion fibrinolytic activity can be sufficient to impair the hæmostatic mechanism, but that it was evidently rather variable in each patient studied As we had been unable to produce significant alteration of fibrinolytic activity with corticotrophin and cortisone in healthy people and in patients with rheumatoid arthritis,[8] the investigation was not carried further

The results obtained with corticotrophin by Dr Kwaan and his colleagues are of the greatest importance and interest It might be rewarding to try the effect of corticotrophin in cirrhotic patients with uncontrollable hæmorrhage, together with observations on fibrinolytic activity and no doubt they have this in mind

Gloucester Royal Hospital

GEORGE R FEARNLEY

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[1] *Antibiot Chemother* 1956 6, 135

[2] Fearnley G R , Revell R , Tweed, J M *Clin Sci* 1952, 11, 309

[3] Truelove S C *Ibid* 1953 12 75

[4] Biggs R Macfarlane, R G , Pilling J *Lancet* 1947 i, 402

[5] Fearnley, G R , Tweed, J M *Clin Sci* 1953 12 81

[6] Fearnley, G R , Lackner R *Brit J Hæmat* 1955, 1, 189

[7] Fearnley, G R *Nature, Lond* 1953 172, 544

[8] Fearnley G R Lackner, R Meanock R I Unpublished data 1953

Medical Education

REVISION OF THE CURRICULUM

Proposals of the Royal College of Physicians

OVERLOADING of the curriculum is a confession of ucational failure. But so long as medical schools try provide a comprehensive training in all branches of medicine, their curricula will be increasingly overloaded. The Royal College of Physicians believes that the essential first step towards reform is to encourage teaching authorities to study their problem afresh, with liberty to experiment; and it therefore proposes[1] that the detailed *Recommendations* issued from time to time by the General Medical Council should be discontinued, and replaced by a general statement on educational objectives. The college's views on these objectives will be found in the following extracts from a further memorandum, signed by Sir Russell Brain, which it has now sent to the council.

The Aim: a Basic Professional Education

To give, before registration, a full training for any ranch of medicine has become impossible, and to try o do so has become harmful. Instead of a comprehensive vocational training the aim in future should be to give the student a basic professional education of high standard: he should acquire a soundly rooted stock of knowledge on which any branch can be grafted later. It is true that a great many facts must be assimilated by anyone who is going to do any kind of medical work; but, both for the future general practitioner and for the future specialist, factual knowledge is in the long run less important than the ability to learn and go on learning.

On qualification the student will be neither a general practitioner nor a specialist, but should be fit to practise under supervision. His training in science should have given him a scientific outlook, and his training in clinical techniques should have given him skill in collecting information. His methods of thought should enable him to approach any clinical problem rationally, but he should already possess knowledge and experience of the commoner diseases and disorders of function, especially in their early stages, and of the management of emergencies. He should appreciate the doctor's responsibilities to his patient and to the community, and he should be a person of sympathy and understanding.

Premedical Education

Whether a medical curriculum produces graduates with these qualities depends partly on the education the students have received before entering upon their medical studies. The General Medical Council in 1947 described the desideratum here as "a broad general education including the principles of Physical and Biological science," and it would now be reasonable to ask each teaching authority to consider whether or not this kind of education is in fact promoted by the conditions on which students are accepted for medical training.

Insistence on the attainment of a high standard (the "advanced" level of the General Certificate of Education) in three or even four scientific subjects may have the advantage of eliminating candidates who cannot be expected to cope with the scientific side of medical education, and it therefore has some value as a means of selecting students who will later qualify. But it has countervailing disadvantages: first, that the candidate, being induced to amass temporarily a great body of facts, may be led thus early into unsound habits of learning; and secondly that, for most of the future members of the medical profession, a genuinely general education is made to stop at the age of 16 or earlier. Probably few teaching authorities believe that the study of scie from this early age, to the exclusion of other school subje is the proper basis for medical education; yet the effe their regulations is to ensure that the large majority of entrants come to their medical schools with this already specialised education. From 16 these boys and girls have been taught little or nothing but science, and often they have been taught it less for its own sake than as a subject of examination.

In selecting future medical students all teaching authorities, presumably, attach importance to achievements outside science; yet by their own restrictive conditions—for which the General Medical Council are not to blame—they may deprive themselves of liberty to choose candidates whose general attainments they would recognise as outstanding.

A teaching authority, though it may ask for General Certificate of Education passes at "ordinary" level in English, a foreign language, mathematics, chemistry, physics, and zoology (or biology), ought not to insist on passes at "advanced" level in more than three subjects, one of which should be non scientific. Concentration of effort on two scientific subjects, rather than three or four, should leave a boy free for sixth-form work in other disciplines which can help to make him a more cultivated person and eventually a better doctor.

Preclinical Studies

At the age of 18—but no earlier—the student who has been adequately prepared may enter upon his preclinical studies.

The purposes of these studies are to obtain further understanding of scientific method, to strengthen scientific habits of thought, and to learn, in outline, what is known about the structure and function of the normal body and mind. These purposes will be fulfilled chiefly through training in anatomy, physiology, biochemistry, and psychology; but the overwhelming size and continuous expansion of each of these subjects makes it essential that the student's courses in them should be explicitly designed and undertaken as parts of the basic education of a doctor—not as training for a future anatomist, physiologist, biochemist, or psychologist. Furthermore, as part of a continuous process of education, their selective presentation should be closely connected, in the minds of teacher and student alike, with the studies in biology, chemistry, and physics that have gone before, and with the clinical studies that lie ahead.

Generally devoting two years to preclinical studies, some teaching authorities start in the later terms to turn the student's attention from health to disease, with teaching in pharmacology and general pathology, and sometimes with clinical demonstrations. In some medical schools abroad there is, indeed, no formal preclinical period, since the student does some work in the wards from the beginning of his course. Whatever the means adopted, the main object will be achieved if the student is led to look on his academic studies as a useful part of his education for medicine, and if he tries to learn thoroughly in order to equip himself for his later work, not superficially in order to pass the next examination.

The proposal that the preclinical subjects should be taught "in outline" does not imply that they are unimportant. Clearly their importance is fundamental, and every encouragement should be given to some students to study them more fully as subjects for an honours degree. But in actual fact the endeavour to teach them comprehensively to everybody has very often led the student to regard them as something to be committed to memory and then forgotten, and it has tended to obscure their fundamental relationship with clinical medicine. As this relationship cannot be fully appreciated without some knowledge of disease, medical schools will do well to arrange that the teaching of preclinical subjects (especially physiology) shall continue during the clinical period, when it will usually be given to best advantage by members of the

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[1] See *Lancet*, 1955, ii, 132.

In 1910–47 his colleagues on the staff of the Royal, and the board of management under the chairmanship of Senator Herbert Quin, succeeded in establishing a neurosurgical department for Northern Ireland at the hospital, and appointed Mr Calvert its first director Part of one of the general surgical wards was set aside for the purpose, and operating-theatre and staff provided, and in 1917 the new department began to function In 1953, through the sustained interest of the chairman of the hospital and the approval of the Northern Ireland Hospitals Authority, a new theatre suite and wards were opened, and here in the past three years, at Quin House, he at last saw the realisation of all his hopes and ambitions to establish neurosurgery on a sound footing in Northern Ireland In 1954 he had the great pleasure of acting as host to the Society of British Neurosurgeons on the occasion of their first visit to Belfast He gave then a typically honest and severely critical account of his own personal experiences with a series of cases of spontaneous subarachnoid hæmorrhage which he had treated as surgical emergencies Last summer he went to Canada for the joint meeting between British and Canadian neurologists and neurosurgeons, and spent some time at the Institute of Neurology in Montreal and other centres in the United States In the autumn he had been elected vice-president of the Ulster Medical Society

Simple statement of the chief events in a successful life does not always indicate the sources of a man's claim to greatness As a doctor, in every sense of the word, Cecil Calvert was one of the most outstanding men the Belfast School has produced But he seldom published any of his work although we often urged him to do so Writing did not come easily to him, for he had an exceptionally fine knowledge of neurological literature and was overcritical of the worth of his own observations Shortly before his death he expressed a desire to give up part of his routine work in favour of making a special study of surgical aspects of the Parkinson syndrome and other extrapyramidal states, but he never claimed to have any particular aptitude for research As a clinical neurologist he was the best we had Often ill-defined physical signs which, if not missed, were accepted by others as being atypical though not inimical to the diagnosis suggested, proved as a result of his careful appraisal to be signposts ultimately leading to the true localisation and nature of the underlying lesion Where he differed from most of us, and may possibly even be considered as unique, was in the freshness of outlook he could summon without effort to bear on each new clinical problem, a truly remarkable faculty which had to be seen to be believed and which showed no signs of failing at any period in his lifetime He might weary of the topic under discussion at a committee meeting but he was never bored at the bedside or when taking a patient's history, however laborious and time-consuming this might prove to be To him there were no "interesting" cases to whet his appetite or "purely functional" problems to be dismissed after a perfunctory examination Each new patient, no matter what his symptoms, was treated as a distinct entity and with that measure of kindly consideration and depth of absorption as could only arise from the conviction that the whole purpose of his being was to elucidate the particular problem then holding his attention When he had completed his examination he would spend some time making notes in his distinctive neat script, and then he was ready for the next patient Another characteristic trait was the problem which the question of fees presented to him Before he gave up private practice, if patients offered to pay he accepted a modest fee, or more often put them off by saying it would do some other time, and his procrastination in sending out accounts was, of course, well known

Mr Calvert's elder brother, Dr Edwin G B Calvert, is senior physician to the Royal Northern Hospital, London and he has two sisters, Mrs R R Sayers and Mrs Allen, wife of Prof F M B Allen He married in 1930, his wife, Eileen, being the second daughter of the late Mr and Mrs Henry Healey of The Fort, Lisburn From her he received devoted loyalty and support Many visitors to their lovely home at the Spa, Ballynahinch, and later at Newtownbreda will remember the graciousness and warmth of the hospitality she provided To his intimate friends he often admitted how much he owed to her, and indeed this could easily be discern by all who knew them, each having a deep regard and affection for the qualities of the other

R S A

During the late war, Cecil Calvert was chosen b Sir Hugh Cairns to be officer in charge of the surgical division at the Military Hospital for Head Injur (Oxford), and in this capacity he shouldered the ma burden of brain surgery in that hospital The mos difficult and time-consuming cases were generally p on his operating-list, as everyone knew that he would spare no effort and grudge no time in achieving his h challenging standards, for only the best would satisfy him

Perhaps the worst types of brain wound, from th surgical point of view, were those which shattered th floor of the anterior fossa The debridement of the wound had to be followed by a tedious repair of the torn meninges, and Calvert's success with these difficult cases was unrivalled During the invasion of Europe there were fresh cases admitted in groups nearly every day, and his life during long periods consisted of operating sleeping and eating

Calvert was so modest and unassuming that we often wondered whether he realised the importance of his work, and certainly he would vigorously disclaim any attempt to describe it in terms commensurate with its great worth As a professional colleague and friend no-one could have been easier to work with Clinical problems were discussed with all who could possibly help, advice was carefully listened to, and differing views would be balanced fairly against his own before a final decision was taken A keen sense of humour led to words of kindly banter being exchanged, but there was never any possibility that either personal dignity or prestige of his specialty would be allowed to interfere with the main object of his work, which was to do the best that was humanly possible for the patient

By his tragic and sudden death at the height of his career, British neurosurgery has suffered a grievous loss, and many of us have lost a great friend

W R B

FRANCIS EVELYN JARDINE

M B Edin, F R C S E

As we announced last week Mr Frank Jardine died on March 27 at his home at Elie, Fife, to which he had retired

He was educated at George Heriot's School and at the University of Edinburgh After he graduated in 1908, he held house-appointments at the Royal Infirmary and later became private assistant to Francis Caird, whose surgical disciple he was In 1912 he took the F R C S and in 1919 he was appointed assistant surgeon to the Royal Infirmary He also served on the staffs of the Vert Memorial Hospital, Haddington, the Dumfries and Galloway Royal Infirmary, the Kirkcaldy Hospital, and the Royal Victoria Tuberculosis Trust From 1917 to 1949 he held office as president of the Royal College of Surgeons of Edinburgh, and in 1950 he retired from the staff of the Royal Infirmary

W Q W writes

"Frank Jardine's surgical technique was based on that of Caird, and, though in some respects he was excessively conservative, his methods, on the whole, were sound and successful He was associated with the department of anatom in the University of Edinburgh for many years, first as demonstrator and later as lecturer in applied anatomy, and there is no doubt that his thorough knowledge of anatomy contributed a great deal to his success as a surgeon He was an excellent teacher and his simple direct style and often homely or humorous illustrations made him a great favour with undergraduates He understood hospital patients we and was able quickly to get on easy terms with them hi exchanges, sometimes in the vernacular, were often mos entertaining to his students and were appreciated by th patients Apart from his professional career, he will be lon remembered for his personal qualities He had a gift fo friendship, which included his own teachers his colleagues hi patients, his students, and his nursing staff His hospitality both at Edinburgh and Elie, leaves grateful memories t many He had a great sense of fun and appeared to see onl the brighter side of life his ready wit and quickness a repartee made him excellent company whether in his own home or at social gatherings His recreations were golf and given time and opportunity, the teacher will study the varying needs of individual students so that each may be aided, guided, and inspired to learn for himself

The Council's Responsibility

The duty of the General Medical Council to ensure that, registration, practitioners possess "the requisite nowledge and skill for the efficient practice of their rofession" has hitherto been discharged (1) by recommendations as to the conditions on which teaching authorities should grant registrable qualifications, and (2) by inspection of the qualifying examinations of the licensing bodies Discontinuance of the issue of detailed recommendations (as proposed by the college) is now possible because the General Medical Council's power of inspection has been extended by the Medical Act, 1950, to the medical schools in which the candidates for registration are taught Believing the quality of these schools to be of primary importance, the council may decide to make use of this power of inspecting them, and will thus be in a position to make recommendations specifically to individual schools rather than generally to all

Examinations are potential instruments of education though they should not control its course, and the therefore form an integral part of a curriculum The college suggests that, to encourage teaching authorities to review their curricula fully, the council should issue no general instructions on the content or timing of any examinations, for such instructions would limit the scope of the review and might prevent the development of a method of progressive assessment which could be an alternative to the present examination system Since a curriculum and its examinations need to be considered together, the council's inspection of a medical school's examinations should henceforward be part of their inspection of the medical school itself

In inviting teaching authorities to reconsider the curricula, and licensing bodies to reconsider their examin tions, the council might ask each such authority or bo to submit, within two years, a statement on its pol and on how this policy is to be realised

Special Articles

TOOTHBRUSH HYGIENE IN HOSPITAL

FRANK BROOK
F.D S , H.D D
ASSISTANT DENTAL SURGEON, LEEDS GENERAL INFIRMARY ,
CHAIRMAN OF LEEDS (GROUP B) HOSPITAL MANAGEMENT COMMITTEE

ORAL hygiene is difficult to maintain in patients with severe mental disease In the training of nurses stress is d on the importance of a clean mouth, but in over- owded and understaffed wards there is a wide gulf etween theory and practice

In many hospitals the nurse hands out the toothbrushes immediately before their use, and collects them afterwards For each brush to be inspected and placed in its individual container, ready for the same patient to use next time, takes more time than can normally be given

In some hospitals the brushes are tagged with the names of the patients, but are then placed in an antiseptic solution in a single container , the bristles of different brushes often come into contact with one another, and some antiseptics injure the attachment of the bristles to the head of the brush

THE ANTISEPTIC

Viefhaus[1] in 1932 reported that toothbrushes can be rilised quickly and efficiently with a 1 in 200 solution 'Carvasept,' which is, I am informed,[2] a preparation f monochlorisothymol Viefhaus said that after dipping he brush in the solution enough antiseptic remained on he bristles to make them spore free in ten minutes There were no deleterious effects on the brushes, even when they were immersed in the solution for three weeks, and the bristles remained hard and elastic Furthermore, the odour and flavour of monochlorisothymol were in no way unpleasant, and were, in fact, more pleasant than certain mouthwashes

Preparation —Monochlorisothymol[3] is insoluble in water, but a stable 10% emulsion may be prepared from the following materials[4]

Monochlorisothymol	100 ml	Oleic acid *B P*	2
Castor oil *B P*	50 g	Alcohol 95 % *B P*	1
Potassium hydroxide *B P*	10 5 g	Water sufficient to produce	

Dissolve the potassium hydroxide in 10 ml of d water and mix this with a solution of the castor oil in of the alcohol Allow to stand for one hour, or until portion remains clear when diluted with 19 times its of water

Stir in the oleic acid until a few drops of the solution a bluish green colour with bromothymol blue (*B P*) Dissolve the monochlorisothymol in the remainder of the alcohol and mix it with the above solution Carefully add sufficient water to 1000 ml and mix well

To obtain the 1 in 200 dilution required for sterilising toothbrushes, add a litre of water to 50 ml of this 10% emulsion

Investigations —Bristles from 6 used toothbrushes gave an average bacterial count of 1200 million organisms per bristle After soaking in a 1 in 200 solution of monochlorisothymol for various periods the brushes were washed in sterile saline and the bristles were cultured Organisms were present on brushes soaked for five, fifteen, and thirty minutes, but not on those soaked for one hour or longer[5]

Experiments on mice suggest that monochlorisothymol is not toxic in concentrations likely to be used for sterilising toothbrushes

The conclusion reached was that used toothbrushe should be soaked in a 1 in 200 solution of monochloris thymol for two hours, and washed in water before they are used again

THE STERILISING CABINET AND ITS USE

This is not a new idea

Bartlett[6] described toothbrush cabinets varying in size from those holding 100 brushes to those holding 20 No brush came into contact with its neighbour, and the brushes were renewed monthly, or oftener, as circumstances demanded Each cabinet was equipped with a metal container holding a fresh solution of 10% formalin, which was inaccessible to the patients

The toothbrush cabinet which is in use at Meanwood Park Hospital, Leeds (see figure), is made of stainless steel, the inside measurements being 15 × 12 × 7½ in[7] The lid is perforated so that the brushes may dry, and is divided into two equal parts by a vertical partition The first-class observer and a good bird man He was a constant attender at meetings of the British Ornithologists Club He rarely spoke in the formal discussions and I do not believe that I ever heard him read a paper, but his comments and remarks delivered in his honest-to God manner were always pithy and to the point I remember a heated and apparently interminable argument between two eminent ornithologists upon the exact method employed by the cuckoo in laying its egg and *swallowing* it, as had been claimed The question arose as to what the cuckoo did next During an awkward lull came a typical "snork" which expressed in vivid ward-room phrases his opinion of the question The male members endeavoured to hide their mirth, but the ladies gazed at each other like hen pheasants startled by the bark of a fox

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[1] Viefhaus K *Arch Hyg*, *Berl* 1932, 107 155
[2] By Mr R Cobb, of the medical department of Messrs Boots Pure Drug Co
[3] Obtainable from Messrs Howards, of Ilford
[4] This method was devised by Mr J G Dare of the pharmacology department University of Leeds
[5] Investigations by Prof C L Oakley, of the bacteriology department University of Leeds
[6] Bartlett D S *Med Bull Veterans Adm*, *Wash.* 1931, 7, 961
[7] The cabinet is obtainable from Messrs Chas F Thackray, Leeds.

A memorial meeting for Prof Samson Wright has been arranged by the Middlesex Hospital Medical School and the Friends of the Hebrew University of Jerusalem It will be held on Thursday, April 19, at 5 p m at the University of London Institute of Education, Senate House, W C 1

Births, Marriages, and Deaths

BIRTHS

Flatt—On March 20 in New York Hospital, U S A, to Adele, wife of Andrian Flatt, M D, F R C S—a son

Hollman—On March 31 at University College Hospital, London to Catharine and Arthur Hollman—a daughter, Anne Sheila sister to Margaret and Susan

Rivlin—On April 4, at Liverpool, to Dr Mona Rivlin (née Harris) wife of Dr J J Rivlin—a daughter

Wilkinson—On March 8 at Hammersmith Hospital W 12 to Vera (née Bell), wife of Dr R W Wilkinson—a daughter

Appointments

Barling, A S M R C S appointed factory doctor Market Deeping Lincolnshire

Bergin, J T, M B N U I registrar in mental deficiency and child psychiatry, Little Plumstead group of hospitals

Bickerstaff, E R, M D Birm M R C P part time consultant neurologist Shrewsbury group

Boyle P J M B N U I D A asst county and school M O, Staffordshire

Brown T J G M B Sydney surgical registrar North Cambridgeshire Hospital, Wisbech

Champ, C J M D Lond M R C O G consultant obstetrician and gynæcologist, Amersham General Hospital

Davitt, Sheelagh M, M B N U I M O school health, Manchester

Griffiths, C I M B Birm, D M R D whole time consultant radiologist, Lichfield, Sutton Coldfield and Tamworth and Birmingham (Dudley Road) groups

Hillman F, M B Belf M R C P I whole time asst pathologist (S H M O) Lancaster and Kendal group of hospitals

Lawson, J I M M B Edin, F F A R C S, D A anæsthetist, Dundee Royal Infirmary

Potter J M M B Camb F R C S part time consultant neurosurgeon Manchester Royal Infirmary and Parkside (Mental) Hospital, Macclesfield

Reinold, D G M R C S registrar in general surgery, Royal Cornwall Infirmary, Truro

Sladden R A D M Oxfd D T M consultant pathologist Northampton and Kettering area

Summers, Frank M B Lond M O H Lambeth

Wells A L M B Camb, D L O, D OBST appointed factory doctor Beccles, Suffolk

South Western Regional Hospital Board

Barry D M R M B Dubl D M R D consultant radiologist, South Somerset clinical area

Chandler C C D M B Lond F F A R C S, D A anæsthetic registrar Frenchay Hospital, Bristol

Nair L E M B Madras F R C S senior surgical registrar, thoracic unit Hawkmoor Chest Hospital Bovey Tracey

East Anglian Regional Hospital Board

Gibson S W N M B Belf F R C S D O consultant ophthalmic surgeon, Norfolk and Norwich hospital group

Kay M D M B Cape Town medical registrar, Ipswich and East Suffolk Hospital

Naunton W J M B Camb D O M S consultant ophthalmic surgeon Norfolk and Norwich hospital group

The Hospital for Sick Children, Great Ormond Street, London

Bain D W M B Lond, F R C S surgical outpatient asst

Benson P F M B Lond M R C P D C H house physician

Cohen Maurice M B Lond house surgeon

MacDermot Violet D M R C S D C H senior house officer, department of neurology and neurosurgery

McKee J A M D house physician

Mandell B B M B Witwatersrand house surgeon orthopædic and plastic departments

Stephens Rosemary M B Lond D C H asst medical registrar

White R H R M B Camb M R C P D C H house physician

Notes and News

WELLCOME MUSEUM OF ORTHOPÆDICS

At the Institute of Orthopædics [1] on April 4 Sir Henry D opened a new Wellcome museum With what he described as a modest allocation of money, and certainly with a modest allowance of space, the organisers have evidently given a great deal of care, time, and knowledge to the creation of this museum Indeed, Sir Henry implied that if the Wellcome Trustees could rely on the institute's success as a precedent they would hesitate ever to make more generous grants

The era when morbid anatomical specimens were regarded as the fountainhead of all medical teaching has passed it is the intimate structure of the cells and the chemical changes in the blood that now chiefly claim our attention A museum today must therefore do far more than provide space for row upon row of dust collecting pots, and, to be useful to the clinician, a museum of bone and joint pathology requires, in particular, X-ray plates, microscopic slides, and clinical and biochemical data The way in which, in this Wellcome museum, almost complete visual representation has been given *to a number of orthopædic diseases reflects the highest credit* on Dr H A Sissons and his team In the section of metabolic bone diseases especially, they have done remarkably well—by judicious selection and uncrowded display of naked-eye specimens, histological slides, and radiographic plates, with concise, illuminated captions

The present exhibition, entitled Pathology of Bones and Joints, will remain open until April 27

MELLANBY AND THE VITAMINS

At the time of his death Sir Edward Mellanby was chairman of a committee which had been entrusted by the British Council with the task of organising a symposium on Recent Research on Vitamins As a tribute to a great investigator in this field, the current number of the *British Medical Bulletin*, in which the symposium has been published, is arranged as a memorial volume Sir Rudolf Peters has contributed an introduction, and Sir Charles Harington a short appreciation of Mellanby's work and character Dame Harriette Chick and Margaret Hume refer to his many years of service in presiding over the Accessory Food Factors Committee

One of Mellanby's main interests was the study of bone formation, and particularly the influence on bone of vitamins A and D In the symposium Honor B Fell describes investigations, in which she collaborated with Mellanby, on the effect of excess of vitamin A in disorganising the growth of bone in tissue culture W I M Holman and R A McCance review the rôle of several vitamins on bone formation, and they cover Mellanby's early work on vitamin D and on the anti *calcifying action of phytic acid Vitamin* A is the main subject of an article by R A Morton and T W Goodwin, and this vitamin also figures in contributions by H M Sinclair on vitamins and the skin, by Antoinette Pirie on vitamin deficiency and vision, and by M E Coates, S K Kon, and J W G Porter on vitamins in animal nutrition

E Lester Smith describes the structure of vitamin B_{12} as elucidated by Sir Alexander Todd, Dorothy Hodgkin, and their colleagues the locating of the cobalt atom and cyanide group at the centre of an incomplete porphyrin system has been a great triumph both for British chemists and for X ray crystallography L J Witts discusses the levels of B_{12} and other B vitamins in the blood and gastro intestinal tract particularly in relation to pernicious anæmia C E Dalgliesh traces the complex paths by which the amino acid tryptophane can be converted into the vitamin nicotinamide, another vitamin, pyridoxine, takes part in the conversion Adrien Albert reviews the important subject of antivitamins anti metabolites, and chemotherapy Discussing vitamins and the protection of the liver, C H Best, C C Lucas, and Jessie H Ridout refer mainly to the lipotropic action of choline and other substances with labile methyl groups

Outlining our knowledge of the biochemistry of vitamin C, L J Harris points to topics requiring further research, such as the reasons for the somewhat haphazard distribution of vitamin C in animal and plant life L W Mapson deals with the effect of commercial processing on the vitamin content of foods New ground is broken by T Moore in an article on t they were. We now have big chairs and little chairs, have chairs with larger wheels in front and those h smaller wheels behind, some are made of wicker, ne of wood, and some of iron, some take up more om than a bedstead, while others can be folded up and rried about There are a hundred-and-one other efinements—straight backs with round seats, round backs with square seats, and square seats with round holes The matter is clearly one for a specialist, and in due course we had word that the Ministry's Senior Wheelchair Consultant was on his way

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[1] The Institute of Orthopædics (University of London) 234 Great Portland Street London W 1

Hasty arrangements were made so that everything would be ready on his arrival The patient s bi-weekly bath was antedated, fresh flowers appeared on the bedside locker, and the house-physician brought the notes up to date At last he arrived, armed to the teeth with official-looking documents. Irrelevant items, such as obstetric history and the width of the neighbours' front garden gate were painstakingly recorded, and then he asked to see the patient To our amazement, he confined himself to a detailed dental examination and, carefully noting that 70% of the upper and 100% of the lower teeth were false, he packed his instruments and left

Not only are we sorely perplexed—we are exceedingly worried All this happened six months ago and the patient has since had the left upper canine extracted Will the wheelchair, when it comes, still fit?

* * *

The *Pharmaceutical Pocket Book* stands between the tinctures and the syrups I don't know why. One of my dispensers put it there years ago, and there it stays Not untouched, and not quite unread I glance at it sometimes when the summer evening surgery is slack nd I can smoke a pipe among the bottles Its dictionary f synonyms is always rewarding, with Abernethy's Pill eading like a string of racehorses Basham's Mixture, Black Juice, and Blue Butter The "C's" bring Chinese Blistering Beetle, Clap Mixture, Crab's Eyes, and Cube Root, followed by Fiddle Gum, Guinea Grains, Essence of Smoke, and Everlasting Pills, Poke Root, Polishing Crocus, Surfeit Water, and Tincture of Steel. Asafœtida answers surprisingly to both Food of the Gods and Devil's Dung Aloes is a favourite, for Lady Hesketh —and Lady Webster have pills of aloes and mastic, Chapman s and Gregory's Dinner Pills combine it with ipecacuanha and rhubarb, Marshall Hall's Pills present with liquorice, hardsoap, and treacle, and its compound ecoction—or Apozem—is also known as the Balsam of afe But some might prefer the milder Lenitive Electuary —or confection of senna Atramentum Nigrum (black nk) and Uvæ Passæ Minores (currants) might not get past on an E C 10, but there could be no objection to the King of Denmark's Chest Mixture of extract of liquorice, fennel water, and anisated liquid ammonia But Red Bottle is my favourite, with its suggestion of simple tricolour dispensing However, not all the long list is so satisfying To read, for instance, that Cabotz means kousso and Carrageen chondrus is merely exasperating The book is still between the tinctures and the syrups, and I often wonder when I catch sight of it what chondrus is and whether you drink kousso or rub it in the scalp

* * *

The child mind has an upside down, non-adult, non-victorian attitude to life. If this was more universally recognised the rewrite of existing plots for children's books and plays would perhaps supply work to psychiatric ior registrars in their spare time I took my children t week to see *Beauty and the Beast* done by a good mpany In the car on the way home a post-mortem as carried out as to whom each child liked best The atter was clinched by Elizabeth, age 9 "I preferred," he said, using her present favourite word, 'the Prince when he was a pooser" I can see now that the actors should have been feline and the beast human It's all so obvious

* * *

PRESCRIBERS' NOTES II

Effective against conditions caused by the administration of antibiotics

Thrushes are singing in my patients throats,
I feed them daily crumbs of penicillin.
Ah! where would be those liquid, bubbling notes
If I had had no E C 10 to fill in!

Letters to the Editor

THE ROYAL COLLEGE OF PHYSICIANS

SIR,—The leader entitled The Gold-headed Cane, in the *British Medical Journal* of April 7, received publicity in the lay press and I am therefore asking you, as well as the Editor of the *Journal*, to publish this letter

The leader calls for comment for two reasons It seriously misrepresents the work of the Royal College of Physicians, and it exemplifies a growing threat to freedom in medicine It complains that the policy of the College is faltering, and shows "confusion of purpose" and that it seems "to be a little doubtful about what its responses should be to the Welfare State and its centre-piece the National Health Service" In fact the policy of the College has from the beginning been a firm and consistent one of cooperating with the Government of the day, and taking a share in the decisions on all matters arising out of the Health Service, including remuneration, of which the leader, somewhat inconsistently, goes on to complain Those, however, who have followed the policy of the British Medical Association and views of the *British Medical Journal* on the Health Service will be familiar with their vacillation, and if one wants examples of confusion of purpose one need look no further than the B M A whose leaders recently had to eat their words on the heroin ban, and withdraw their evidence from the Royal Commission on Marriage and Divorce

The leader complains that the College Officers are out of touch with the Fellows and Members It is true that the democratic practice of the College is not identical with that of the B M A, and that its tradition gives the President considerable freedom of action, safeguarded by requiring him and the other College Officers to be re elected annually But every Fellow has a right to attend Comitia, and no Fellow ought to complain that a subject has not been discussed there if he has himself failed to attend and raise it The allusion to Members seems to be based on sheer ignorance, for Members' meetings are held twice a year with the President in the chair, and Members are free to express their views on any subject arranged by their own committee, as well as electing two representatives to the Council

But the leader also misrepresents the College by implying that medical politics is its main interest It entirely neglects to mention the large amount of work done by the College committees which have made substantial contributions to undergraduate and postgraduate medical education, and expressed the views of the College on many clinical, scientific, and sociological topics And the College is even now developing plans for extending its building and expanding these activities

I note in passing that in discussing the limitation of the tenure of office of Presidents of the College and of other institutions the leader does not mention that the Chairman of the Council of the B M A has served in that office since 1949, but such limitation, as the B M A will no doubt agree, is a matter for decision by the bodies concerned

But the main trend of the leader is the clear implication, which finds support elsewhere in the same issue of the *Journal*, that the B M A should occupy a position of exclusive privilege and power in medicine When the B M A organises a conference on medical education, it is the duty of the Colleges to cooperate, even though they may prefer to confine themselves to their own work in this field. When the B M A is negotiating about medical remuneration, it is the duty of the Colleges to keep silent. When the B M A rules that broadcasting and television appearances by doctors should be anonymous, personal opinions and particular circumstances are not to count.

All these instances show that medicine is not free from the danger, already evident in the industrial field, of the

University of St Andrews

On July 3 the honorary degree of LL D will be conferred on Sir James Learmonth, regius professor of clinical surgery in the University of Edinburgh

International College of Surgeons

Sectional meetings of this college will be held at Amsterdam (April 28 and 29) and at Nantes (May 14–16) A Continental clinical cruise will also be held during May Further particulars may be had from Dr J F Brailsford, 20, Highfield Road, Edgbaston Birmingham, 15

Central Midwives Board

Mr Arnold Walker has been re elected as chairman and Prof A A Moncrieff as deputy chairman

London School of Hygiene and Tropical Medicine

Sir James Kilpatrick has been appointed to succeed Prof Bradford Hill, F R S , as dean of the school He will take office on March 1, 1957, when he retires from his present post of director general of the medical services of the Royal Air Force

Queen's Institute of District Nursing

This institute is to hold a meeting at Church House, London, S W 1, on Wednesday, June 6, at 2 30 P M , to discuss the part of the district nurse in the prevention and care of mental ill health Dr Kenneth Soddy and Dr L S Davies will speak Further particulars may be had from the general secretary of the institute, 57, Lower Belgrave Street, S W 1

Research in Leukæmia

The Leukemia Society, Inc , formerly the Robert Roesler de Villiers Foundation, will award grants in aid and fellowships to support research on leukæmia during 1956–57 Further particulars may be had from the Regius Professor of Physic, University Department of Medicine, Tennis Court Road, Cambridge

International Cybernetics Congress

This congress is to be held, under the patronage of the Belgian ministry of education and of UNESCO, at Namur from June 26 to 29 The programme will be divided into the following sections principles and methods of cybernetics, mechanical brains, automation, cybernetics and life Further particulars may be had from the commercial counsellor, Belgian Embassy, 103 Eaton Square, London, S W 1

Reablement of the Blind

The World Council for the Welfare of the Blind and the World Veterans Federation are sponsoring a seminar on this subject which will be held at the Royal National Institute for the Blind, 224, Great Portland Street, London, W 1, on Monday, April 23, at 10 A M Mr Iain Macleod Minister of Labour and National Service, will be the principal speaker

Ophthalmological Society of the United Kingdom

The annual congress of this society will be held at 1, Wimpole Street, London W 1, on Thursday, Friday and Saturday, April 26, 27, and 28 On Thursday at 9 45 A M Sir Stewart Duke Elder, Mr P L Blaxter, Mr S J H Miller and Prof G P Sourdille will be the opening speakers in a discussion on the Early *Diagnosis of Glaucoma* On Friday at 2 P M Mr A I B Goldsmith Dr M Lederman and Dr J A Dudgeon will speak in a symposium on Herpetic Infections of the Outer Eye

The Doctor in the Chair

Alderman G H Goulden, the mayor of Salford who is also deputy chairman of the local executive council protested at a meeting of the city council (*Manchester Guardian* April 5) at the election to the chairmanship of the executive council of a doctor under contract with the National Health Service Alderman G W Davis said that at a meeting of an executive council he found himself surrounded by doctors dentists pharmacists and other professional men At the election of the chairman there had been 6 laymen to 17 professional men Alderman Dr Joseph Shlosberg pointed out that when complaints against professional men were being heard it was customary for an equal number of laymen and professional men to sit under a chairman with a knowledge of law Councillor John Hall described the administration of the health service as topsy turvy with non medical superintendents running hospitals and medical men in places where laymen would be expected

International Society of Surgery

A general meeting of British members of the society w be held at 3 15 P M on Friday, April 20, in the Royal C of Surgeons, Lincoln's Inn Fields, London, W C 2

Institute of British Photographers

Medical Group —A conference will be held by the g at St Bartholomew's Hospital, London, E C 1, on Satu April 21 at 2 P M Tickets can be had from the m secretary of the institute, 49, Gordon Square, W C 1

Family Planning Association

On Tuesday, April 17, at 6 15 P M , this associatio holding a meeting at Caxton Hall London, S W 1, at Mr J Bronowski, PH D , Mr Julian Huxley F R S , a Canon Mervyn Stockwood will answer questions on Pa hood—by Choice or by Chance

Aims of Medical Education

The London region of the British Medical Students Association is holding a symposium on this subject at the Lond Hospital, E 1, on Saturday, April 21 Tickets may be h from the B M S A , B M A House, Tavistock Square Lond W C 1

International Meeting on Electro-encephalograph

The E E G Society are holding an international Europea meeting from May 24 to 26 at the Royal College of Surg of England, Lincoln's Inn Fields, London, W C 2 Th subjects chosen for discussion are instrumentation recording, and processing methods, and drug effects and E E Non members may obtain further particulars from Dr S L Sherwood, National Institute for Medical Research Mill Hi N W 7

Guildford Group Hospital Management Committee has to over 100 local general practitioners a pamphlet describing t services available in the district for old people A summary of t information has been printed on a leaflet which may be gummed into the fly leaf of a pocket diary

The National Association for Mental Health (39, Queen An Street, London W 1) has published a pamphlet by Miss Adri Trainor L R A M , on *Teaching the Mentally Handicapped Chil Speak* (Pp 20 2s) Miss Trainor describes methods for train the silent child the mongol child and the child who can speak

Diary of the Week

APRIL 15 TO 21

Tuesday, 17th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn Fiel
W C 2
5 P M Mr W J W Sharrard Muscle Paralysis in Poliomyeli
(Hunterian lecture)

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
5 P M *Comparative Medicine* Prof G A H Buttle, Dr L G
Goodwin Dr S B Kendall Prof L Boyland Prof J
Knox Synergy in Chemotherapy
5 15 P M *General Practice* Dr G I Watson Prof J M
Mackintosh Dr Kenneth Carter Therapeutic Re

Thursday, 19th

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND
9 15 A M (15 Lincoln's Inn Fields W C 2) Mr D J Waterst
Mr H H Nixon Mr Arnold Gourevitch Mr J J Mas
Brown Neonatal Intestinal Obstruction (Beginning o
three day annual meeting)

BRITISH INSTITUTE OF RADIOLOGY 32 Welbeck Street W 1
5 P M Prof George de Hevesy Application of Radio
Tracers in Radiobiology (Silvanus Thompson lecture)

MANCHESTER MEDICAL SOCIETY
8 P M (University of Manchester) *Anæsthetics* Dr T Dundee
Facts and Fancies Dr J F Riding Postoperativ
Vomiting

Friday, 20th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
4 P M Prof Carl Semb (Oslo) Partial Resection of the Kidney
(Moynihan lecture)

ROYAL SOCIETY OF MEDICINE
5 P M *Epidemiology and Preventive Medicine* Dr W P D
Logan Epidemiology of Mental Illness
8 30 P M *Radiology Obstetrics and Gynæcology* Prof H L
Kottmeier (Stockholm) The Radiumhemmet Experie
in the Treatment of Ovarian Tumours

FACULTY OF RADIOLOGISTS
4 45 P M (15 Lincoln's Inn Fields W C 2) Mr B Ware
Dr B M Wheatley Dr J R Clarkson Mr W
Eastwood Cæsium 137

ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington W 2
5 P M Dr Leonard Colebrook F R S The Story of Puerperal
Fever

ses of meningitis admitted to small isolation hospitals thout adequate pathological facilities, and where tment cannot help but be unsatisfactory Indeed, me such hospitals do not even have a resident medical icer

Your plea for a carefully planned study of the treat- ent and outcome of purulent meningitis is timely ch a trial should be carried out on a country-wide sis

Royal Infirmary,
Huddersfield

W P SWEETNAM

B C G

SIR,—In your leading article (March 3) on the recent edical Research Council B C G trial you state that Many of us will long regret that we did not press for ch a trial sooner ”

In this connection I would draw your attention to some ents which occurred so long ago as 1943, when at a meeting the Tuberculosis Association (now the British Tuberculosis ssociation) it was unanimously agreed, following upon a scussion on B C G by international experts, that the Minister Health be approached with a view to conducting a trial this country Nothing further could be done until the end the war, but shortly after its close a “ Memorandum on C G ” was prepared by Prof W H Tytler for a joint mmittee of the Tuberculosis Association, the Joint Tuber losis Council, and the National Association for the Pre- ention of Tuberculosis, for the consideration of the then inister of Health and the Secretary of State for Scotland 1947 the research committee of the B T A was inaugurated nd immediately set about drawing up a practical scheme for C G trials which was made available to the Ministry of ealth

In the report of the B C G trial, no mention is made of he B T A and the part it has played over a long period f years in initiating such a trial Much of the credit for his forward-looking outlook must go, therefore, to the ld tuberculosis officers and sanatorium medical officers f the pre National Health Service days and to the two ther organisations associated with the memorandum

British Tuberculosis Association
59 Portland Place,
London W 1

W E SNELL
President

THE BASE DEGREES BY WHICH WE RISE

SIR,—Peter Davey combines ignorance with facetious- ess in his letter to Barbara published last week May correct a few of the misrepresentations and add the pinions of a younger pathologist upon this vexed ubject ?

The D C P, but not the D.PATH, is awarded by the Uni ersity of London, to internal or external students who pass the examination The internal candidates are students of the Postgraduate Medical School, and since trainee pathologists in this country cannot afford to spend a further academic year undergoing full time instruction, it is natural that most of them are Colonials However, any pathologist who can show evidence of having spent at least one year studying all four branches of clinical pathology can become an external candidate The statement that the examination is too easy for internal students and too hard for external students is a reflection upon the examiners and is not true

Peter Davey has not yet met anyone who has bothered to take the D.PATH If the old grey mare will bring him in this direction I will be pleased to meet him I will tell him that this diploma is awarded by the Conjoint Board in England and that before sitting the examination the candidate must produce evidence of having studied and practised pathology for three years, two of them at a teaching centre

The possession of either of these diplomas indicates that the candidate has reached a certain practical standard in all four branches of clinical pathology In academic departments it is common for a pathologist to specialise in one subject without any background knowledge of general clinical pathology, this is undesirable

My next point concerns the Edinburgh Membership, there is no such thing as an M R C.P (PATH) of Edinburgh All candidates have to pass papers in general medicine and therapeutics and have to satisfy the examiners in clinical medicine In addition a special subject is offered These range from anæsthetics to obstetrics, pathology (in the sense of morbid anatomy and histology), bacteriology, clinical chemistry, and hæmatology are four separate subjects Any one of these, but not all, may be offered by a candidate who must, however, also pass the clinical examination

Neither this examination, nor the M D, nor the PH D, nor the writing of papers offers evidence of general knowledge and technical ability in clinical pathology

A new examination may be desirable, but in the mean time the D PATH should be considered further with a possible view to increasing its standard and value One obvious defect is that the practical examination, held in Queen Square, is rather limited It should be held over a three day period in a hospital laboratory

Peter Davey lays stress on the writing of papers I hope he expects a higher standard of accuracy in these than in his own jottings which occupy more than two pages of your valuable space

Cambridge

H J WOODLIFF

*** In discussing the possible creation of a Faculty of Pathologists by one or more of the Royal Colleges, Dr Peter Davey said “The R C P won't have us” This should be regarded as a prophecy rather than a statement of fact, and for our part we hope it may prove to have been unduly pessimistic —ED L

PROSPECTS FOR LABORATORY TECHNICIANS

SIR,—Your annotation last week expresses clearly ideas which I have been trying to put forward It seems that laboratory technicians would be well advised to hitch their waggon to the Scientific Civil Service and do away with the individual payments against establishment

Group Pathological Laboratory,
Lakin Road, Warwick

A P PRIOR

VISITING IN MENTAL HOSPITALS

SIR,—Your leading article of March 24 favours unrestricted or very frequent visiting of patients in mental hospitals I am very doubtful whether you are right

You say that there are no insurmountable reasons why all hospitals should not allow daily visits But at present there is certainly a shortage of medical and nursing staff, and attending to visitors takes a lot of time Secondly, the mental patient, whether we like it or not, is differently afflicted from a general hospital patient, and he and his family react differently to his illness Though we may change the names of places and persons, it remains clear that nearly all relatives feel uneasy about, or are actually repelled by, the mentally ill they attempt to deny the gravity of the disease or its very presence—probably because they almost always feel guilty, and feel that the illness is a slur on them and the family The patient may feel very much the same Very often the family either try to sever their connections with the patient (especially if he is a chronic patient and of a bothersome or bizarre type) or endeavour, often successfully, to have him discharged against advice These factors become more manifest if frequent visits are made Moreover, psychological disturbance is not restricted to patients but tends to spill over into their families

There should not be any special difficulty in the way of the psychiatrist meeting the family, as you suggest there may be I think that the frequency of visiting should be left entirely to the informal and sympathetic individual judgment, arrived at after consultation with the relatives and the patient My own experience suggests that psychiatrists are, on the whole, much more willing to talk things over with the relatives than are most doctors in other specialties

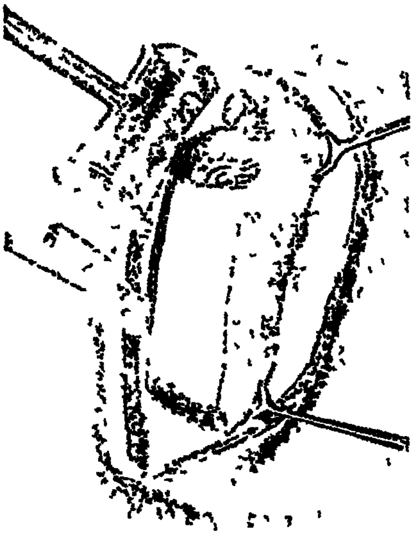

Fig 2—The edge of the sternum is being shaved off with a Lebsche chisel. The dotted line indicates where the costal cartilages will be sectioned.

and some had excision of the sternal head of the pectoralis major. There has been no operative mortality.

The primary tumour in 46 patients has been in the inner hemisphere of the breast, it has been central in 9 and in the upper outer quadrant in 2. Cases have been carefully selected, only inner hemisphere and central growths being treated for the most part. This has been a deliberate policy prompted by Handley and Thackray's biopsy finding that invasion of the internal mammary chain was much commoner when the primary tumour was in the inner hemisphere or central areas of the breast than when it was in the outer hemisphere.

Though age has been no bar, only the fitter of the older patients have been selected for operation; in fact 5 were over the age of 70, the oldest being 75.

Pathological investigation of the specimens removed at operation showed that the state of the lymph nodes was as follows:

Nodes invaded	*No of cases*
None	19 (33%)
Axillary only	15 (27%)
Internal mammary only	11 (19%)
Axillary and internal mammary	12 (21%)

The fact that only a half of the cases have shown axillary metastases is evidence that the series, so far as degree of spread is concerned, is less advanced than most others reported. Nevertheless 23 (40%) of the 57 patients showed invasion of the internal mammary chain, and of these the internal mammary chain alone was invaded in 11 (19%). Tables I and II give a more detailed analysis of the deposits according to site of the primary growth and frequency of invasion of internal mammary nodes in the different spaces.

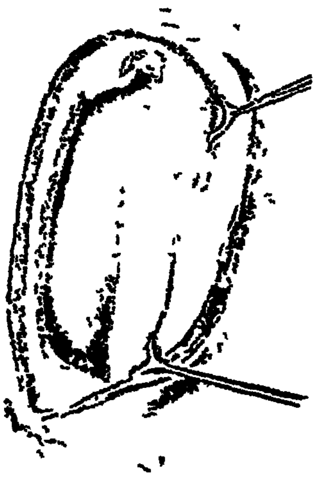

Fig 3—The rectangular area of the chest wall together with the underlying internal mammary vessels and lymph nodes has been removed leaving the pleura intact.

The first 2 patients in the series were operated on in 1952, 8 were operated on in 1953, 30 in 1954, and 17 in 1955. Sufficient time has thus not elapsed to indicate the long-term results. Table III shows the relation between length of follow-up and recurrence or death from carcinoma of the breast. 46 patients are alive without recurrence. Of these 29 had no internal mammary node invasion. The remaining 17 cases have shown invasion of the internal mammary nodes in the following intercostal space distribution:

Spaces invaded	*No of cases*
Upper three	[illegible]
First only	5
Second only	[illegible]
Third only	2
Fourth only	1
First and second	1
Second and fourth	1

Included among these 17 cases is 1 example of lymphatic permeation, 1 of venous invasion, and 1 of invasion of the connective tissues of the upper three spaces. Although no clinical evidence of recurrence has been found seven months, twenty-one months, and ten months respectively, their condition is watched with interest.

Table IV gives details of those 11 patients in whom recurrences have developed and who are either still alive at the time of follow-up or are dead from metastases. No less than 5 showed invasion of the first space internal mammary node out of a total of 13 cases in the whole series in which this node was found to be invaded. It is perhaps this evidence which has led us to consider that the first space should be explored at an early stage of the operation to determine whether invasion is present and, if it is, to abandon the extended operation in favour of a simple mastectomy and radiotherapy. This opinion leans towards that expressed by McDonald et al (1953).

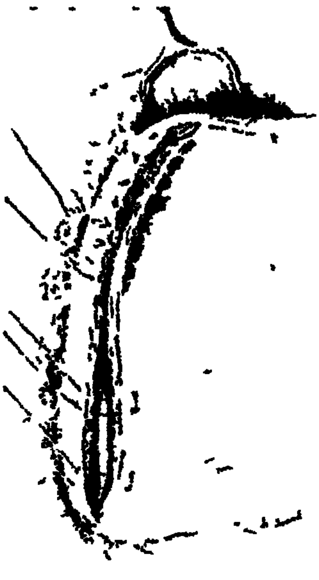

Fig 4—The cut edges of the pectoralis major are sutured over the chest wall defect.

2 patients developed apparent second primary tumours in the opposite breast. Both came in close sequence in the early part of this series and we wondered whether the operation might somehow have provoked the second carcinoma. However both second tumours showed different histological features from their predecessors, and we felt that this quashed all suspicion that the operation might have been responsible.

Of more immediate interest than the recurrence rate, which cannot yet be properly assessed, is the morbidity and immediate postoperative course of these patients. The conclusion may be stated now that there is no

TABLE I—QUADRANT DISTRIBUTION OF PRIMARY TUMOUR AND LYMPH-NODE METASTASES

—	Upper outer	Upper inner	Central	Lower outer	Lower inner	Total
All nodes free		16	1		2	19
Axillary nodes alone	2	8	3		2	15
Int mammary nodes invaded alone		10			1	11
Axillary and int mammary nodes invaded		7	5			12
Total	2	41	9			[illegible]

erican tests are widely used in this country, and when test has not been re standardised, caution is always ded in interpreting the results

The M.M.P.I has not been re standardised, and Cramond's results suggest that the "lie" scale at y rate should not be used in Britain until standardisan data on a British population are available

Woodford Green, Essex JANET CARR

WHOLE-TIME SPECIALISTS

SIR,

"The process of deterioration arising from a sense of ievance on the part of the staff may be a slow one, particuly in a service with the high traditions of the British vil Service, and by the time the tendency manifests itself eparable damage may have been done"—Report of the vil Service Commission

These sentiments apply with equal force to wholeme specialists, most of whom signed contracts in July, 949, after being assured that the then Minister of Health d agreed to accept the recommendations of the onsultant Spens Committee, and that "remuneration as regarded as a subject suitable for arbitration"

The Ministry's refusal to honour its assurances is breach of good faith which cannot be excused by the ibsequent discovery that they were not legally binding his discovery has, however, aroused grave misgivings mongst whole-time specialists about the way in which e negotiations have been conducted since the earliest ays

If, as some still believe, "Spens remains the yardstick f consultant remuneration" then not a single financial ecommendation about whole time service has been fully nplemented The Spens report advised that a wholeme consultant's salary should be from £1500 to £2500 a ear in terms of 1939 values, and that in bringing it p to date due regard should be paid not only to changes the value of money but also to the increased earnings other professions and other branches of medicine

Assuming the specialist is married with two young hildren, we see from the following table (the position efore the 1954 increases is given in parentheses) how the ecommendation has been given effect.

	Gross income today (£)	*Net income after deduction of tax (£)*
Whole time S.H.M.O		
Minimum	1500 (1300)	1251 (1094)
Maximum	1950 (1750)	1553 (1386)
Whole time consultant		
Minimum	2100 (1700)	1636 (1354)
Maximum	3100 (2750)	2091 (1883)
	Equivalent net income in 1938 (£)	*Corresponding gross income in 1938 (£)*
Whole time S.H.M.O		
Minimum	487 (481)	494 (489)
Maximum	605 (610)	638 (640)
Whole time consultant		
Minimum	637 (596)	678 (623)
Maximum	815 (829)	908 (914)

The cost of living has risen by 35% since July, 1949, compared with the 1954 increases of 14% in S.H.M.O salaries and 25–14% in consultant salaries, allowance being made for the Government's contribution to superannuation in all cases The benefit of the 1954 increases has now been wiped out by the subsequent rise in the cost of living, leaving whole-time specialists much worse off today than in 1949

A great deal of nonsense has been talked about the increases bringing whole time consultants' salaries into line with those of general practitioners after the Danckwerts Award in March, 1952 The award of a 100% betterment factor was richly deserved by the general practitioners, who have always conducted their negotiations in a business-like manner Although it did not mean that individual earnings were doubled, it gave the average general practitioner (except the 1000 shortlist men) £3240 a year gross (this figure was given during the debate on the Award and was not denied by the Government) Even though practice expenses amount to over a third of the practitioner's gross income, he scores heavily over the whole-time consultant because he obtains reasonable income-tax relief

The Spens Committee *assumed that* whole-*time* specialists would be paid "any sums which represent expenses reasonably incurred in the course of their work" in addition to the salaries recommended, and these allowances would not be liable to income-tax, and stated

> "The Evidence Committee has brought to our notice a number of items of expense which must be met if the specialist is to perform his duties efficiently These include car expense, expenses of travel apart from the use of a car, the cost of renewal of instruments and other equipment, the cost of books and journals, preparation of scientific papers, and subscriptions to professional societies, printing, stationery and telephone costs, expenses of attendance at national and international professional meetings, and the expenses of visiting hospitals and clinics at home and abroad, and entertaining visiting colleagues"

Few of these expense allowances have been granted none are adequately met

A whole time specialist on call for emergency and domiciliary visits must run a car, yet he is paid for only a fraction of the mileage he covers in the board's service, he is not paid for "routine" journeys to his main hospital even when he must travel by car because he is on call for emergency domiciliary visits or has to undertake other journeys on hospital business Management committees spend limited sums on hospital libraries and so provide some of the books and journals required Although the specialist must have a telephone because of his work, he is paid no portion of the rental, only the cost of outgoing professional calls if he can remember to jot them down In fact many whole time specialists who were formerly employed by local authorities and are now doing the same work under the N H S have had their car and telephone expenses drastically cut Study leave in theory, but not in practice, covers the cost of attending professional meetings Nothing has been done about any of the other expenses

The only expense item in the list on which the whole time specialist is allowed income-tax relief is his £2 a year subscription to a medical defence society

Comparing the terms and conditions of whole time service, we find that the difference in the maximum basic salary of a whole time consultant (£3100) and a part-time doing 9 sessions a week ($9\frac{1}{2}/11$ of £3100 = £2677) is £423, or £185 after deduction of tax

To compensate for his lower salary the part-timer has the following privileges

1 He gets a basic fee of 4 guineas for each of the first 32 domiciliary visits a year (£134), after that both whole-time and part-time specialists are paid at the same rate for the next 168

2 He is paid a travelling allowance of up to £190 a year (which, of course, is free of tax) for routine visits to his main hospital.

3 He is allowed up to 1 hour's travelling time out of each $3\frac{1}{2}$-hour session

4 He is allowed private practice and can thus secure income tax relief on many of his expenses

The fact that the whole-time specialist is, in effect, paid at a lower rate for doing exactly the same work as the part-time, and is denied reasonable expense allowances and income-tax relief, causes bitter resentment The most recent example is the new agreement about domiciliary visits

Up to now, whole time specialists have not been paid for these visits, though the Spens Committee advised that they should be The fact that under the new agreement whole time specialists will not be paid for the first 32 visits a year is degrading to whole-timers and makes the "concession" practically worthless

Only a *few whole-time* specialists are compelled by the terms of their contract to undertake these visits why should

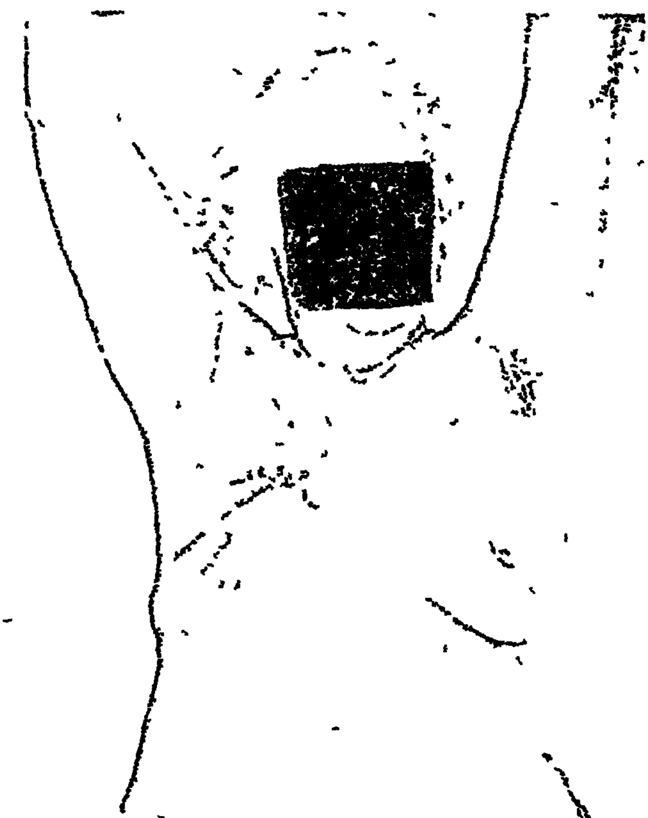

Fig 5—A patient, fourteen days after the operation to show that arm movement may rapidly return to normal

this never occurs Fig 5, showing a patient fourteen days after operation, demonstrates that a full range of movements is possible at an early stage

Œdema of the Arm —This is no commoner than after ordinary radical mastectomy No case of frank brawny arm has occurred Slight swelling of the upper arm has been noted, but is no greater than after standard radical mastectomy

Cosmetic Appearance —There is no significant difference in cosmetic appearance In some earlier cases where the whole sternal head of the pectoralis major was excised, there is some respiratory movement over the excised segment of chest wall In those where the pectoralis major has been left, it is not possible to tell from inspection alone that any of the chest wall is missing and the appearance is much better than after a Halsted operation, because the chest is not hollow below the clavicle

Length of Stay in Hospital —This was twenty four days as an average compared with twenty-one days for the standard operation Hospital beds are thus not much more occupied by this extension of the operation

Discussion

It is necessary first to consider some aspects of the theoretical basis of this operation The preservation of the pectoralis major in a procedure which claims to be radical is a departure from accepted routine The chief reason for ablation of this muscle is to enable the axilla to be easily reached Except in very advanced cases, invasion of the pectoralis major by carcinoma is rare, nor have we seen recurrences in the pectoralis major after its preservation though one of us (D H P) has made preservation a feature of breast carcinoma operations since 1930 The axilla can be reached and adequately cleared if the pectoralis major is preserved by relaxation and retraction The arguments on point are fully stated elsewhere (Patey and Dyson 19 It will suffice to say here that we believe preservat of the pectoralis major is compatible with a truly rad mastectomy

The operation described is not a monobloc proced This may be disadvantageous and is against that princi of cancer surgery which states that a primary tum and its metastases should be removed in one piece. I is no doubt desirable to achieve this if possible, but the present connection the preservation of the pector major (which makes a monobloc operation impossib seems a *very solid practical advantage to weigh agai* a more theoretical disadvantage

The various ways of extending radical surgery f breast tumours beyond its conventional boundaries hav met with some hostility on the score of danger a deformity *Our results show that an extended operati* is not significantly more dangerous, and this is also tru of Urban's technique , and far from being more mutilat than the classical Halsted operation, it is less so becau the pectoralis major is preserved and the chest wall n denuded of its muscular covering

Others have preceded us in devising surgical technique for attacking the internal mammary chain We ow *much to the ideas of Margottini and Bucalossi* (194 Wangensteen (1949), and particularly to Urban (195 who were first in the field They in their turn have pa generous tribute to the stimulus which the patholog investigations at the Middlesex Hospital played i suggesting the need for their operations They have bee followed by Bremer (1953), Sugarbaker (1953), Andreas et al (1954), Redon and Lacour (1954), and Abrao a Gentil (1955) While the technique we have described not so radical as some, we believe that it achieves compromise between doing too much and doing to little

At present two diverging lines of thought are curre in the treatment of breast cancer On the one hand ar those who believe in extending the scope of surgery in th sort of way which has been detailed On the other han *are those who think that surgery should be curtailed an* deep X ray therapy should play the principal role Th latter view has been sponsored chiefly by McWhirte and there can be no question *that his latest re* (McWhirter 1955) at least equal those obtained standard surgical methods X ray therapy will no however, "sterilise" invaded lymph nodes *with a* certainty This has been shown repeatedly *for th* axillary lymph nodes, and one of us (*Handley a Thackray 1954*) has produced biopsy evidence *that ev* after therapy the internal mammary nodes may cont histologically normal carcinoma cells There is th good reason for testing what more radical surgery achieve, because theoretically it may yield better resul Only if it were shown that blood spread is a consta early feature in the dissemination of breast carcinom or that there were other primary paths of lympha spread—e g , directly to the intercostal spaces in t region of the lateral perforating arteries—would theoretical reason for extending surgery be vitiated

There remains the difficulty of nomenclature operations which include excision of the internal ma mary chain *The term "extended radical mastectomy* has been used to distinguish these procedures from Halsted operation This term, coming at a time wh there is a widespread feeling that the extirpative surg of breast cancer has gone as far as is wise, is unfortun because the word "extended" carries an atmosphere the unjustifiable In fact the Halsted operation is re a semiradical mastectomy Pathologically the sort operation which we have described is merely remedyin deficiencies of technique in the old standard procedu those in the control group 4 were thought to have proved similarly

These results are not statistically significant, but some the children who received mestinon continue to prove and have been noticed to relapse if the drug is thdrawn It would seem that further trials are certainly stified

A supply of 'Mestinon' was kindly provided by Roche oducts Ltd

Department of Child Health
University of Liverpool

R J DERHAM

DOCTORS IN COMMERCE

SIR,—One wonders how many of your readers will have oticed an advertisement of a well known drug house on 44 in your issue of April 7, which announces several icancies for "medical representatives," and invites pplications from pharmaceutical chemists and qualified hysicians

I consider—and I believe many of my colleagues will e with me—that a medical qualification should not in us country be used in this connection I am aware iat on the Continent widespread medical unemployment as driven many young physicians into the arms of the rug houses, and I have myself witnessed the unedifying pectacle of a young physician going cap in hand to sell roducts of his particular firm This has not happened ere as yet, but the above mentioned advertisement hould give our elders food for thought as to the increasing conomic straits of our young graduates

It is quite a different matter for a medical man to ork for an ethical drug house in a purely advisory apacity, or in a scientific field such as pharmacology ndeed a healthy critical and objectively creative influence ay be exerted by conscientious physicians in such posts

As a practical measure to put a stop to the attempt o use medical graduates as commercial travellers, I ould suggest that our medical journals take the lead in ot allowing any further such advertisements, and also hat as many members of our profession as possible be oused to show our displeasure at such practices to any ther pharmaceutical companies which may be contemplating such a move

As a medical graduate working myself in a scientific apacity for a pharmaceutical company, I beg you to llow me to sign myself

SCIENTIST

*** We agree with our correspondent, and regret that, y an oversight, we did not represent this view to the irm which sent us the advertisement —ED L

ECZEMA VACCINATUM

SIR,—In regard to Dr Napier's comment (Jan 14) on our failure to find any published reports of strict localisation of vaccinial lesions on the eczematous patches[1] I would like to say that we missed the report by Sommerville et al[2]

This was not listed in the *Quarterly Cumulative Index Medicus* under eczema vaccinatum, eczema or vaccinia—probably because these workers used the term Kaposi s varicelliform eruption, which has been abandoned by many and is used as a synonym for eczema herpeticum by many others

In none of the ten cases described by Sommerville et al was strict localisation of vaccinial lesions to the eczematous patches mentioned Dr Napier s comment about the frequency of this localisation is, thus, surprising Since in eczema vaccinatum (as well as in eczema herpeticum) the eczema determines the generalisation of vaccinia as well as the localisation of most vaccinial lesions, it is reasonable to expect that when vaccinial lesions are strictly confined to the eczematous patches (as in our case) this important characteristic should be emphasised, because of its bearing on the pathogenesis of the vaccinial eruption After all, the localisation of vaccinial lesions on the eczematous patches is not a mere coincidence

Regarding Dr Napier's thesis of direct inoculation of vaccinia virus in the eczematous lesions, this hypothesis is the older of the two concerning the pathogenesis of vaccinial skin lesions , it is also the more obvious and may seem the likelier But most, if not all of those who have tested this hypothesis do not favour it but that of hæmatogenous spread While the existence of lesions on the inoculation site is generally admitted, these lesions rarely appear in man (except after inoculation against smallpox)

As to the significance of the enlarged lymph glands, I again disagree with Dr Napier From our words "a hard painful lymph gland" he deduces that "surely this indicated infection travelling inwards and not outwards" We mentioned that the first lymph gland to appear did so "on the first day of the present illness" simultaneously with sore throat, fever anorexia restlessness, and "the eczematous patches became swollen hot and painful" From these data it is obvious that at least another lymphoid tissue organ—the tonsils—reacted at the same time as the right crural lymph gland This and other clear indications of a systemic reaction contradict Dr Napier's contention that "surely this indicated infection travelling inwards and not outwards" Besides, the enlargement of a lymph gland in the left crural region developed two days after the systemic symptoms and signs

Virus Section
Instituto Adolfo Lutz
Sao Paulo Brazil

LUIS F DE SALLES-GOMES

CORONARY-ARTERY DISEASE

SIR,—In the past decade observations in the post mortem room and in the laboratory as well as dietetic studies in the field have suggested lines of thought on the pathogenesis of atherosclerosis which may have practical bearing on the treatment and prognosis of ischæmic heart-disease This term is used to include coronary occlusion and thrombosis, myocardial infarction, and fibrosis leading to coronary insufficiency All these conditions are dependent on atherosclerosis

It is not possible by direct evidence to prove that atherosclerosis (formerly atheroma) is a reversible process . at first thought it seems impossible that thickened, diseased, narrowed, and possibly occluded arteries could revert to relative normality or that the atherosclerotic brittle aorta of the old man might change There is, however, some inferential and circumstantial evidence that such changes can take place

For some years I have carefully examined the coronary arteries while doing routine necropsies After a time it became apparent that without any deliberate forethought I expected to find atherosclerotic coronary arteries when examining the body of a well-nourished male over 50 , my guess often proved correct When examining a thin or wasted subject of the same age-group I expected to find relatively healthy coronary arteries , more often than not this presumption was correct

Wilens[1] showed that at necropsy severe atherosclerosis is twice as common in obese as in undernourished subjects 35 years of age or older A high proportion of those found to be undernourished at necropsy had been well nourished or even obese before the onset of the terminal wasting disease It would seem that during a period of severe weight loss significant resorption of pre existing atherosclerotic deposits occurs

In doing routine necropsies I noticed the relative absence of atherosclerosis in the coronary arteries and aortas of subjects that had been treated with stilbœstrol for prostatic carcinoma, compared with other male subjects of the same age group[2] Not only was the atherosclerosis relatively decreased but surprisingly the aortas of the stilbœstrol-treated group seemed to have regained the elasticity of youth Rivin et al[3] confirm these findings except for the aortic changes

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[1] de Salles Gomes L F , Bassol O N , Patricio L D *Lancet* 1955 ii 1275
[2] Sommerville J Napier, W Dick A *Brit J Derm* 1951 63 203

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[1] Wilens S L *Arch intern Med* 1947 79, 129
[2] Aldin R *Brit med J* 1955 ii 630
[3] Rivin A L Dimitroff S P *Circulation* 1954 9 533

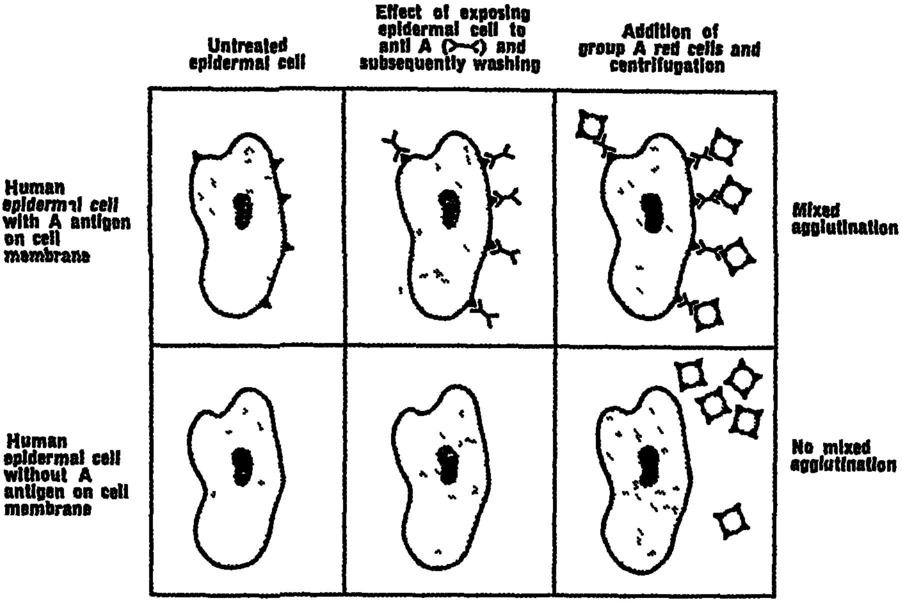

Untreated epidermal cell
Effect of exposing epidermal cell to anti A (>—<) and subsequently washing
Addition of group A red cells and centrifugation
Human epidermal cell with A antigen on cell membrane
Mixed agglutination
Human epidermal cell without A antigen on cell membrane
No mixed agglutination

Fig 1—Mixed erythrocyte epidermal cell agglutination reaction for detection of the A (and B) antigen on epidermal cells of human skin

surgery The tissue, spread on tulle gras and folded in gauze wrung out in saline solution, was still suitable after storage for one or two weeks at 4°C

Suspensions of isolated epidermal cells were prepared from the stored split skin according to the method described by Medawar (1948) by a tryptic digestion process In brief, digestion separates the skin into two layers, allowing the dermis to be peeled off, leaving a flat sheet of pure epidermis This epidermal layer is rendered into a suspension by scraping the loosened cells into Tyrode's solution Cell clusters are broken up into a fine suspension by repeated drawing in and out of a fine bore pipett The cells are then wash twice in Tyrode's solution

Suspensions of Human Grou A, Group-B, and Group O R Cells

A few drops of blood were obtained by ear-prick and collected into 0 6% tri-sodiu citrate in saline solution Afte two washes in saline solution they were resuspended in a 1 in 100 dilution of inactivated normal rabbit serum previously absorbed free from antibodies for human red cell (hereafter called N R S dilu ent) The purpose of the 1 in 100 dilution of rabbit serum was to prevent the red cells from sticking to the glass slides and coverslips when the test is read

Glassware

Siliconed glassware was used in the tests

Anti A and Anti-B Grouping Sera

These were human sera issued by the National Blood Transfusion Service for routine blood typing

Experimental Study

Demonstration of A and B Antigens on Epidermal Cells

Five drops of a suspension of the human epidermal cells under study were placed in each of two tubes (8 × 50 mm) Five drops of heat inactivated human anti A grouping serum were added to one tube and anti-B to the other tube The mixtures were

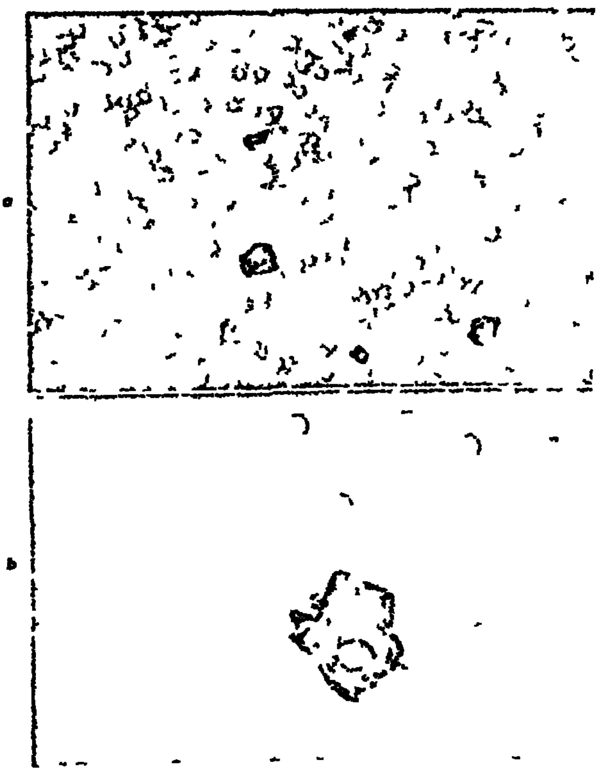


Fig 2—Mixed erythrocyte-epidermal cell agglutination reaction negative result—red cells have no affinity for the serum treated epidermal cells (Phase-contrast microscopy a × 125, b × 500)

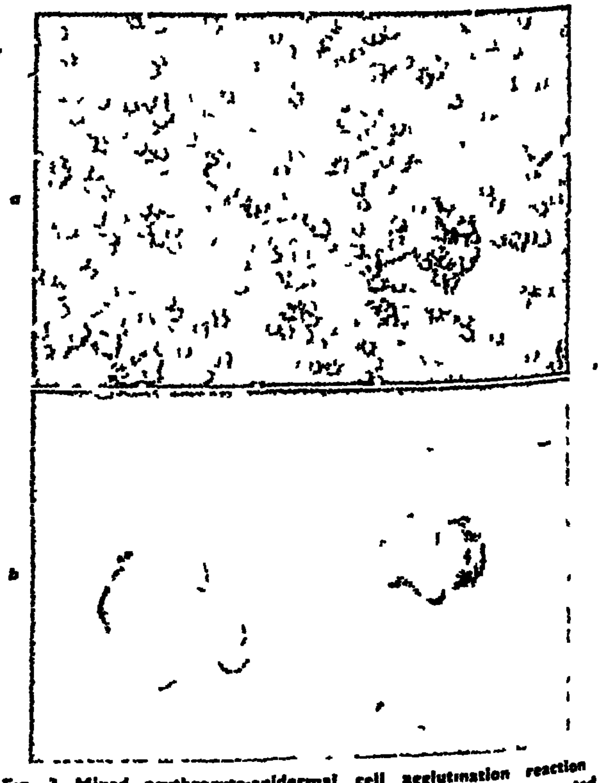


Fig 3—Mixed erythrocyte-epidermal cell agglutination reaction positive result—red cells adhering specifically to the serum treated epidermal cells (Phase-contrast microscopy a, × 125 b, × 500)

Balloon and tube systems of smaller diameter will make the swallowing more popular

Though I have encountered no harm from lavage with 1 200,000 adrenaline, wider experience is necessary to ensure that no harm will be done in any particular case

London, S W 10 F E WEALE

DEFICIENCY OF ESSENTIAL FATTY ACIDS

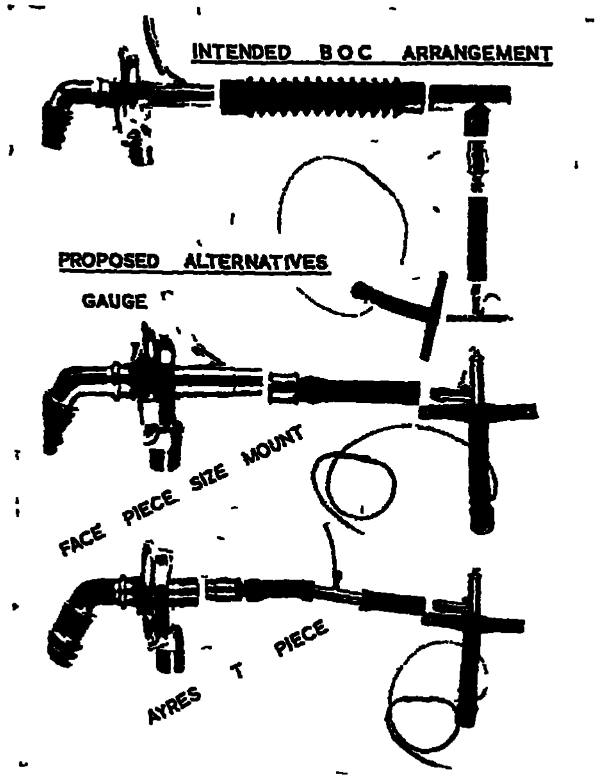
SIR,—With reference to Dr Sinclair's stimulating letter last week, I should like to add that when essential fatty acids are applied to mammalian epidermis there is immediate absorption

The results in cases of psoriasis and acne, after treatment in wet high thermal conditions combined with application of fatty acids, are very encouraging The fatty acids used are the essential fatty acids combined with the saturated and unsaturated fatty acids of the acetic, acrylic, and scorbic series The difficulty has been to prepare these substances without their pungent odours Lanolin and fats, as vehicles for medicaments, must give way to fatty acids on account of the extremely good penetration values of the latter

Tunbridge Wells E F ST JOHN LYBURN

BEAVER MARK II RESPIRATOR

SIR,—It seems that there is some doubt among the recipients of Beaver Mark II respirators as to how these should be connected to tracheotomised patients I apologise that through my negligence this is not illustrated either in the B O C catalogue or in the instructions circulated via the Ministry of Health I hope that the accompanying figure (by courtesy of the Institute of Neurology at the National Hospital) will clarify the arrangement Personally I prefer the "alternative" fittings for reasons of simplicity, and elimination of dead space and potential water trap The figure also shows the moulded rubber, cuffed tracheotomy tubes that have proved completely satisfactory



National Hospital
Queen Square
London W C 1

ROBERT BEAVER

IN THE MENTAL HOSPITAL

SIR,—Your valuable series has given stimulating accounts of ideas and findings in the special field of the "forgotten patient" Perhaps I may be permitted to draw attention to an experiment which might develop into a profitable example of how care, occupation, and daily routine can be combined in order to serve the mentally handicapped

The Camphill Village Trust has been conducting this experiment since September, 1955, on a recently acquired estate in the Cleveland Hills in Yorkshire The Trust was founded by a group consisting of parents of handicapped children and staff of the Camphill and Sheiling Schools (residential schools for handicapped children) Enough funds were raised to secure a start, and the first 25 "villagers" (16 men and 9 women ranging in age from 18 to 38) are now living and working together under the leadership of the Reverend Peter Roth

The aims of the village community are threefold

1 That in a few years, after the initial difficulties of finance and building are overcome, the village be established as a self supporting community, similar to the Papworth Settlement At the moment there are three farms which are already working and run entirely by the villagers, a start has been made towards a weaving shop, and pottery, joinery, and bookbinding departments will be added in time

2 That for none of the villagers fees are to be paid Parents and relatives are invited to make some financial contribution to the Trust if they are able and willing to do so The Trust is to run the village by voluntary contributions until it becomes self supporting Thus everyone in need of this kind of environment will have the possibility of obtaining it Furthermore the villagers know that it is their effort that provides their livelihood Under this arrangement it is hoped to establish in each one of them a fundamental self assurance and dignity, the conviction that it is "their" village which they build and promote will be a great stimulating force

3 That the villagers live together in a small unit of four or five with their foster-parents, who not only look after them but share their life and work No rigid distinction between "staff" and "inmates" is made, social activities are common, lectures and classes are attended by everyone

It is much too early to speak of results, but most of the villagers have settled down very happily, and already show much enthusiasm for their duties and a sense of responsibility which previously had been lacking

Milltimber
Aberdeenshire

KARL KONIG

VACCINIA VERSUS POLIOMYELITIS

SIR,—Dr MacIver (Feb 4) reports an investigation suggesting that the paralytic form of poliomyelitis seldom attacks children who have been vaccinated against smallpox in the previous few years We have taken up his suggestion that larger material be studied and have examined the vaccination state of 111 children in Vienna, under 4 years of age, who contracted paralytic poliomyelitis in the years 1951–55, comparing the relationship between the vaccinated and unvaccinated children in this group with the relationship between the vaccinated and unvaccinated coeval children in the whole population of Vienna The results of this investigation are shown in the accompanying table

VACCINATION STATE OF ALL CHILDREN AND OF CHILDREN WITH PARALYTIC POLIOMYELITIS IN VIENNA, 1951–55

Age (yr)	All children		Children with paralytic poliomyelitis	
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated
1	14 445	45,269	2	15
2	43 660	18 155	20	11
3	50 776	18 023	20	10
4	55,466	23 577	27	6

FACTOR IN ARACHIS OIL DEPRESSING SENSITIVITY TO TUBERCULIN IN B C G-INFECTED GUINEAPIGS

D A LONG
M D Lond

A J P MARTIN
M A, Ph D Camb, F R S

MEMBERS OF SCIENTIFIC STAFF, NATIONAL INSTITUTE FOR MEDICAL RESEARCH, MILL HILL, LONDON

ROUTINE testing, by the method of Long and Miles (1950), of an antirheumatic preparation for which cortisone-like activity was claimed showed that it slightly but significantly depressed the sensitivity of B C G-infected guineapigs to tuberculin, but the antiallergic activity was found to be in the arachis oil in which the drug was suspended and not in the drug itself

Fractionation of the arachis oil produced material which, in doses of 6×10^{-8} g per kg of body-weight, maximally reduced sensitivity to tuberculin in sensitised guineapigs The maximal reduction that can be achieved is slightly greater than that possible with cortisone acetate, which requires a dose of 5 mg per kg of body-weight

The antiallergic factor in arachis oil appears to be combined in several different phospholipids with differing solubilities The activity persists after alkaline hydrolysis of the phospholipids, and the active substance appears to be an amine with about 10-14 carbon atoms in it

Coburn and Moore (1943) showed that feeding dried egg-yolk to underprivileged children prevented the recurrence of rheumatic fever in spite of repeated attacks of hæmolytic streptococcal infection Wallis (1954) found that the consumption of eggs was significantly less in children who developed rheumatic fever than in a comparable group who did not Coburn et al (1954) have separated from egg-yolk a phospholipid fraction which possesses antianaphylactic activity in guineapigs and to which the antirheumatic properties of eggs may be due Following Coburn's lead we have found that egg-oil possesses antiallergic activity in the Long and Miles (1950) test and that the active substance appears, in its chemical and biological properties, to be similar to, if not identical with, the substance in arachis oil It thus seems probable that the antianaphylactic substance of Coburn is similar to, or the same as, the antiallergic substance in arachis oil

The antirheumatic property of egg-yolk may be due to its content of biologically valuable protein (Long 1954a) or to the antiallergic factor The protein itself does not possess antiallergic activity

Methods

The biological test is made by measuring the diameter of the lesion produced by injecting two different doses (32 and 320 I U) of Old Tuberculin intracutaneously into guineapigs infected at least a month previously with B C G The active substances were injected subcutaneously dissolved in 1 ml of biologically inactive oil or in aqueous emulsion (Merck & Co, Aqueous Vehicle No 1") (similar results being obtained by either method) five or six hours *before the injection of Old* Tuberculin The diameters of the lesions were read next day Administration by mouth twenty four hours before the tuberculin test also depressed sensitivity, hence similar substances in the diet would presumably be assimilated in man

To detect with certainty a tenfold difference of activity it was necessary to use ten guineapigs in a group In any one experiment eighty guineapigs were used affording seven tests of substance or dose level and one control The guineapigs were used once only

The fractionation methods had to be carefully sele in view of the impossibility of obtaining an accurate of the potency of any substance A method was only value if a clear-cut division into "active" and "inactive" fractions was obtained Usually no procedure w adopted unless the fraction to be discarded proved to b "inactive" at ten times the dose that the fracti retained was "active"

In two successive winters work had to be suspende because the biological tests gave inconsistent resul The variation within the groups increased greatly a later a syndrome developed analogous to kwashiorkor i man This disease occurred in winter in many labora tories (*cf* Paget 1954) in which, as in our case, Bruce and *Parkes* (1947) pelleted diet 18 was the main source of food The addition of skimmed milk to the diet both cured and prevented the disease Skimmed milk was therefore substituted for 5% of the grass meal of diet 18 This modified diet, 18A, which is available commercially from Associated London Flour Millers, enabled us to make satisfactory assays irrespective of season Diet 18A was supplemented, as was diet 18 in previous wo (Long and Miles 1950), by unlimited hay and cabbag

Chemical Methods

A preliminary experiment showed that shaking arach oil (active at about 1 ml) three times with an equ volume each time of methanol extracted the whole the activity (The residue was used as a vehicle f administering active fractions) The combined extra were about twenty times as active as the original o and probably almost the whole of the activity was the first extract When the extract had stood for som weeks, a bulky precipitate was formed which could b centrifuged down and contained most of the activit Extracting this precipitate, which was about a quart of the whole, with 40°-60° b p petroleum ether an later, with acetone left a very small amount of extremel insoluble material, active in single doses of 1 mg p guineapig, which was typical of a phospholipid in it solubility behaviour and physical properties By far th greater part of the activity was left in the soluble part though the activity per unit weight was much le Th suggests that the active substance could be combined in range of phospholipids of differing solubilities

Arachis oil was obviously not the best source of th phospholipid, and it was confirmed that more activ extracts could be obtained from ground-nuts and und from hexane extracted ground-nuts, by extraction wi methanol However, a more convenient source wa "vegetable lecithin" from ground-nuts, which is com mercially available as a by product of the manufacture arachis oil and is active at 1-10 mg

The activity persisted after hydrolysis with alcohol potash, and was found in the non saponifiable fractio There was no evidence of loss of activity, but a su stantial loss could have occurred unnoticed Lar amounts of sterols were crystallised from the no saponifiable matter and were without activity T remaining material, a deep brown oil, became semi sol on standing overnight Molecular distillation at 100 removed all the activity The distillate, which appear to have the whole of the original activity, was a pa yellow oil A small amount of more volatile mater collected in the cold trap and had an activity about tenth of that of the main distillate, suggesting th *distillation at a lower temperature would have be* profitable

By titration with perchloric acid in glacial acetic ac with methyl violet as the indicator, it was found that these fractions contained small amounts of amines T active distillate was therefore distributed betwe acidified 80% methanol water and cyclohexane T activity was confined to the acidified solution In

Obituary

CECIL ARMSTRONG CALVERT

M.B Belf., F.R.C.S.I

Mr. Calvert director of neurosurgery at the Royal Victoria Hospital, Belfast, was killed in a motor accident on April 4, when on his way to the funeral of the late Mr A. H. M Eaton of Omagh The car in which he was travelling collided with another vehicle and his companions Prof F. M. B Allen and Dr. Ivan McCaw, were seriously injured

At his funeral service last Saturday, St Anne's Cathedral was filled to overflowing, and the streets outside were lined with people. This was because he was a man of outstanding quality, and the following accounts of him, by two friends show why he was so much respected and so much liked

* * *

[Green, Belfast

Cecil Calvert was approaching sixty-two at the time of his death although he looked younger and still had more than ample vigour for the exacting nature of his work. He himself however, was not convinced of this; for recently, one evening about 10 o'clock he begged to be excused because he was feeling unaccountably tired. That day had been begun by operating from 2–9 A.M. on a patient with severe head injuries Having completed this task he had gone home for breakfast and a bath returning at 11 to operate on another patient, this time with a ruptured intracranial aneurysm He had successfully exposed and secured this by wrapping it with muscle and the patient had been safely returned to bed by 6 P.M., after which he had just had time for a hasty meal before proceeding to a meeting of the Surgical Journal Club, at which the above incident occurred

He was the second of the three sons of the late Mr and Mrs. James Calvert of Lurgan, his mother being an Armstrong of Tullyweel, Fivemiletown, co Fermanagh Educated at Lurgan College, his first serious interest was in astronomy, and it was with the idea of providing a livelihood, whilst he pursued further studies in this field that he decided first to enter the banking profession Both of his brothers had elected to do medicine, a course to which he was not attracted until later, in 1916 in which year his younger brother Howard, then serving in the Army was killed in action Entering the Queen's University of Belfast in 1917, he had a distinguished undergraduate career and qualified in 1922 obtaining first-class honours and an exhibition in the final examinations After spending a year as resident in the Royal Victoria Hospital he applied himself to postgraduate study in surgery and was admitted to the fellowship of the Royal College of Surgeons of Ireland in 1926 Meanwhile his potential qualities had been recognised and he was appointed surgical registrar and tutor successively Afterwards he worked for some years as clinical assistant to S T Irwin and with R J. McConnell two members of the visiting surgical staff of the Royal for whom he had particular regard, and for whose help in his early days he was always ready to acknowledge his indebtedness

It was about the same time that he met Geoffrey Jefferson through whom I believe he was probably inspired to interest himself especially in the surgery of the nervous system. This interest was fostered by his election to membership of the Society of British Neurosurgeons in 1926 Thereafter, he was rarely absent from meetings of the society, and with other members travelled widely in Europe, missing no opportunity of learning about new techniques and advances in this special field.

At home he had been appointed to the Ulster Hospital for Children and Women, and in 1933 to the honorary visiting staff of the Royal Victoria Hospital. He had begun consulting practice taking rooms in 2, Lower Crescent which were let to him by the late Miss Bostock, then a personage in the nursing profession and just retired from her position as matron of the hospital As his quite exceptional qualities became more widely known pressure of work steadily increased, and soon he was doing his full share of surgery and night emergencies at the hospital, outpatient sessions, teaching, and making long journeys at all hours into the country, often to operate on difficult cases and in hastily improvised surroundings On one occasion during an exceptionally hard winter, he had to abandon his car in a drift and proceed on foot through the snow for many miles carrying his instruments and other sterilised equipment to answer the call of a doctor in Ballyclare at the bedside of a patient with an acute abdomen

Such a life would have provided ample satisfaction for most men but between 1930–39 he found time to undertake, entirely on his own initiative many operations on the brain and spinal cord which being lengthy procedures had to be undertaken at night, and then only when a theatre was available Even so there was never any difficulty in getting volunteers to assist him and usually about 9 or 10 of an evening when preparations had been completed the operation would begin The results as is not surprising in the light of present knowledge were not always encouraging it required courage to go on, and good humour and tact to brave the often disapproving looks of the night sister at such frequent disruptions of her routine; but in time she became his staunch ally So he carried on often not leaving the hospital until 6 in the morning only to return two or three hours later (as fresh as if he had had a full night's rest) to grapple with a heavy outpatient clinic

Shortly after the outbreak of war in 1939 he volunteered for military service and accepted the invitation of the late Sir Hugh Cairns to join him and others at the Military Hospital for Head Injuries Oxford Here he worked until the conclusion of hostilities, being promoted to the rank of lieut.-colonel His exceptional skill as a brain surgeon, his phenomenal yet apparently effortless capacity for sustained physical and mental activity, and the care and thought he bestowed on the wounded men committed to his charge commanded the respect and affection of all those who worked with him. Whilst at Oxford he made some outstanding contributions to the surgery of wounds of the head which were published in the War Surgery Supplement of the *British Journal of Surgery* (1947)* The first was on Orbito-facio-cranial Gunshot Wounds and the second appeared jointly with his chief Cairns Peter Daniel, and G B Northcroft under the title of Delayed Complications after Head Wounds with Special Reference to Intracranial Infection

In 1946 he gave the annual oration to students at the opening of the hospital winter term, selecting as title for his address the Development of Neurosurgery (*Ulster med J* 1946, 15 141) At its conclusion he made the following comments the significance of which (as they applied to himself) may not have struck us then as forcibly as they now do He said

> This brief record of the contributions to neurosurgery fails to take note of the spirit which infused the daily lives of the great men who laid its foundations and built up its various departments Amongst other attributes common to them all was honesty of purpose, a simple desire for the truth and nothing but the truth" He went on: 'one might say of each of them as Shakespeare said of Brutus—'His life was gentle and the elements so mixed in him that nature might stand up and say to all the world, This was a man '

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* Earlier pre-war publications had been Whitla's Dictionary of Treatment (8th Ed.), of which he was joint editor, and a paper on Congenital Talipes Equino Varus (*Ulster med J*, 1933) He also published a paper on Injuries of the Frontal and Ethmoidal Sinuses during the war (*Proc. R Soc Med*, 1942)

The active substance appears to be an amine with about 10-14 carbon atoms

Vegetable lecithin, from peanuts or soybean, provides a rich source of the factor

A similar, if not identical, substance is concentrated in egg yolk

The possible relationship of this factor to the work of Coburn et al (1954) on the antirheumatic properties of egg-yolk is discussed

We are indebted to Dr Knud Tolderlund, of the Statens Seruminstitut, Copenhagen, for the B C G, and to Miss M V Mussett for the statistical analysis on which our observations are based

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EFFECTS OF DIVIDING THE PITUITARY STALK IN MAN

DOROTHY S RUSSELL
M A Oxfd, M D Lond, Sc D Camb, LL D Glasg, F R C P
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF LONDON
From the Bernhard Baron Institute of Pathology, the London Hospital

PUBLISHED reports on the results of dividing the pituitary stalk during intracranial operations are both few and discordant Dott (1938, case 2) recorded no untoward effects in respect of pituitary function On the other hand in Cushing's case (1912) death followed, in acute pituitary cachexia, 3 days after the operation Post mortem examination revealed that the stalk had been divided at its junction with the gland, and that the anterior lobe had undergone necrosis In 1940 Dandy reported the case, in a girl of 17, in which he had divided the stalk midway between the brain and the diaphragma sellæ Postoperatively there was permanent diabetes insipidus but no dysfunction of the anterior lobe the patient subsequently married and was twice pregnant Rasmussen's case (1940) is excluded because his description indicates that the stalk was not in fact completely divided, and, further, the *anterior pituitary* was deliberately cauterised at operation

In the present communication, illustrated by three cases, an attempt will be made to reconcile these divergent results in the light of recent investigations of the intimate vasculature of the pituitary body (Xuereb et al 1954)

Case-records

FIRST CASE

A man of 41 was operated upon *for a suprasellar craniopharyngioma* by the late Sir Hugh Cairns in 1933 For the previous 4-5 years there had been some impairment of anterior pituitary function—increase of weight impotence and lack of energy On examination he was slender and pale, with a thin wrinkled and slightly scaly skin He had a thin beard but hair was absent from the trunk and pubic hair was of feminine distribution His external *genitalia were small* A sugar tolerance test gave a low and rather flattened curve Daily intake and output of fluids varied from 1124 to 1537 *ml*

After operation, when the pituitary stalk was accidentally divided he remained stuporose with a tendency to delirium

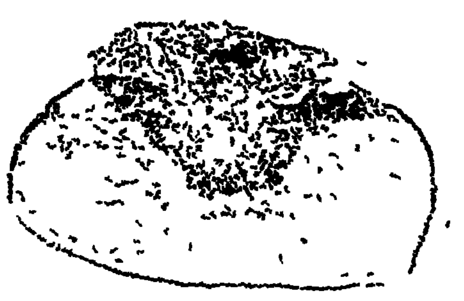

Fig 1 (case 1)—Horizontal section of pituitary showing necrosis of anterior lobe (pale) and fringe of surviving cells (dark) (Haematoxylin and eosin × 45)

He made few spontaneous movements, and developed spasticity *of* all limbs, with a transitory extensor plantar response on the right His temperature remained at 96 F except *for* two excursions above normal within the first 4 hours Pulse rate was from 100 to 120, blood pressure remained at 60/50 mm Hg, and rose only to 85/70 mm after a blood transfusion A single injection of 0 75 ml of a crude extract of whole pituitary (prepared by a commercial firm) produced a temporary rise to 110/90 mm 4 hours later

He became progressively more emaciated during the 1[illegible] days of his survival, and facial hair ceased growth though previously he had shaved daily The skin over his malar eminences became shiny and waxy Urinary incontinence *prevented any estimate of fluid output, but his daily intake* varied from 592 to 2631 ml and he was disinclined to drink

Macroscopic Examination (P M 399 1933)

At necropsy operative division of the stalk was confirmed though its remains were not identified There was a ragged gap in the floor of the third ventricle exposing the interior of the cystic tumour The sella turcica was shallow the dorsum sellæ being *greatly* eroded The pituitary body (0 35 g) was slightly *flattened, and on horizontal* section the anterior lobe appeared pale and opaque, the posterior lobe normal *The adrenals (7 4 g) and thyroid gland* [illegible] appeared normal Both testes were small (11 8 g)

Microscopic Examination

Pituitary—The *anterior* lobe is necrotic except for a narrow subcapsular zone, a few cells deep, which expands into a somewhat broader irregular strip against the junction with the posterior lobe (fig 1) Internal to this peripheral rim is a zone of young granulation tissue containing numerous foam cells The *posterior* lobe is normal apart from a slight increase in the number of pituicytes

Other endocrine organs—The *adrenal* cortex is narrow the zona glomerulosa prominent and well preserved while the nuclei of the zona fasciculata are often shrunken and pyknotic The zona reticularis is focally infiltrated with plasma cells and there is less nuclear degeneration The medulla appears normal The *thyroid is normal,* containing abundant colloid In the *testis* there is slight diffuse atrophy of seminiferous tubules, with fibrous thickening of their basement membranes Although many spermatogonia and spermatocytes are in stages of division there is no evidence of spermatogenesis, and the tubules of the rete are empty The three *parathyroid glands,* examined *appear normal*

SECOND CASE

A girl aged 8 well developed and intelligent for her age, was admitted to hospital in 1951 with symptoms and physical signs referable to a suprasellar craniopharyngioma A radical attempt at its removal was complicated by division of the pituitary stalk though this was not actually seen at operation *She survived for 33 days* during which she lay for the most part unconscious and unresponsive though she occasionally attempted to obey commands She made no spontaneous movements, but would *move slightly in response* to pinprick Flaccidity of the limbs developed, with absent reflexes Within 24 hours of the operation blood *pressure* fell to 90/60 mm, temperature rose to 102 F, and pulse and respiration rates to 160 and 70 respectively With the *administration* of pressor substances and of cortisone, and later corticotrophin, her general condition improved appreciably, *and* the blood pressure rose to 115/65 mm, though it fluctuated considerably and was sometimes too low to estimate *There was never any* n his later years, gardening, both of which he was able to njoy to the full at his charming home at Elie where he had a appy time with his family and grandchildren

Mr Jardine leaves a widow and three *daughters*

BARBARA TCHAYKOVSKY
M D, B Sc Lond D.P H

Barbara Tchaykovsky, who died in her 81st year on Feb 5, was the eldest child of Nicholas Tchaykovsky, the well-known Russian educationalist and reformer, who, under the Czarist regime, was forced to leave his country in the '70s of the last century After a period in the United States, where Barbara was born, the family came to England and settled in Harrow, which remained their permanent home She was educated at the North London Collegiate School for Girls, Bedford College for Women, and the Royal Free Hospital She was a brilliant student, and, although her medical studies were protracted because she had to earn her living by teaching and coaching, she graduated M B Lond in 1906 and M D in 1908, when she was awarded the university gold medal in State medicine She had already obtained the D P H

After qualification she was appointed a part-time school medical officer under the London County Council, a position which she held until her retirement under the age-limit in 1940 She also held appointments as medical officer to a few private schools During the whole of her professional life she gave her spare time her energies, and her means, to the furtherance of the maternity and child-welfare movement In 1912 she founded a dental clinic for the school-children of Harrow and district, at a time when there was no provision for treatment of the dental defects revealed at school medical inspections This was followed in 1915 by the foundation of the Wealdstone Day Nursery and, associated with it, the first baby clinic and antenatal clinic Her efforts were largely responsible for the establishment of the first municipal baby clinic in the district and for the formation of a special maternity and child-welfare subcommittee of the local public-health committee on which she herself served for over twenty years She also founded the Council of Child Welfare for Harrow and District, which coordinated the voluntary services dealing with antenatal, dental massage, and sun treatments an observation ward for ailing babies, *and a* clinic for child guidance It was not until 1937 that responsibility for all these activities, created largely through her personal energy and enthusiasm, was jointly assumed by the Middlesex County Council the Harrow Urban District Council, and the Harrow Hospital

H C writes "Dr Tchaykovsky was endowed with a typical Russian temperament, marked by great enthusiasm and driving power She was generous to a fault and would respond without stint from her modest resources to appeals for help She will be greatly missed by her friends, who loved her for her personal qualities and admired her for her devoted public service"

THOMAS ROBSON
M D Lond, *M R C P*

Dr Robson, senior physician to the Royal Victoria Hospital, Bournemouth, who died at his home on March 22 at the age of 54, was born in Cardiff, the son of a consulting engineer Educated at the Cardiff High School *he* began his medical studies in Cardiff and continued them at St Thomas's Hospital He qualified in 1923 and after a period as resident physician under Dr Frank Eve at the Royal Infirmary Hull, he went into practice at Royston Herts While in this general practice he took the M D Lond and M R C P In 1930 he moved to *Bournemouth* where he was for some years in partnership with the late Dr Bottomley He became physician to the Cornelia and East Dorset Hospital, Poole and was *later* appointed an assistant physician to the Royal Victoria and West Hants Hospital, Bournemouth in 1939 he became a full physician He took an active *part not only* in the clinical work of the hospital but also on its administrative side, and for some years was *vice-chairman of* the board of management He was also the secretary of the Bournemouth Medical Society

T R A writes

Tom Robson was always a bonny *fighter* Though born in Wales, his roots were in the North Tyne, the home of the turbulent Robson clan of whom Trevelyan says "they paid little heed to the things writ or even to the feudal power of the Percies' Collaterals of George Stephenson, his people were railway engineers who drove the iron roads through Britain, and this iron and this driving force were part of his nature Here indeed was a physician with the brain of an engineer, clear cut as a precision tool, penetrating to the root of the matter, all trimmings and superfluities shorn away, a brilliant diagnostician He fought to establish the position of the physician and to prevent the splitting of general medicine into too many branches He believed that when all laboratory tests had been assayed and all specialists had had their say there would always be the need for someone with a wide knowledge, not only of medicine but of life and philosophy, to give a final opinion He fought against death when it approached his patients, as if it were a personal affront, all his forces were mobilised, no time or effort was spared He rejoiced over each victory and mourned each loss His great capacity for work and his complete inability to relax finally ended in his own defeat, after a long courageous struggle against ill health "After life's fitful fever he sleeps well" He will live long in the memories of both doctors and patients in this part of the country

Dr Robson is survived by his wife and a daughter Dr Margaret Robson, and a son who obtained an open scholarship at St John's Cambridge, and is studying medicine there

Dr J E O'LOGHLEN

K B writes

In these days when it is fashionable to stress the importance of general practice, the death of Dr O'Loghlen should not pass without notice, since few of the last generation can have done more to enhance its status His versatility was remarkable He was skilled in the practice of the many minor surgical *procedures which fall* within the scope of the general practitioner—and indeed some major procedures *for his rectal* work attracted and kept patients from far afield He neglected no *specialty In medicine* his knowledge and ability were great, while a host *of* patients have reason to be grateful to him *for* his gifts in the diagnosis of orthopædic ailments of all kinds and *their* treatment, especially by manipulation His ability seemed *sometimes* to be based on a special sense, but was in reality founded on a solid basis of anatomy, the *study of which* he *continued* throughout his life

His concern was always where possible for the re education of his patients and the prevention of the faulty habits which *had led to their disease* His storehouse of advice particularly about minor ailments, was an unending *surprise* He gave his time in strict proportion to his patients needs wasting little on the idle and the trivial, but showing the utmost *concern for those* who were really ill He always kept in touch with those whom he had had to refer to a *specialist*— He wore his great kindness of heart under a cloak, but those who knew him were not misled

Mr F J F BARRINGTON

R E S writes

"*I knew* Mr Barrington because he hired my father's shooting in Norfolk and he invited me to join him on several occasions He understood the way of birds and would walk *long* distances *for them* I often thought his insistence on being on the outside had its advantages and was convinced of it when at the end of a long walk we approached a field of *kale* on the outer side of which was a strip of stubble Down this he walked a little ahead of me and at the end was as fresh as is the month of May compared with us who emerged soaked to the umbilicus and with wet mildew clinging to our jackets But all was soon forgotten as he handed round his flask remarking that he thought the risk of contagion was small I feel sure those Saturdays from September to January restored his mental energy and kept him a fellow of infinite jest of most excellent fancy ' "

P H M -B writes

Barrington was by every measure an exceptional personality As I saw his lank slim figure, hatless as usual carrying the inevitable despatch case, swinging down Harley Street before turning into Marylebone Road the night before he died, I little thought that I *had* seen the last of my old friend Although I well knew the wide field of science over which his mind ranged, it was in natural history, and especially in ornithology, that we met on common ground Snorker was a

Other endocrine organs—In the *adrenals* degeneration of the zona fasciculata resembles that described in case 1, but cellular infiltration of the zona reticularis is less conspicuous The seminiferous tubules of the *testis* have undergone slight atrophy There is no evidence of spermatogenesis the cellular picture being similar to that observed in case 1 The tubules of the rete and head of the epididymis are packed with necrotic cells and poorly preserved spermatids Apart from focal carcinomatous infiltration of the stroma, the appearances of the *thyroid* are normal and there is abundant colloid

Discussion

In cases 1 and 2 necrosis of the anterior lobe resulted from operative division of the pituitary stalk In case 2 the development of purulent leptomeningitis can be excluded as a cause in the light of the clinical history In case 3 a similar necrosis was induced by carcinomatous permeation of the portal vessels In all three, acute anterior-lobe deficiency preceded death the length of survival in cases 1 and 3 being closely similar in the absence of hormone therapy In none was there any evidence of diabetes insipidus It is, however recognised that an intact anterior lobe is essential to the development of this syndrome, though precisely how this operates is controversial

Case 3 has the merit of demonstrating the essential part played by the portal vessels of the stalk in maintaining the nutrition of the anterior lobe Experimental confirmation of this is provided by Daniel and Prichard (1956) who found that arresting the blood flow in the portal vessels of the rat by cauterisation resulted in necrosis of the anterior pituitary But, owing to certain differences in the vascular supply in the rat, these necroses were not as extensive as those observed in the present human examples Sheehan (1937) has emphasised the importance of thrombosis in the sinuses below the level of the stalk in determining the development of Simmonds's disease after obstetric shock

The degenerative changes observed in the adrenal and testis of cases 1 and 3 illustrate the effects of recent deprivation of corticotrophic and gonadotrophic hormone

Recent anatomical studies (Xuereb et al 1954, McConnell 1953) have made it clear that the superior hypophyseal arteries do not directly supply the anterior pituitary But, having entered its substance, they subdivide and certain branches anastomose with twigs from the inferior hypophyseal arteries in the neighbourhood of the lower infundibular stem (i e, that part of the stalk which lies below the level of the diaphragma sellæ) According to Xuereb et al, branches from these anastomotic segments, as well as the terminal twigs of the superior hypophyseal arteries, ascend into the lower infundibular stem and break up into capillary tufts Blood is collected from these into short portal vessels which descend into the anterior lobe and, with the longer portal vessels descending from superior levels distribute blood to the sinusoids of the gland (fig 4) The extent of the circulatory disturbance inflicted on the anterior lobe should therefore be proportionate to the de interruption of portal supply, as already postulated b Xuereb et al the lower the level of division the le extensive will be the necrosis In Cushing's case we ha the valuable information that division was at the junc of the stalk with the gland, and necrosis was minim In case 1 above it may be inferred that division was at similar level, in case 2, where more of the gland surviv it was probably higher Division, in Dandy's case, at t middle of the stalk inflicted diabetes insipidus thro interruption of the supraopticohypophyseal tract nerve-fibres, but clearly did not damage the anter lobe sufficiently to impair its function

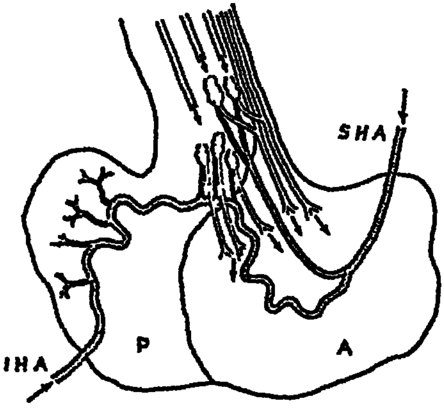

Fig 4—Diagram of relevant features of pituitary circulation (adapted from Xuereb et al) A anterior lobe, P posterior lobe SHA superior, and IHA, inferior, hypophyseal arteries The long and short portal vessels are represented breaking up into the sinusoids of the anterior lobe

At the present time hypophysectomy is performed i the treatment of advanced carcinoma of the breast Th object of the operation is to remove all anterior l tissue, and I submit that a simpler procedure—divi of the stalk at its junction with the gland, and caut of the cut segment, which should include destruction o the lower infundibular stem—may be equally effectiv If so the hazards to the patient would be reduced and th surgeon's task considerably simplified In the Londo Hospital Mr Northfield has adopted this modification i several cases, but as yet it is too soon to assess the full endocrinological effects

Summary

The effects of dividing the human pituitary stalk hav been examined in the light of three cases which came t post mortem examination, and of the existing literature

The extent to which necrosis of the anterior lobe wil result seems to depend directly upon the completenes with which the portal vessels are interrupted, and henc the level of division

It is suggested that division of the stalk at its junctio with the gland may be as effective clinically as tota hypophysectomy

I am indebted to Mr D W C Northfield for the cli notes of case 2

ADDENDUM

Since this paper was written one of Mr Northfield's cases came to necropsy two days after stalk section had been performed The gland (weight 0 8 g) was divided after fixation into eight sagittal pieces and sectioned serially Microscopically the posterior lobe is well preserved and partly occupied by secondary carcinoma The greater part of the anterior lobe is necrotic, with marginal infiltration of such tissue by neutrophil leucocytes A zone of surviving cells is closely related to the boundary between the anterior and posterior lobes an fans out laterally beneath the capsule on the postero inferior aspect of the gland The zone is irregular i outline and its lateral extensions are occasionally interrupted by the necrosis Elsewhere a thin interrupted zone, up to two acini thick, of surviving tissue lies beneath the capsule with the exception of the dorsal surface

To gain a rough estimate of the amount of surviving tissue, forty-four representative sections were projected and the living and necrotic areas outlined on paper, an these areas were then cut out and separately weighed By this means it was estimated that 8 4% of anterior lob survived This is probably excessive because degenerating cells are often mingled with those that appear we preserved

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amin E he reviews experiments by Taylor on the protec n of rats against the hæmolysis induced by hyperoxia, and ggests that the known low vitamin E levels in premature fants may be a contributory factor in the precipitation of ernicterus or retrolental fibroplasia after exposure to oxygen a stimulating end to the symposium, B S Platt's topics nclude civilisation and the sophistication of food, the application of the principles of nutrition through the agency of fficial organisations, such as F A O and W H O, and oncepts of balance, whether between different vitamins in he body, between nutrients in a diet, or even between the ize of the world and the number of its inhabitants

As scientific editor, Professor Platt has produced a symposium which Mellanby would have commended for the way it sets out the achievements of the science of nutrition, and particularly its application to clinical medicine

A HOSPITAL CENTENARY

THE Hospital of St John & St Elizabeth, London, this ear celebrates the centenary of its foundation It is a Catholic foundation, though the majority of its patients are on Catholics, and it is outside the National Health Service Patients are asked to pay what they can afford, and on average they contribute about £4 a week towards their total expenses of £15 Otherwise the hospital depends on voluntary contribution Admissions rose from 1783 in 1947 to 2578 in 1954 Over the same years the hospital's annual income increased from £42,000 to £92,000 and expenditure from £75,000 to £110,000 The hospital has opened a centenary appeal for £250,000 to clear the accumulated deficit, renew equipment, and provide more accommodation for training rses Donations should be sent to the fund, c/o Barclays ank, 54, Lombard Street, E C 3

MEDICAL RESEARCH IN MALAYA

THE Colonial Development and Welfare Act of 1946 was planned to promote the welfare of Colonial territories by financial grants for approved schemes The benefit to Malayan medicine from this aid has been incalculable, and its proposed extension to 1966 foreshadows continued support

The report for 1954 of the Institute for Medical Research at Kuala Lumpur is replete with information on bacteriology, serology, biochemistry, nutrition, pathology, virus research, medicine, zoology, entomology, and malariology The institute, rected by Dr J. W Field, has been linked with the Research epartment of the United States Army and Graduate School ollaboration began in 1947 with a clinical trial of chloramhenicol in the treatment of scrub typhus Since 1948 five American medical research teams, financed by the U S Treasury, have worked in the institute, and now a small American group is engaged there on the transmission of Japanese-B encephalitis, the leptospiral infections, and the efficacy of leech repellants Recent years have also witnessed increased liaison with the Army Medical Services, for which the jungle operations against Communist terrorists, the excellent hospital facilities of the Army in Malaya, and the deployment of many keen young doctors have been responsible The Army service has for the first time in Malaya isolated apanese B virus from a human infection In February, 1954, aboratories for the study of virus diseases were opened

This report gives some indication of the increasing value and amount of work undertaken at the institute

THE AMBULANCE SERVICE

CONCERNED by the increasing cost of the ambulance service (in the past three years this has risen by some 30% to about £10 million a year) and by its difficulty in meeting all demands, e Ministry of Health has made a fresh approach to hospital d local health authorities Over 60% of all calls on the ervice come from hospitals, and hospital authorities are sked to appoint a single person in each hospital to coördinate requests for ambulance transport The decision whether an ambulance or hospital car is needed should, says the Ministry,[1] be a medical responsibility, and only exceptionally should this responsibility be delegated to the nursing staff Local health authorities are asked[2] to ensure that the medical officer of health is closely associated with the ambulance service, and suggestions for more economical and efficient operation include use of radio communication and of hemmed canvas sheet stretchers with removable poles, to lift patients from an ambulance stretcher on to a hospital bed, thus saving delay of the ambulance through its having to wait for the return of its stretcher

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1 H M (56)28

2 Circular 5/56

FOUNDERS OF DERMATOLOGY

IN the Harveian oration for 1951 Sir Archibald Gray gave an account of the history of dermatology from the time of Harvey[1] He has now used the Prosser White oration to discuss the Founders of Modern Dermatology[2]

In the main he describes the work of three men—Joseph Jacques Plenck (1738–1807) who worked in Vienna, and two Yorkshiremen, Robert Willan (1757–1812) and Thomas Bateman (1778–1821) Willan came to London in 1781 and worked for more than twenty years as physician to the Public Dispensary in Carey Street where he was joined by Bateman in 1801 Willan set out to define the lesions and collate the various disorders of the skin, producing a simple classification on a morphological basis, and Bateman popularised Willan's work in a book which ran into many editions Plenck had produced a classification at an earlier date

Most of Sir Archibald's address consists in a critical and detailed assessment of Plenck's and Willan's contributions Plenck undoubtedly had the originality to introduce the morphological system of nomenclature Willan copied and clarified this, but what is more important is that he introduced a nomenclature which with some modifications has been universally accepted He, more than anyone, is recognised as the founder of modern dermatology Willan was also interested in epidemic diseases, and published annually from 1796 to 1800 monthly reports on the weather and prevailing diseases in London which is considered a pioneer work, and which was continued by Bateman from 1804 to 1816 He was partly responsible for the founding in 1801 of what afterwards became the London Fever Hospital, and was one of the original extraordinary physicians

MEDICAL FILMS

THE following films have been added to the library of th International Cripples Association

Treatment of Poliomyelitis with Curare and Stretch (16 mm, silent, black-and-white, 10 minutes U S A, 19 Victor H Raisman, M D, Kew Gardens Hospital, New Yor —This shows the improvement in a 17 year old boy un treatment with curare and stretching, at intervals from three weeks to two years after a severe attack of poliomyelitis The emphasis is on the results obtained rather than on details of the treatment, and there is no indication of the dosage of curare used This film is of interest to physiotherapists For specialists in physical medicine it includes insufficient clinical detail

Bugnet's Neurotherapeutic Method (16 mm, sound, black-and-white, 29 minutes Netherlands, 1954)—This film outlines the theory, application, and results of Bugnet's therapy for re-educating muscles after poliomyelitis It opens with a short introduction in which the principle of muscle activation by bombardment with stimuli is explained and the underlying physiology is shown on charts Examples of the use of the standing, walking, and grasp reflexes are shown The second half of the film is devoted to a series of cases illustrating the application of the technique This long film leaves no clear impression of the procedure or its advantages The exposition is muddled and the conclusions are confused

Mrs Hazard's House (16 mm, sound, colour, 11 minutes U S A Adviser Harry F Dietrich, M D)—This is a propaganda film, encouraging greater care in the prevention of accidents to children in the home

It opens with a visit to Mrs Hazard's house in which various hazards are depicted in a series of still cartoon pictures while Mrs Hazard describes the accidents she devises to change children into statistics Dr Dietrich is then introduced, and he remarks that accidents in the home cause more deaths annually than do disease or traffic accidents Finally a few examples of hazards in the American home of a young couple with an infant are shown, and the film ends by recommending that leaflets be obtained from local health authorities

Though designed for American audiences, this film might be useful in this country for selected general audiences

Further information about these films may be obtained from Dr Francis Bach 1a Devonshire Place, London W 1

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1 *Lancet* 1951, ii, 795

2 *Trans St John's Hosp derm Soc* Autumn, 1955

TABLE II—SURVIVAL AND CONTENT OF ADENOSINE TRIPHOSPHATE CONTENT OF CELLS INCUBATED WITH NUCLEOSIDE AFTER 3 WEEKS' STORAGE RESTORED AT 4°C FOR VARIOUS PERIODS AND REINCUBATED BEFORE TRANSFUSION

Storage (days)	Nucleoside	% survival at 48 hr		Adenosine triphosphate (µg of phosphorus per ml of cells)		
				Before incubation	After incubation	
		Nucleoside	Glucose		Nucleoside	Glucose
28	Guanosine	82	48	39	58	31
42	Guanosine	75	21	30	49	nil
56	Guanosine	67	17	28	39	nil

In table II are shown similar experiments in which blood had been incubated with the nucleoside at the end of three weeks' storage and then reincubated before its final transfusion. Here again there is increased survival of the treated cells, and their survival is better after long storage periods when treated in this way, *whereas there is but little difference between the two* groups after shorter periods of storage. These experiments were *performed* on three separated specimens of stored blood, which all responded well to nucleoside revival. However, as pointed out elsewhere (Prankerd 1956) there is some variability in the metabolic response of cells to incubation with nucleosides, and recently two specimens of stored blood have been found in which there was no satisfactory revival.

Fig. 2 shows a record of blood-pressure in a narcotised cat after the intravenous administration of various amounts of the two nucleosides. The drop in blood-pressure after adenosine contrasts clearly with the absence of any *change after guanosine.* *No abnormalities* on electrocardiography were observed although such have been reported in guineapigs given adenosine (Drury 1936).

To demonstrate the *innocuity* of *guanosine* when given to man, records of pulse, blood pressure, temperature, and biochemical tests are shown in fig. 3 of a uræmic patient who was given a pint of six-week old blood revived before transfusion by an hour's incubation with 750 mg. of guanosine. Electrocardiograms were taken frequently during transfusion, and no abnormal effects observed. The patient's hæmoglobin increased by an amount compatible with complete survival of the transfused cells twenty-four hours later, and after forty-eight hours there was no indirect evidence of excessive hæmolysis.

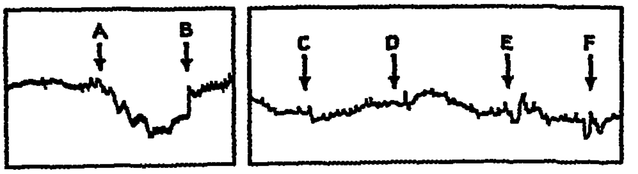


Fig. 2—Blood pressure tracings from narcotised cat. A–B, injection of adenosine 5 mg. C–D, injection of guanosine 5 mg. E–F, injection of guanosine 50 mg.

DISCUSSION

The benefit of reviving stored blood with nucleosides is clearly demonstrated by these experiments, and it appears that reasonably good survival can be obtained even in eight week old blood which has been revived after three weeks' storage and again before transfusion. The mechanism of this revival is *probably metabolic* and related to the increase in the intracellular content of adenosine triphosphate. Elsewhere (Prankerd 1956) the detailed metabolic changes taking place in stored blood have been reported, *together* with the effects of nucleosides. The conclusion from these studies was th after three weeks' storage, red cells lose their abi to phosphorylate glucose, and that this deficiency related to the decrease in intracellular adenosine t phosphate. Nucleosides enable red cells to resynth adenosine triphosphate; and, *once this has happened,* a *sufficient extent, phosphorylation* of glucose can again.

The mechanism of the nucleoside effect was disc in an earlier paper (Prankerd and Altman 1954b), which it was suggested that Dische's (1938, 19 observations were relevant. He observed that red- hæmolysates incubated with adenosine formed tr and hexose phosphates, all intermediates in the glycoly sequence. We concluded that, with intact erythrocyte the nucleosides were split by a nucleoside phosphoryla in the cell surface, and that the ribose phosph which *formed after the splitting* could be metabol by way of steps in the hexosemonophosphate shunt. These steps are shown diagrammatically below.

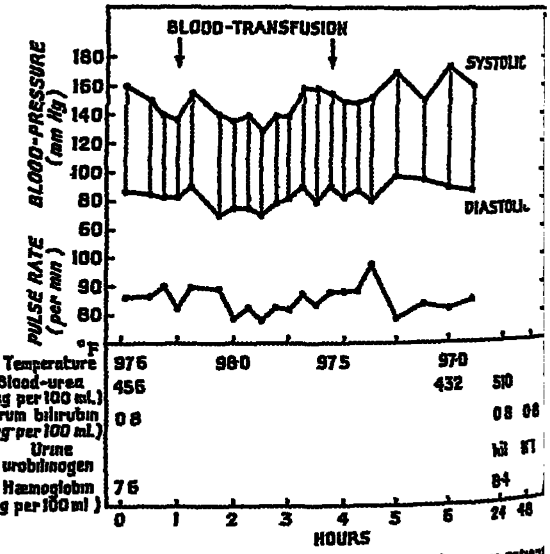
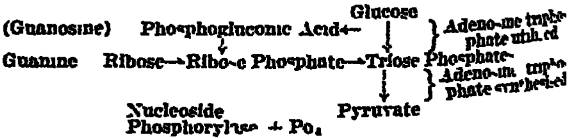


Fig. 3—Blood-pressure, pulse-rate, and biochemical changes in patient transfused with six-week-stored blood revived with guanosine.


Glucose
(Guanosine)
Phosphogluconic Acid
Adenosine triphosphate utilised
Guanine
Ribose
Ribose Phosphate
Triose Phosphate
Adenosine triphosphate synthesised
Nucleoside Phosphorylase + PO4
Pyruvate

The really significant point seems to be that, where adenosine triphosphate is required for the phosphoryla tion of glucose, it is not required with the ribose of th nucleoside, and it can therefore be resynthesised eve when the cell stores are severely depleted of it.

The chemical structures of adenosine and guanosi are shown in fig. 4, and the difference in toxicity betwee the *two seems to* be related to the chemical differen between them. The substitution of the amino group between them. The substitution of the amino group the 6th carbon of adenosine by oxygen in guanosi may account for the loss of toxicity. A number of oth nucleosides not showing this *amino group* have also be

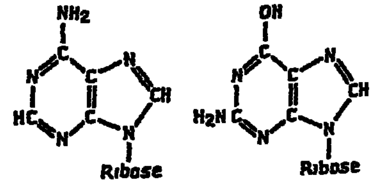


Fig. 4—Chemical structures of adenosine and guanosine.

EXCISION OF THE INTERNAL MAMMARY CHAIN IN RADICAL MASTECTOMY

RESULTS IN 57 CASES

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THE breast has at least two primary lymphatic drainage systems, the larger the axillary, the smaller the internal mammary Whereas the axillary nodes are invaded in about two thirds of patients with "operable" carcinoma of the breast, the internal mammary chain is involved in one-third (Handley and Thackray 1954) The classical radical mastectomy, which takes account only of the axillary system, is therefore foredoomed to failure on one occasion in three by reason of its neglect of the internal mammary lymph-nodes

Surgeons in an endeavour to deal with this unsatisfactory situation have, among other expedients, attempted to make breast surgery truly radical by excising both primary lymphatic drainage systems at the same time as the primary growth We describe here a simple technique for such an operation, and its immediate results in 57 cases There must of course be a lapse of some years before the late results can be assessed, but the present analysis shows that the internal mammary chain can be extirpated without significantly adding to the mortality, morbidity, or deformity of the classical operation

Technique

Several techniques have now been described for excising the internal mammary chain as an addition to "radical" mastectomy The method to be described differs from these chiefly in that it preserves the whole pectoralis major muscle

The operation begins with the same skin incisions as a radical mastectomy Thin skin flaps are raised to the usual limits of the proposed excision At the inner and upper corner of the wound the fascia is then reflected downwards and outwards off the pectoralis major muscle, sufficiently to allow this muscle to be split in the direction of its fibres over the first intercostal space A biopsy of the underlying internal mammary lymph-node is then made by incising the muscles of the 1st intercostal space, to discover whether the node is invaded by carcinoma If it is, the operation is terminated as a simple mastectomy If it is not, the internal mammary vessels are double tied as high as possible (a process which is facilitated by nibbling away the lower border of the first costal cartilage) and divided The first space is then left for the moment, and the reflection of the pectoral fascia and breast from the pectoralis major proceeds as far as the lower border of the muscle By lifting the arm so that it points towards the ceiling and by retracting the pectoralis major, the pectoralis minor can be sectioned close to the coracoid process, and at its lower attachment, and the axillary contents cleared in the usual way up to the lateral border of the first rib , the pectoralis major with its main nerve supply is preserved The breast, with its attached axillary tissue, is removed as a specimen similar to that from a classical radical mastectomy, except that it lacks the pectoralis major muscle

The arm is replaced on an arm board and the sternal head of the pectoralis major is divided just lateral and parallel to the edge of the sternum to reveal the costal cartilages and intercostal muscles The fifth costal cartilage is removed and the internal mammary vessels are double tied and divided at their lower end

A block of the chest wall, measuring about 4 in by 1 in and including the second, third, and fourth costal cartilages, the intervening intercostal muscles, and the internal mammary vascular bundle, has now to be removed, if possible without opening the pleura The first intercostal space is re entered and the pleura gently pushed by blunt dissection away from the inner side of the chest wall as far down as possible , it may sometimes be torn in this manœuvre The costal cartilages are divided at their medial and lateral ends by slipping a Kocher's enucleator under them one by one, and cutting them with a solid scalpel Alternatively the lateral edge of the sternum may be shaved off with a Lebsche chisel to free the medial ends of the cartilages A little further dissection frees the specimen, and until it is removed there are a few small vessels which cannot be adequately secured When hæmostasis is complete the cut edges of the sternal head of pectoralis major are reunited with mattress sutures, and the gap in the chest wall thus closed The skin is sutured and drainage provided only for the axilla grafting being used if necessary

Figs 1–4 show the main points of the operative technique

The chest wall dissection adds approximately half an hour to the time taken for a Halsted operation

Results

We have now treated 57 patients by some form of therapeutic removal of the internal mammary chain The earlier cases did not always follow the description given 3, for example, were done by Urban's technique,

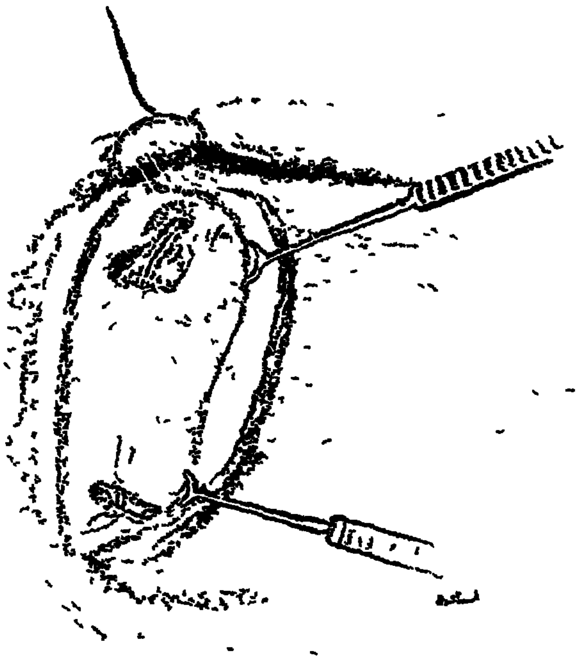

Fig 1—The breast and axillary contents have been removed and the pectoralis major muscle has been cut across the direction of its fibres, to reveal the costal cartilages The first and fifth intercostal spaces have been opened and the internal mammary vessels double-tied in the spaces

Experiment II

An attempt was therefore made to obtain 20 samples of liquor amnii in this way Patients who agreed to submit to the test were selected for paracentesis between the 32nd and 36th weeks of pregnancy if there seemed to be sufficient liquor amnii present to allow a sample to be taken safely 3 patients with obvious hydramnios were included in this number Samples were taken with a lumbar-puncture needle inserted through the abdominal wall in the midline just below the umbilicus after the injection of a small quantity of 1% procaine, 5–10 ml of fluid was withdrawn

Results —Paracentesis yielded suitable samples in only 13 of the 20 patients In 3 patients no liquor was aspirated at all and the attempt was not persisted with, in 3 others a little bloodstained fluid alone was obtained, which was considered unsuitable for examination, in 1 patient 2 ml of pure blood immediately filled the syringe when the plunger was withdrawn, and this attempt also was abandoned, 1 patient from whom bloodstained fluid alone was withdrawn began at once premature labour at 36 weeks' gestation Examination of the 13 samples obtained successfully enabled the sex of the fœtus to be diagnosed correctly in all (6 male, 7 female) In these samples relatively more cells suitable for study were observed than in samples taken by artificial rupture of the membranes later in pregnancy

Discussion

It seems clear from these results that, by careful examination of the nuclei of epithelial cells contained in specimens of liquor amnii, the sex of the fœtus can be accurately predicted Difficulties in interpretation were due to cell shrinkage simulating sex-chromatin masses and to debris partly obscuring nuclear details The number of nuclei unsuitable for study was sometimes great, the search for sufficient nuclei with good definition being then more arduous and time consuming, in 2 of the specimens examined sufficient suitable nuclei could not be found to allow a prediction to be made On the basis of such a small study it is impossible to assess how often these unsuitable specimens might be obtained

For the test to have any practical value, however, it is necessary for the liquor to be obtained with perfect safety some time before term No method of doing this other than by paracentesis uteri seems possible, and the small risk involved in the manœuvre seems to preclude this method for widespread general use The theoretical risk of injury to the fœtus or the placenta, or even the uterus, in introducing a needle through the uterine wall in this manner can readily be appreciated, and the untoward incidents in the 20 paracenteses, though they cannot be regraded as serious, were the deciding factor in the decision not to pursue this investigation further Neither the aspiration of pure blood nor the onset of premature labour was followed by serious consequences, but their occurrence indicates that there is a risk, albeit very small, from this procedure No risk at all can be justified for the purpose of predicting what will soon be known for certain

Summary and Conclusions

The discovery that genetic sex can be diagnosed on the presence of chromatin masses in female nuclei in human tissues suggested that this test might be applied to diagnosis of the sex of the fœtus before birth

Accordingly 20 specimens of liquor amnii were obtained between the 26th and 42nd weeks of gestation by artificial rupture of the membranes or at cæsarean section, and the centrifuged deposit was examined after staining

The sex of the fœtus was correctly diagnosed in 18, the 2 others were unsuitable for accurate prediction

To test the practicability of using this method to determine the sex of the fœtus before birth, 20 other patients were selected for abdominal paracentesis between the 32nd and 36th weeks of pregnancy

Only 13 suitable samples of liquor amnii were obtained and the sex of the fœtus was predicted correctly in all—6 male and 7 female

In the remaining 7 cases no liquor was obtained at all from 3, a small amount of bloody fluid from 3, and pure blood from 1, 1 of these patients went at once into premature labour at 36 weeks' gestation

Although these incidents were not followed by serious consequences they seem to indicate that the method involves a small risk, mainly to the fœtus, and is therefore unsuitable for general use to discover a child's sex which would soon be known for certain

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TRACTION-MANIPULATION AND PLASTIC CORSETS IN THE TREATMENT OF DISC LESIONS OF THE LUMBAR SPINE

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MANIPULATIVE surgery has been looked on with misgivings by most doctors because it has been largely in the hands of unqualified practitioners, some of whom have made unfortunate mistakes, such as loosening up a fixed tuberculous hip joint Such mistakes will continue to be made so long as the initial diagnosis is in lay hands Careful clinical diagnosis, including radiography, to exclude any more serious underlying condition is essential in every case before any manipulation is undertaken

Various forms of manipulation for disc lesions have been practised—usually hyperextension sometimes combined with rotational movements and sometimes with traction

Traction is undoubtedly the safest, it may be applied by simply making a patient hang by his arms from a horizontal bar This procedure often eases the pain, but traction applied through harness attached to the patient's thorax and pelvis, with the patient prone, is much less exhausting and can therefore be applied longer The degree of traction can be controlled by a spring balance

The ability to place the patient in hyperextension while the traction is still operating is an additional help in the manipulative reduction of a prolapsed disc

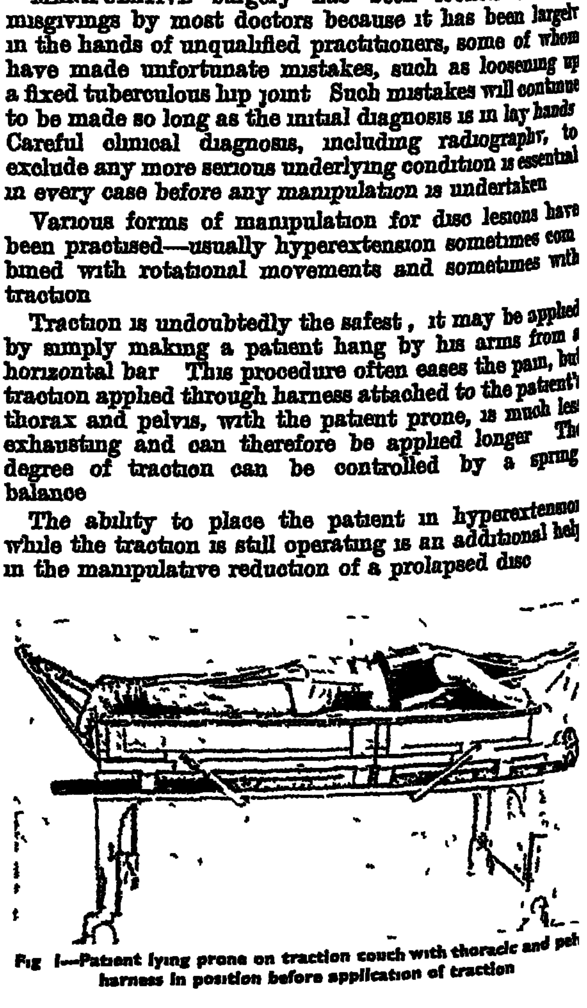

Fig 1—Patient lying prone on traction couch with thoracic and pel harness in position before application of traction

TABLE II—INCIDENCE OF INTERNAL-MAMMARY-NODE INVOLVEMENT BY INTERCOSTAL SPACES

—	Right breast	Left breast	Total
Invasion of first space node	3	10	13
Invasion of second space node	4	9	13
Invasion of third-space node	3	4	7
Invasion of fourth-space node	2	2	4
Total cases with internal mammary node invasion	11	12	23
Total cases in the series	29	28	57

37 spaces were invaded in 23 cases

substantial increase in the disability or postoperative complications over what may be expected from the standard radical mastectomy It is very difficult to put the comparison into figures because these cases have been followed with greater care than ordinary radical mastectomies and we have no exact yardstick for com- rison But the following details are not based on mere mon but are arrived at with the detailed case notes iore us

Shock —There is slightly more shock in these patients ian after ordinary radical mastectomy but it has ever caused anxiety Rather more of the cases receive wo pints of blood after operation than after radical mastectomy, but some have needed none The added loss of blood at operation has been so small that it cannot be considered to have seriously affected transfusion needs

Pulmonary Complications —These are slightly more common than after radical mastectomy, but here again no serious concern has been caused Small effusions and small areas of collapse have been noted and 2 patients have had small pulmonary emboli It must be said on the one hand that the chest was very carefully watched in this series and more minor complications have thus perhaps been found and on the other hand that vigorous preoperative and postoperative breathing exercises, tipping and chest percussion may have reduced the incidence of complications

Wound Complications —There has been less trouble from flap sloughing and marginal necrosis than after the standard radical mastectomy This may in part be due to exclusion of the very old and of those with very advanced growths and in part to our removing as a routine more skin than is usual with the corollary of frequent skin-grafting In fact, no less than 39 cases were skin-grafted

Fluid Collections under the Flaps —These have not been more evident than after a standard radical mastectomy The routine use of suction drainage has in any case made fluid collections after breast operations much rarer than they used to be

Complications of the Chest Wall Defect —These have not been seen The patients do not complain of pain in the area of the defect nor of discomfort

Arm Movement —The return of arm movement is always slower if the sternal head of pectoralis major is preserved than if it is sacrificed It is slower still if the pectoralis major is divided as we have described to expose the intercostal spaces There is thus a definite drawback in slowness of recovery in arm movement The ultimate result nevertheless seems to be nearly as good as with our standard radical mastectomy Division of the pectoralis major does not appear to result in ischaemic contracture of either portion of the muscle, but one would like further experience before concluding that

TABLE III—FOLLOW UP TO SEPTEMBER 1955

—	1–3 mos	4–6 mos	7–12 mos	13–18 mos	19–24 mos	25 mos and over	Totals
Alive without recurrence	10	4	12	14	2	4	46
Alive with recurrence	0	1	1	1	1	1	5
Dead from carcinoma of breast	0	2	0	1	2	1	6
Total	10	7	13	16	5	6	57

There were no operative deaths and no patient has died from other causes

TABLE IV—DETAILS OF CASES SHOWING RECURRENCE

Case no	Age (yr)	Site of primary (quad)	Histological findings: Primary	Histological findings: Axilla	Histological findings: Int mammary	Time of recurrence (mo noted)	Site of recurrence	Subsequent treatment	Total follow-up period (mos)	Outcome
1	42	Upper inner	Spheroidal	1 gland invaded	Free	2	Cerebral	D X P	4	Alive
2	63	Central	Spheroidal	Invaded	3rd and 4th invaded	24	Supraclavicular retrosternal	D X R	26	Alive
3	56	Upper inner	Spheroidal	Free	1st invaded	14	1st space sternum	Tele-cobalt	17	Alive
4	55	Upper outer	Spheroidal some tubules	Invaded	Free	10	Nodule in scar	D X R	17	Alive
5	43	Upper inner	Spheroidal	Free	Free	17	Cerebral	D X R	19	Alive
6	53	Central	Very cellular spheroidal	Invaded	1st 2nd and 3rd invaded	12	Skeletal hepatic pulmonary	Testosterone	22	Dead
7	64	Upper inner (preop D X R)	No viable tumour	Viable tumour	No tumour seen	3	Skeletal skin nodules	Nil	6	Dead
8	60	Upper inner	Spheroidal with marked tubule form	Free	1st and 2nd invaded	15	Skeletal hepatic cerebral	Testosterone	21	Dead
9	59	Lower inner	Spheroidal	Free	Free	3	Hepatic peritoneal	Testosterone	6	Dead
10	42	Upper inner	Spheroidal	Invaded	1st and 2nd invaded	24	Skeletal pulmonary	D X R	33	Dead
11	52	Upper inner	Spheroidal	Free	1st invaded	15	Skeletal pulmonary	Testosterone	18	Dead

D X R = deep X ray therapy

extent in the first few days but then gradually subsided Partial immediate relief occurred in 36 (72%), 14 of these had more than one manipulation, and in 6 a considerable degree of pain returned later An operation was eventually required in 4 No immediate relief was obtained in 1 case (2%) and so this form of treatment was discontinued 2 cases (4%) were made worse as soon as the traction was applied, it was immediately discontinued, and the aggravation ceased Anæsthesia was not used in any of these cases, the patient's response is probably a safeguard against doing any harm in unsuitable conditions

Of the 50 patients 44 had a temporary lumbar support made, and this is considered a great safeguard against recurrence The results after 6–12 months (table II) showed that the 11 patients who were completely relieved immediately had no recurrence, and of the 36 who obtained partial immediate relief only 6 had a recurrence

TABLE I—EFFECTS OF TRACTION AND HYPEREXTENSION IN 50 CASES OF SEVERE LOW-BACK AND SCIATIC PAIN

Effect	No of cases	Remarks
Complete immediate relief of pain	11 (22%)	In 5 of these cases the pain returned to a slight extent in a few days but then gradually subsided
Partial immediate relief	36 (72%)	14 of these had more than 1 manipulation In 6 a considerable degree of pain returned later, and in 4 operation was carried out
No immediate relief	1 (2%)	Treatment discontinued
Made worse	2 (4%)	Traction discontinued immediately
Cases in which some form of plaster plastic, or other disc support was also used	44 (88%)	Used in nearly all the later cases as a preventive measure against recurrences

The series is small but it gives some idea of the effectiveness of traction in relieving severe attacks of backache and sciatic pain It is a very useful treatment, much to be preferred to rest in bed and "twilight sleep," and, combined with a supporting corset, allows the patient to be up and about with a considerable margin of safety against a recurrence This manipulation and the application of the plastic support are usually done in the outpatient department, thus freeing hospital beds for other patients

Plastic Supports for Lumbar Spine

Plastic supports moulded directly on to the patient are used in the treatment of disc lesions either with or without manipulation, and have many advantages over plaster or any other form of support or belt for this purpose

The method of application is that described by Brennan (1954, 1955) using polyethylene as a supporting material and a heat insulated layer of polyurethane which not only prevents the patient from being burnt but also makes an excellent soft lining material for the support

Plastic Corset

Design —The design of plastic support (figs 6–8) used at Norwich is based on that of a disc support previously used by me and is made with a solid back-piece The front is narrower than the back and is split in two to allow the support to be removed and reapplied Two straps and buckles are attached in front to keep it snugly in position and to allow for adjustment This front portion is particularly important because, when the two halves are buckled together, it restricts forward flexion at the lumbar spine far better than does any posterior support alone Large pieces are cut out at the sides not only to make moulding easier but also to allow adequate ventilation

TABLE II—RESULTS SIX MONTHS OR LONGER AFTER MANIPULATION

Result	No of cases
Completely relieved	11 (22%)
Relieved to a considerable extent but still avoiding lifting heavy weights	30 (60%)
Not relieved	9 (18%)

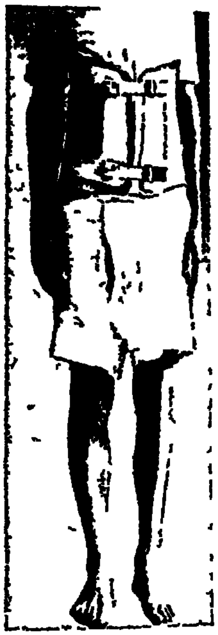

Fig 6—Patient standing with plastic support buckled snugly in position

Material —The support is cut out of a $^3/_{16}$ inch sheet of polyethylene lined with a $^1/_4$-inch sheet of polyurethane of a slightly larger size so as to overlap the polyethylene by $^1/_2$ inch at the edges

Measurements —Individual measurements are required for each patient, and the corset is cut out before it is applied The circumference of the patient's body is measured at the level of the xiphisternum (upper margin of the support) and at the level of the tips of the greater trochanters (lower margin) These measurements should be reduced by $^1/_2$ inch when the polyethylene is being cut so as to allow for a gap in front for adjustment with the straps and buckles The front is $1^1/_2$–2 inches less in depth, the lower margin in front being concave downwards on each side to clear the thighs when the patient sits down The midline posteriorly is marked to facilitate correct application later, and the patient's name is written on with a wax pencil

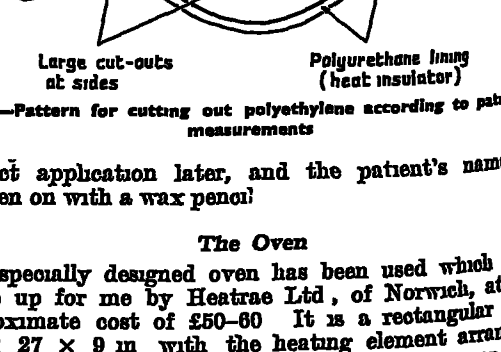
Site for rivets for attaching straps and buckles
Polyethylene
Large cut-outs at sides
Polyurethane lining (heat insulator)

Fig 7—Pattern for cutting out polyethylene according to patient's measurements

The Oven

A specially designed oven has been used which was made up for me by Heatrae Ltd, of Norwich, at an approximate cost of £50–60 It is a rectangular box 58 × 27 × 9 in with the heating element arranged in the roof to give even distribution of heat over the floor At one side is a four-position switch giving hot, medium, low, and off, and there are also a thermostat control and a thermometer *One side of the oven is* hinged to form a door The oven is large enough to hold an asbestos-covered aluminium tray 49 × 25 in, on which the plastic material is placed The oven takes about a quarter of an hour to reach, with the switch in the d it might properly be called "rational radical mastectomy" The term "extended radical mastectomy" ight be reserved for those procedures in which attempts e made to remove more than the primary lymphatic ainage areas—e g, where a supraclavicular dissection included.

Rational radical mastectomy is still experimental hether it will improve the results of treatment remains) be seen. All that can be claimed at present is that the rocedure rests on a sound theoretical basis and can be arried out with no significant addition to the mortality, orbidity, or deformity of the Halsted operation

Summary

A new technique is described for excision of the ternal mammary lymph nodes in primary operations or carcinoma of the breast

57 patients have been operated upon without mortality, n 55 the primary tumour was either in the inner hemisphere or in the central area of the breast

The disability, deformity, and morbidity of the operation are no greater than after the classical radical mastectomy

Invasion of the internal mammary lymphatic chain was ound in 23 cases (40%)

It will not be possible to assess the value of the operation in terms of cure-rate until further time has elapsed

We are greatly indebted to the Bland-Sutton Institute of Pathology of the Middlesex Hospital Medical School, and in particular to Dr A C Thackray, for the histological work incorporated in this paper, and to Miss E Hewland, the hospital medical artist, for the drawings of the operative technique

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> "Men meet together for many reasons in the course of business They need to instruct or persuade each other They must agree on a course of action They find thinking in public more productive or less painful than thinking in private But there are at least as many reasons for meetings to transact no business Meetings are held because men seek companionship or, at a minimum, wish to escape the tedium of solitary duties They yearn for the prestige which accrues to the man who presides over meetings, and this leads them to convoke assemblages over which they can preside Finally, there is the meeting which is called not because there is business to be done but because it is necessary to create the impression that business is being done Such meetings are more than a substitute for action They are widely regarded as action The fact that no business is transacted at a no business meeting is normally not a serious cause of embarrassment to those attending Numerous formulas have been devised to prevent discomfort Thus scholars, who are great devotees of the no business meeting, rely heavily on the exchange of ideas justification To them the exchange of ideas is an absolute good Any meeting at which ideas are exchanged is therefore, useful This justification is nearly ironclad It is very hard to have a meeting of which it can be said that no ideas were exchanged'—J K GALBRAITH, *The Great Crash, 1929* London 1955

A AND B BLOOD-GROUP ANTIGENS ON HUMAN EPIDERMAL CELLS

DEMONSTRATED BY MIXED AGGLUTINATION

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STUDIES of the antigenic structure of body cells other than red cells have awaited the development of new methods The technique reported here for demonstrating intra-species differences in the antigenic structure of human epidermal cells offers certain possibilities

Isolated epidermal cells or aggregates of these cells prepared from small sheets of split skin do not give cellular suspensions suitable for agglutination tests The inhomogeneity of the suspension, the irregular shapes of the cells, and the difficulty in obtaining suspensions in sufficient quantity militate against the use of this reaction On the other hand if it were possible to obtain a specific link or attachment between antibodies combining with even a few epidermal cells and different but specially selected indicator cells, the interaction of the individual cells should be easy to observe under the microscope Such specific mixed agglutination or combination between two cell types should occur if both cell types possess a particular antigen in common For instance, Wiener and Herman (1939) showed that horse anti pneumococcus type-14 serum would form mixed agglutinates between type-14 pneumococci and human red cells because both these cells possess a common antigen

If skin epidermal cells of a person of blood-group A possess the A antigen, then accepting that ordinary agglutinating antibodies are at least bivalent, we would expect such epidermal cells to be capable of being linked by anti A to group A red cells Thus on theoretical grounds the phenomenon of specific mixed agglutination or combination should provide a means of revealing whether epidermal cells do in fact contain the A and B blood group antigens on their membranes

The procedure which we have adopted for testing epidermal cells for the A (and B) antigen is illustrated diagrammatically in fig 1 A suspension of epidermal cells from a group-A person is exposed to anti-A, and the cells are subsequently washed free from uncombined antibody Only epidermal cells possessing the A antigen should adsorb anti A and consequently after being washed possess free extending "receptors" with affinity for the A antigen Group-A red cells added at this stage should combine with extending anti A receptors on the treated epidermal cells On the other hand, group-B and group-O red cells should not adhere to the treated epidermal cells

The results recorded here substantiate this reasoning and appear to offer conclusive evidence for the existence of the A and B antigens on epidermal cells of group-A and group-B persons respectively

Materials and Methods

Preparation of Isolated Epidermal Cells from Human Skin

The skin available for this study consisted of small fragments of stored thin split skin procured for plastic

Thrombotic micro-angiopathy was first described by Libman and Moschcowitz in 1925, but it was not until Baehr et al (1936) published four cases that it was generally accepted as an entity Since then there have been an increasing number of reports, mainly from the U S A In the United Kingdom two cases were reported by Symmers (1952), who reviewed the previously published cases, and Revill and Wilson (1954) reported a case which they said was the sixth in this country Ellison and Lloyd (1954) have since added a seventh

We report the present case in the hope that, along with future reports, it may help to establish a full clinical picture, elucidate the nature of the occlusive material (which we believe may be fibrin), and eventually reveal the ætiology of this strange disease

Case-report

A housewife, aged 46, was admitted to the Western Infirmary, *Glasgow*, on *June 9, 1954*, having been ill for six days She had previously been healthy except for "kidney trouble and high blood pressure" during pregnancy at the age of 28 Her menstrual history was normal, and the last period was in November, 1953 There was no history of anæmia or of excessive bleeding, but she said that she "bruised fairly easily" She had not received sulphonamides, 'Sedormid,' or any other drug known to cause purpura Six days before admission she suddenly felt dizzy and almost immediately lost consciousness She recovered in a few seconds and vomited a fairly large quantity of fluid but did not notice its colour or its consistence During the rest of the day she felt weak, breathless, and light headed Next day she had another attack of dizziness but did not lose consciousness, although "everything seemed to go black" She was seen that day by her doctor, who noted that her blood pressure was 160/95 mm Hg No petechiæ were seen on this occasion Three days before admission the patient passed a fairly large quantity of bright red blood per vaginam No clots were seen The bleeding was accompanied by indefinite right sided lower abdominal pain Two days before admission she had another attack of dizziness On the morning of admission to hospital her doctor saw her, recorded a blood pressure of 120/80 mm Hg, and noted increasing pallor, continuing vaginal bleeding, and petechiæ on her arms and body He arranged for her immediate admission to hospital

On examination the patient was well developed, obese, and very pale and her conjunctivæ were faintly tinged with jaundice She had slight dyspnœa, but no cyanosis or œdema A few scattered petechiæ were present in the skin of her forearms, arms, trunk, and legs, but not on the face or in the mucosa of her eyes and mouth There was no clubbing of her fingers Her temperature was 98°F, pulse rate 110, and respirations 22 a minute Her pulse was of good quality and regular rhythm, her blood pressure 120/75 mm Hg, and her apex-beat impalpable, no cardiac abnormality was detected clinically No abnormality of her respiratory system was detected except a few low pitched rhonchi at the left lung base Her tongue, palate, and fauces appeared normal No hepatic or splenic enlargement or any other abdominal abnormality was detected Her pupils were rather small but responded normally, both directly and consensually, to light and near vision Her biceps, triceps, supinator, and knee and ankle jerks were normal, abdominal reflexes absent, and plantar responses both flexor Motor and sensory functions were normal, except that the vibration sense was diminished in both legs There was no evidence of involvement of the cranial nerves

Laboratory investigations—No abnormality was detected in her urine A blood examination showed Hb 35% (Sahli) = 4 9 g per 100 ml, red cells 1,900,000 per c mm, packed cell volume 19%, mean corpuscular volume 100 c µ, mean corpuscular Hb concentration 25 8%, and white cells 8200 per c mm A blood film showed anisocytosis and poikilocytosis, with a few large forms and a few normoblasts White cells were numerous, with a high proportion of bilobed and trilobed neutrophils No platelets were seen, after extensive search Hess's test was negative Bleeding time 13 minutes (Duke's method) Clotting time $4^1/_2$ minutes (capillary method) Direct Coombs test negative The serum was slightly icteric

Sternal marrow puncture on June 10, 1954, revealed a hyperplastic marrow with essentially macronormoblastic erythropoiesis There was an increased number of megakaryocytes some having pyknotic nuclei The cells which exhibited granularity of the cytoplasm only rarely showed the granular material which is the preliminary stage of platelet formation. No hyalinisation of the cytoplasm was seen

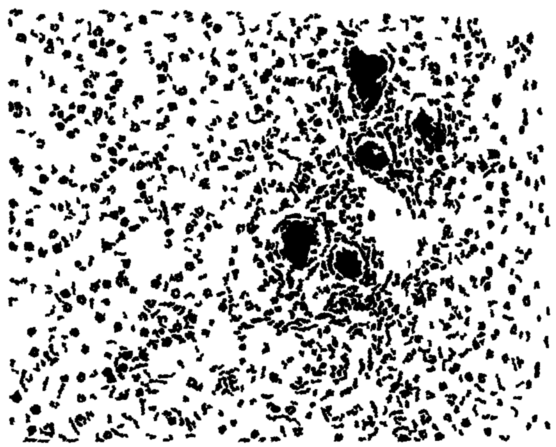

Fig 1—Thrombi in vessels of portal tract.

Treatment and course—A blood transfusion of 2 pints of group B Rh positive blood was given without any untoward reaction on June 10, 1954 Next day the patient became suddenly comatose after a tonic convulsion with cyanosis A few moments after the onset of coma she was breathing stertorously, and all four limbs were completely flaccid Her reflexes were depressed and her plantar responses equivocal Her pupils were contracted but reacted to light There was no nuchal rigidity Retinoscopy revealed no abnormality Lumbar puncture produced crystal clear cerebrospinal fluid under considerable (unmeasured) pressure, no cells were found in the fluid The patient did not regain consciousness *Left hemiplegia was suspected, but there was no definite proof* of this The patient's temperature rose to 101°F that evening

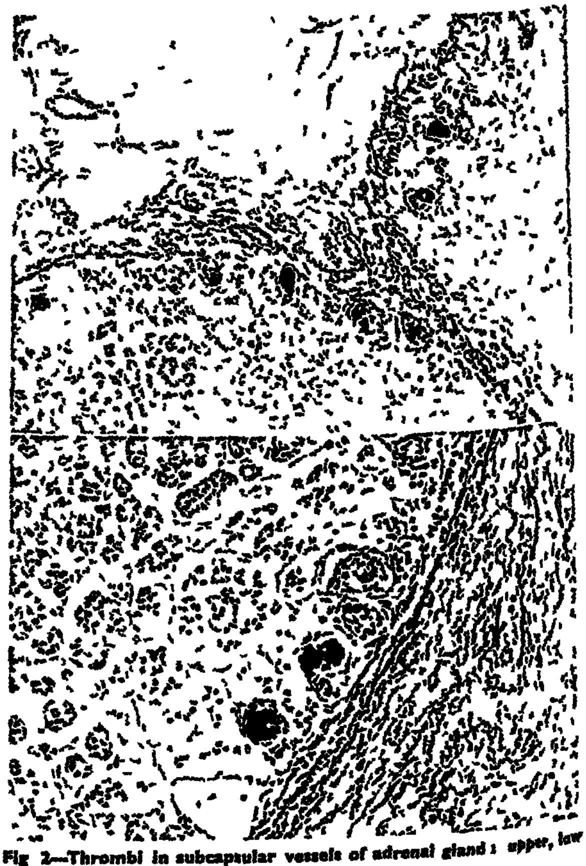

Fig 2—Thrombi in subcapsular vessels of adrenal gland : upper, low power ; lower, high power

incubated for an hour at room-temperature The epidermal cells were then deposited by centrifugation at 1500 r p m for five minutes, washed twice with N R S diluent, and finally resuspended in four drops of the diluent One drop of each suspension was then transferred to three precipitin tubes (5 × 50 mm), and one drop of a 1/2% suspension of group A, group-B, or group-O red cells was added The contents of the tubes were mixed and the cells deposited by centrifugation at 1500 r p m for two minutes The deposited cells, after gentle resuspension, were examined by phase-contrast microscopy for specific linking of red cells to the epidermal cells (figs 2 and 3)

The accompanying table, which summarises the esults, shows that group-A red cells showed a specific ffinity for epidermal cells from group-A persons only nd only if these epidermal cells had been exposed previously to an anti-A grouping serum Thus, anti-A is adsorbed on to epidermal cells of group-A persons only Likewise with group-B red cells, mixed agglutinates were formed with epidermal cells from group B persons only and again only if these latter cells had been exposed previously to anti-B grouping serum Thus anti-B is adsorbed on to epidermal cells of group-B persons only

MIXED ERYTHROCYTE EPIDERMAL CELL AGGLUTINATION BY MEANS OF ANTI A AND ANTI-B GROUPING SERA

Epidermal cells from persons of group	Exposed to grouping serum	Treated epidermal cells washed and 1 drop added to 1 drop red cell suspension of group		
		A	B	O
A	anti A	+ +	–	–
B	anti A	–	–	–
O	anti A	–	–	–
A	anti B	–	–	–
B	anti B	–	+ +	–
O	anti B	–	–	–

+ + mixed erythrocyte epidermal cell agglutination—i e, many red cells adhering to isolated epidermal cells (see fig 3*a* and *b*)
–, no mixed agglutination (see fig 2*a* and *b*)

Up to now epidermal cells from nine group-A persons, five group-O persons, and three group-B persons have been examined, and in all instances the results have conformed with those shown in the table From this it may be concluded that epidermal cells contain the A and B group antigens on their membrane

The anti-A and anti-B grouping sera used in these tests had titres of about 256 and, in most of the experiments, were used undiluted and diluted 1 in 5 However, even with the sera diluted 1 in 50, the reaction still took place, but it was weaker

If at the end of the test the deposited cells are resuspended too violently, the specifically adhering red ells may break away from the epidermal cells These ed cells, however, sometimes remain agglutinated, uggesting that some antibody molecules are transferred totally from the epidermal cells to the red cells

Among the skins examined and found to possess the group antigen, two (one group-A and one group-B) were from persons who were non secretors, hence the occurrence of the A or B group antigen on epidermal cells is not limited to persons possessing the secretor gene On the other hand, the epidermal cells from one group-A person gave a reaction much weaker than the others A second test gave the same results Whether this is the expression of an A subgroup will emerge from further experience

The tube which has group O red cells added serves as a good control for any non-specific combination or agglutination As an example, in one test epidermal cells were used which had been left as a saline suspension at 4°C for a week These cells were from a group-A person and after treatment with anti-A combined with group B red cells as well as those of group A but much more weakly However, group-O red cells were likewise adsorbed This indicated that something was wrong, and when the epidermal cells were examined carefully under the microscope they were seen to be highly contaminated with bacteria

Discussion

The only report we have seen about the A and B antigens and skin is that of Yosida (1928), who concluded that these antigens were absent from skin epithelium. The evidence presented now leaves no doubt that these antigens are present on skin epidermal cells

This finding is not without bearing on the problem of skin homografts Skin cells will now be further examined with sera specific for the other blood group systems, and an attempt will be made to establish their full antigenic structure and to determine which of the intra species antigens are concerned in the homograft reaction

The present observations seem also to be of importance in forensic medicine, because it may be possible to identify the A B O group of an isolated piece of skin completely devoid of blood

We have already applied this principle of mixed agglutination to confirm the presence of the A and B antigens on platelets (Coombs and Bedford 1955), and it seems that the method could be applied to most tissue cells It may therefore afford a useful tool in studies of the antigenic architecture of tissue cells and of problems of ontogeny

With the method described here the antigen being studied on the tissue cells must also exist on the indicator red cells The principle of mixed agglutination, however, may still be used in dealing with an undefined tissue antigen, because recourse may be had to the anti-globulin reaction Here the indicator red cells must also be sensitised with antibody globulin With both tissue cells and indicator red cells sensitised with antibody globulin, mixed agglutination may be brought about by an anti-globulin serum Coombs et al (1956) have used this latter principle in the examination of sera for platelet antibodies In this particular instance the reaction is called the mixed erythrocyte platelet anti-globulin reaction

Summary

The A and B antigens have been demonstrated on skin epidermal cells of group-A and group-B persons respectively by the principle of specific mixed agglutination

Mixed erythrocyte epidermal cell agglutination is possible because both cell types possess a common antigen

R R A C would like to thank both the Nuffield Foundation and the Agricultural Research Council for a joint personal grant We would specially like to place on record our thanks to Dr and Mrs K Joysey and Mr Walter Hatton, group B persons who volunteered skin biopsies for these experiments, to Sister M J Davies and the staff of the ear, nose, and throat theatre, Addenbrooke's Hospital, for their most helpful coöperation at all times, and to Mrs C M Madin Miss M A. Coad, and Mr R H. Matthews for numerous samples of blood Fig 1 was prepared by Mrs C M Madin

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(2) Fibrin was obtained from an inflammatory exudate of lung and fixed in formol corrosive sublimate, and paraffin sections were prepared This material is subsequently referred to as natural fibrin

(3) "Thrombi" from vessels in the present case Sections of liver were used, and the material in the vessels henceforth is called the occlusive mass

Sections of platelet mass, natural fibrin, and the occlusive mass were stained by various methods under identical conditions Unless stated otherwise, the acid and basic dyes were used in 0 5% aqueous solution

Results

The results are shown in the accompanying table

The sections from the mass of prepared platelets showed a rather granular conglomerate mass of material without any recognisable structures It is, therefore, not surprising that the certain recognition of platelets in tissue sections has been a subject for much argument in the past

The picro Mallory technique stains the platelet mass blue, whereas both natural fibrin and the occlusive mass are stained red The other stains show similarities in the stain reactions of the occlusive mass, platelet mass, and fibrin It is, however, probably unjustifiable to correlate the staining reactions seen in sections of tissue with any of the materials isolated from fresh blood fixed, processed, and embedded as described, since the regulation of artefacts is difficult to control Thus, for example, if prepared platelets are contaminated with heparin or dextran, their stain affinities are much altered Likewise the staining characters of fibrin may be altered by washing before fixation

What, then, can be said of the occlusive masses that characterise this hyperergic micro angiopathy? The current view that they are composed of platelets is difficult to disprove because of the difficulty in recognising platelets in tissue sections So far as identification is possible by the use of staining methods on sections, we see no reason to regard these masses as other than fibrin The contrary views (see below) may well have been based on staining methods and methods of fixation rather less satisfactory than those of Lendrum for the demonstration of fibrin

Discussion

The anæmia present in this disease has been generally reported as hæmolytic but with a negative Coombs test, and certainly antibodies to erythrocytes were not demonstrable in the present case The fate of transfused red cells in this disorder has been studied by Adelson and Stefanini (1952), who observed a shortened survival-time, but they likewise could not demonstrate red cell auto antibodies or iso antibodies

The thrombocytopenia has been explained as a consumption of platelets in the formation of myriad thrombi but the commonly held view that the "thrombi" are composed of platelets perhaps merits critical reconsideration because, as we have shown, the "thrombi" have all the tinctorial qualities of fibrin Platelet agglutinins were not detected in the present case, as was also the experience of Bernheim (1943) and Adelson (1952) Adelson, however, found a shortened survival-time of transfused platelets and interpreted this as evidence of a destructive mechanism Possibly this mechanism may be the same as that of idiopathic thrombocytopenic purpura, and it seems difficult to understand why previous workers have felt it necessary to postulate that platelet thrombi are the cause of the thrombocytopenia in thrombotic micro-angiopathy

The episodic character of the clinical course is reflected in the microscopical finding of varied degrees of hyalinisation, organisation, and canalisation of the occluding masses, the appearances indeed suggest that the les had appeared in crops

Splenectomy has been done in a few cases with benefit Presumably, therefore, the spleen plays significant part in this disease Likewise administrat of cortisone or of corticotrophin, given in relatively sm doses, does not appear to influence the course of t disease

No lesions were noted in either skin or bone marr Bone-marrow aspiration has, however, yielded diagnost aid in the past (Cooper et al 1952)

The virtual lack of histological evidence of necros other tissue damage, despite the multiple peripher vascular thrombosis, makes it difficult to explain th curious lethal character of the disease In the pres case adrenal hæmorrhages were unusually severe, an this could well have contributed materially to the fat issue

This curious absence of necrosis rather suggest th the occlusions are confined to a level of the vascular tr where there is an anastomosing network, and it ma well be that, whatever the appearance of the involv vessel, it is always a precapillary arteriole An apparent widening of the vessels that contain thrombi was one o the most obvious features in sections from the pres case Indeed, the walls of some affected vessels were s attenuated that the usual distinction between venule an arteriole was lost Comparable dilations were noted b Orbison (1952), who showed, in reconstructions prepare from Meacham's two cases, that these were situated a the arteriolo-capillary junctions It is possibly significan that Humble (1949) found that the site of dermal bleedin in purpuric patients was the arteriolo capillary junction It therefore appears that damage is done at this particula point in the vascular tree, but it is not clear what relation if any, this anatomical localisation bears to the formatio of occlusive masses

The precise nature of the occlusive material is stil unknown Moschcowitz (1925) believed that it wa formed of agglutinated red cells, but this is no longe generally accepted, the common view being that it is a mass of agglutinated platelets (Lutz 1951) This view was apparently reached by a process of exclusion, since neither bacteria, nor red cells, nor threads of fibrin wer found in the so called thrombi It was next stated b Meacham et al (1951) that the thrombotic material ha the same staining reaction as platelets The pres investigation, though extending and confirming the results, if not their interpretation, shows that the throm botic material stains like fibrin The absence of fibrilla structure does not mean that the material is not fibri A compacted granular material giving the staining reac tions of fibrin is not uncommonly seen along with th fibrillar form in infective and exudative disease of th lung That both these forms are fibrin is very possib in the light of work by Ferry and Morrison (1947), wh showed that fibrinogen, clotted under different cond tions, may yield two distinct types of clot, one retic lated and fibrillar, and the other more homogeneous an compact A granular "clumped" form of fibrin wa described by Howell (1914) in mixtures of fibrinogen an thrombin, where the amount of the latter was insufficien to give a firm clot It is therefore probable that th conversion of fibrinogen to fibrin may give sever morphological variants of fibrin As Robb-Smith (195 points out, there is no a-priori justification for assumin that the mechanism of formation of fibrin is identic in each case

The observed differences in the properties of clo formed under various conditions presumably depend o the manner in which the fibrinogen molecules are link together during polymerisation It is conceivable th in the present disease the conversion of fibrinogen similar extraction with alkaline methanol activity remained in the cyclohexane From this we conclude that the active substance is an amine

Gas liquid chromatograms were run with Apiezon M ' at 197°C and nitrogen as carrier gas (James and Martin 1954) Both the original distillate and the basic fraction obtained from the distribution with acidified methanol proved to be highly complex, and the activity was confined to a zone of volatility roughly equivalent to that of a hydrocarbon containing 14 carbon atoms The recovery of activity from the gas chromatogram was, however, very low Further work at lower temperatures is indicated

Attempts to fractionate on liquid liquid columns between acidified 80% methanol and cyclohexane also did not lead to a striking increase in potency, and further work on these lines is also needed

The fractionation of the largest batch proceeded as follows

13 kg of ' vegetable lecithin " was hydrolysed with 7 25 kg of KOH and 18 litres of ethanol in a steam jacketed pan The KOH was first dissolved in the boiling ethanol and the lecithin added with stirring until fully dissolved The material was left for ninety minutes at 100°C, and much NH_3 and $(CH_3)_3N$ were given off Cold water was run into the jacket until it cooled to about 45°C and the material was then a pasty mass 8 litres of water was added, and the mass liquefied Ice was now added until 30 litres of water and 45 litres of ether had been used The material was well stirred and left to settle overnight, it separated into two layers The upper layer was siphoned off, and to it was added a third of its volume of water An ether layer was separated, and the aqueous layer was extracted with an equal volume of ether in a counter current extractor of about five theoretical plates' efficiency The material remaining in the vat was extracted with 30 litres of ether with simple stirring The ether extracts were combined, washed with a small volume of water, and distilled The residue contained water and alcohol and was collected in a 10 litre bottle, and to it were added 5 litres of ether and 2 litres of water The ether layer was separated and concentrated, and the process was repeated with 500 ml of water and 2 litres of ether The ether layer was evaporated to dryness, and the residue was a *brown oil*, semisolid below 70°C It was *dissolved in 1 5 litres of acetone* and set aside at –5°C The precipitate was filtered off, washed with 1 litre of cold acetone, and discarded The acetone mother liquor and washings were evaporated down and yielded 90 ml of dark brown oil, liquid at first at room temperature and setting overnight to a semisolid

This material was distilled in a molecular still at 100°C, and 22 ml of a pale yellow oil, whose colour deepened on standing, was obtained This was active at 0 3 µg The undistilled residue was inactive at 10 µg

The distillate had a strong smell, which was even stronger in the more volatile material that had collected in the cold trap

15 6 g of the distillate was distributed between 250 ml (80 20 1 by vol) of methanol water conc H_2SO_4, and 250 ml of cyclohexane The methanol layer was run off, and the cyclohexane layer re extracted with 250 ml of the acidified aqueous methanol The combined methanol extracts were made alkaline with NaOH, freed from methanol by distillation, and extracted thrice with ether On evaporation of the ether a dark-brown oil weighing 1 74 g remained This material, the ' basic fraction," was active at 0 03 µg per guineapig

The neutral fraction " from the cyclohexane was inactive at 0 3 µg

When the extraction procedure was repeated with NaOH in place of H_2SO_4, the cyclohexane and methanol fractions were both active at 0 3 µg

20 µl of the basic fraction was applied to a gas chromatogram 120 cm long with a stationary phase of apiezon M at 197°C The nitrogen pressure was 71 cm Hg Fractions were collected in cotton wool moistened with ethanol packed in tubes 12 cm long and 1 cm in diameter (Excess ethanol was first removed by suction on a water pump and the tube then attached to the exit tube of the apparatus with a sleeve of silicone rubber tubing)

Tubes were changed after (*a*) 7½, (*b*) 17½, (c) 27, (*d*) 37, and (c) 56 minutes

CONDITIONS IN WHICH DESENSITISATION DEVELOPED WITH THE AGENTS TESTED

Agent and dose per kg of body weight	Diet deficient in ascorbic acid	Reduced glutathione (150 mg per kg of body-weight)
Cortisone acetate * 5 mg (Long and Miles 1950)	–	–
Alloxan 25–50 mg (Long et al 1951)	–	–
Ethionine 50 mg (Long 1954b)	–	–
Cysteinamine 100 mg (Long 1954c)	–	–
Insulin 2 units compensating phase succeeding hypoglycaemia (Cornforth and Long 1953)	–	–
Dehydro ascorbic acid 50 mg (Long et al 1951)	–	–
Growth hormone 10 mg (Cornforth and Long 1953)	+	–
Glucose 1 phosphate 0 01 mg (Cornforth and Long 1952)	–	+
Lysergic acid diethylamide 0 00018 mg (Cornforth and Long 1952)	–	+
Polyoxyethylene ethers 10 mg (Hart et al 1952)	–	–
N acetylsphingosine 10 mg (Fisher et al 1951)	–	–
Peanut-oil factor 0 000006 mg (Long and Martin unpublished)	–	+

* For activity of related steroids see Long and Spensley (1954)

The tubes were washed out with 10 ml of ethanol, and 1 ml of this solution was considered equivalent to 2 mg of the basic fraction The fractions were tested at 0 5, 0 3, and 0 03 µg equivalent basic fraction Only (c) was active (the tests at 0 3 and 0 03 µg were with five guineapigs each and not fully satisfactory)

It was considered that activity was probably lost in this experiment

Eggs and Other Substances

20 hard boiled egg-yolks were extracted in a Waring Blendor with 2 portions of 500 ml of ether After filtration the ether was evaporated off 100 g of yellow oil was obtained In three weeks a bulky sludge precipitated this was centrifuged down The oil was active at 10 mg, the precipitate was doubtfully active at 10 mg

From 50 ml of oil 1 g of unsaponifiable matter was obtained by ether extraction after alkaline hydrolysis, it contained much cholesterol and was active at 20–200 µg

Linseed oil was active at 1 ml, and soybean lecithin was active at 10 mg, but olive oil, almond oil, and wheat germ oil were all inactive at 1 ml

The extracted egg yolk protein was dried and fed at 500 mg daily for three days and proved to be inactive

Comment

Sensitivity to tuberculin is clearly a complex phenomenon that can be influenced by various factors (see table) The diversity of substances that depress sensitivity is such that no single explanation will suffice Presumably those influenced by a diet deficient in ascorbic acid or by injection with reduced glutathione have some part of their mechanism of action in common Long (1955) discusses possible modes of action of several of these substances

Summary

The response to intradermal tuberculin was used as a measure of allergic hypersensitivity in albino guineapigs infected with B C G

Single subcutaneous injections of arachis oil depressed sensitivity slightly but significantly

Purification resulted in a non-toxic fraction that, in a dose of 0 000006 mg per kg of body-weight depressed sensitivity to a degree comparable with that obtained under similar conditions with cortisone acetate in a dose of 5 mg per kg of body-weight, which is maximally effective

RHESUS (D) FACTOR IN SARCOIDOSIS

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I REPORT here the results of a brief investigation after the chance finding of a negative Rh (D) factor in a young patient with sarcoidosis

32 patients of this department who are suspected of having sarcoidosis had their blood group and Rh (D) factor determined , the accompanying table summarises the diagnostic features in favour of the diagnosis of sarcoidosis and the blood results Genotype examination in respect of c,C,e,E, and d could not be carried out, and the results are expressed in terms of rhesus (D) factor only

The sera were scrutinised for atypical antibodies, and direct Coombs tests were recorded on most samples

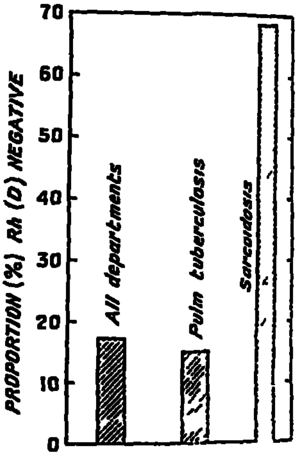
21 of the 32 patients suspected of having sarcoidosis were found to have Rh (D) negative blood, whereas the ABO blood-groups were fairly normally distributed In all the patients with Rh (D) negative blood radiography of the chest revealed pulmonary involvement On the other hand, of the 11 whose blood was Rh (D) positive, 4 (cases 5, 9, 20, and 29) showed no radiographic abnormality at the hila or in the lung fields and in 1 (case 11) there was doubtful enlargement of the left hilum only. In the remaining 6 the lung involvement was widespread, and in case 31 there were also unusual skin lesions

4 patients (cases 2, 4, 13, and 26) presented with ocular signs of sarcoidosis in addition to the lung changes, and their blood was Rh (D) negative A patient with Eale's disease (case 29), however, whose chest radiographs remain consistently normal, was Rh (D) positive Similarly case 31, who has widespread ocular, skin, and lung lesions, proved to be Rh (D) positive The diagnosis in this patient is still subjudice despite " sarcoid like" lesions in a skin biopsy

FINDINGS IN 32 CASES OF SARCOIDOSIS

Case no	Liver biopsy	Chest radiograph	Rh (D) factor	Blood group	Other biopsies
1	Pos	Mottling and hila +	Neg	A	
2		Mottling	Neg	A	Pos keloid biopsy
3	Pos	Mottling and hila +	Neg	A	
4	Pos	Hila +	Neg	B	
5		Normal	Pos	AB	Endometrial sarcoid
6	Neg	Mottling and hila +	Neg	A	
7	Neg	Hila +	Neg	O	
8	Pos	Mottling and hila +	Pos	A	Skin scar—sarcoid
9		Normal	Pos	A	Sarcoid of parotid
10	Neg	Mottling	Neg	B	
11		? lt hilum	Pos	O	Sarcoid in synovia
12	Pos	Mottling and hila +	Neg	O	
13	Pos	Hila +	Neg	A	
14	Pos	Hila +	Neg	A	
15		Hila +	Neg	O	
16	Neg	Mottling	Neg	O	
17	Doubtful	Hila +	Pos	O	
18	Pos	Mottling and hila +	Pos	O	
19		Mottling and hila +	Neg	O	
20		Normal	Pos	A	Sarcoid in muscle biopsy
21		Hila +	Pos	O	
22	Focal necrosis	Hila +	Neg	A	
23	Neg	Mottling	Pos	AB	
24		Hila +	Neg	O	
25		Mottling and hila +	Neg	O	
26		Hila +	Neg	B	
27		Hila +	Neg	O	
28		Mottling	Neg	O	
29		Normal	Pos	A	
30	Neg	Hila +	Neg	A	
31		Mottling	Pos	O	Sarcoid like skin lesions
32		Mottling	Neg	O	

4 patients (cases 5, 9, 11, and 20) in whom the principal manifestations of sarcoidosis originated outside the lungs had Rh (D) positive blood



Proportions of patients with Rh (D) negative blood (1) from all departments (1000 cases) , (2) with pulmonary tuberculosis (93 cases) , and (3) with sarcoidosis (32 cases)

In 5 Rh (D) negative patients sarcoidosis was confirmed by liver biopsy , and in each of 4 Rh (D) positive patients liver biopsy was also positive In 1 Rh (D) positive patient the biopsy of the liver was of doubtful value ; and in 1 (case 22), whose blood was Rh (D) negative, the liver showed focal necrosis 1 Rh (D) positive and 5 Rh (D) negative patients had negative liver biopsies

Rhesus Factor in Other Groups

Of 1000 patients of all departments of this hospital who had their blood-group and Rh (D) factor determined in the period September to November, 1955, 173—i e, 17 3%—were Rh (D) negative 93 patients with pulmonary tuberculosis who were known at one time to have had positive sputa showed a somewhat similar Rh (D) factor distribution , of these 93 patients, tested at this hospital or at the Lambeth and South Western Hospital, 14 (15 1%) were Rh (D) negative (see figure)

DISCUSSION

In the present series of cases of sarcoidosis the prevalence of hilar lymph-node and lung involvement was higher in patients with Rh (D) negative blood than in others Of the total of 32 patients 21—66%—were Rh (D) negative , this proportion is probably significantly greater than that in the general population, and suggests that Rh (D) negative patients react more commonly than Rh (D) positive patients with the production of sarcoidosis (see figure)

No conclusions can be drawn from these figures in respect of susceptibility to sarcoidosis among Rh (D) negative patients, and much larger series are required for any statistical analysis

I suggest that the examination of the Rh factor is of some additional help where sarcoidosis is suspected The fairly large proportion of Rh (D) negative patients observed in this inquiry compares with the positive Kveim's tests in 12 of the 16 cases of sarcoidosis recorded by James and Thomson (1955)

Summary

Of 32 patients suspected of having sarcoidosis 21 were found to have Rh (D) negative blood as well as radiographic evidence of hilar or lung involvement Of 11 whose blood was Rh (D) positive, 4 had normal chest radiographs

This small series suggests that Rh (D) negative blood is commoner in patients with sarcoidosis than in the general population

I thank Dr J H Anderson for permission to study these patients, who are under his care, and Dr J L Pinniger and his technical staff for the determinations of the blood groups and Rh factor of the patients with sarcoidosis

REFERENCE

James, G D Thomson, A D (1955) *Quart J Med* 24, 49

idence of diabetes insipidus her fluid intake being at first 419 ml. daily, later reduced to 887 ml. on account of lack of bsorption from the stomach

She developed a pyogenic intracranial infection from a enicillin resistant staphylococcus, and the spread of this nfection was responsible for death

Macroscopic Examination (P.M. 95 1951)

Necropsy revealed purulent pachy- and leptomeningitis The pituitary stalk was not found Surrounded by thick exudate, the floor of the third ventricle was replaced by an operative deficit leading into the cystic cavity of the tumour There was recent thrombosis of the superior longitudinal and right lateral sinuses The pituitary gland (0 6 g) was flattened n an expanded sella turcica

The right adrenal was swollen and destroyed by recent hæmorrhage, the left appeared normal

Microscopic Examination

Pituitary—There is patchy necrosis of about half of the parenchyma of the *anterior* lobe The necrotic areas are infiltrated in places with lymphocytes and plasma cells The residual parenchyma is poorly preserved, the cells being in stages of degeneration The basophils are pale, swollen, and agranular, the perinuclear cytoplasm appears stringy but at the periphery it is homogeneous and slightly hyaline In the acidophil cells the granules are often clumped

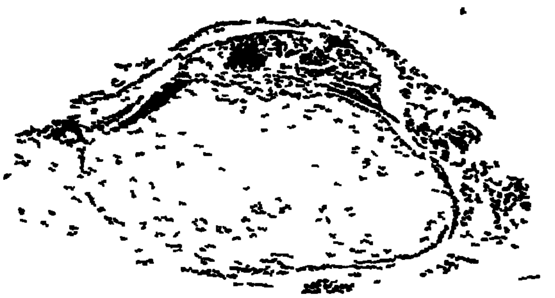


Fig 2 (case 3)—Horizontal section of pituitary as in fig I (H and E ×35)

Four large sinusoids near the centre of the anterior lobe are thrombosed, with early organisation of the thrombus The *posterior* lobe is normal

Other endocrine organs—The hæmorrhage in the right *adrenal* is associated with thrombosis of the central vein, the gland is infarcted The capsule is infiltrated with numerous leucocytes and two large groups of gram positive cocci occupy softened areas in the substance of the gland. The left adrenal contains abundant lipoid, two of the capsular veins are plugged with ante mortem thrombus, and the cortex shows focal hyperæmia The *thymus*, *spleen*, and *lymph nodes* are heavily depleted of small lymphocytes The *thyroid* is normal

Anterior-pituitary insufficiency was recognised in the postoperative course of both of these patients It is probable that, in case 2, life was prolonged by hormone therapy, but this masked the spread of pyogenic infection which, as the pathological examination showed eventually spread systemically with the promotion of thrombosis in the adrenal veins In 1933 hormone therapy was not available, and the postoperative picture in case I was that of unmitigated anterior lobe insufficiency These two cases therefore, agree with Cushing s early observation that division of the stalk can result in severe necrosis of the anterior lobe A brief note is now added on a third case in which, although anatomical division of the stalk was not inflicted, the pathological findings throw considerable light on the vascular pathways implicated in the production of this necrosis

THIRD CASE

A man aged 44 had complained of pain in the right upper limb for 4 months, and more recently of severe pain in the back and behind both eyes He was admitted to hospital in April 1939 in stupor His wife related that 5 days earlier, he had become hysterical and taken to his bed where he had since remained He deteriorated mentally and, though able to recognise his wife was dull and rambled in his speech He lost weight rapidly and became pale On the day before admission he was restless, feverish, and sweating and had visual hallucinations

On examination he was semicomatose, with eyes half closed and mumbling perpetually He occasionally attempted to answer questions His skin was sallow with yellowish-brown pigmentation of the face There were sordes on the lips and his tongue was dry and furred Enlarged supraclavicular glands, and radiographic evidence of tumour deposits in the pelvis and vertebræ were found, but the primary source of these was not determined Blood pressure 100/50 mm and 103·65 mm 4 days later *Nervous system* neck-rigidity present, no papillœdema, right external rectus palsy and nystagmus Blood examination showed a leuco-erythroblastic anæmia Lumbar puncture yielded faintly yellow cerebrospinal fluid mixed with blood at a pressure of 170 mm, containing 20 lymphocytes per ml Urine cloud of albumin Blood urea 0 055 g per 100 ml

No disturbance of water balance was noted but records of intake and output were not kept He became increasingly drowsy, and resentful of attention Urinary incontinence developed and he died, with signs of pneumonia 6 days after admission

Macroscopic Examination (P.M. 164 1939)

Primary carcinoma of the pylorus was found, with extensive carcinomatosis of the lymph nodes and skeleton including the skull There was pachymeningitis carcinomatosa of the left parietal region and over the base with recent thrombosis of the cavernous sinuses The brain and pituitary stalk appeared unaltered, but the anterior lobe of the pituitary (1 2 g) was pale and opaque The adrenals (10 4 g), testes (25 6 g), and thyroid (36 5 g) appeared normal except for a partly calcified adenoma in the thyroid

Microscopic Examination

Pituitary—The appearances of the *anterior* lobe closely resemble those of case 1 and the age of the lesion as judged by the peripheral granulation tissue, is similar (fig 2) The capsule is thickened by recent hæmorrhage and chronic inflammatory cellular exudate, while many of the small veins are permeated with carcinoma The *posterior* lobe is infiltrated at its margin by a few groups of tumour cells, associated with areas of hæmorrhage and some inflammatory cellular infiltration

In coronal sections through the hypothalamus and pituitary stalk there are small areas of recent hæmorrhage in the tuber cinereum and in the stalk In the latter there are also areas of necrosis and many of the portal vessels are plugged with carcinoma cells and thrombus (fig 3) This involvement of the portal vessels extends throughout the length of the stalk to its level of attachment with the gland Branches of the superior hypophyseal arteries over the surface of the stalk are normal and patent

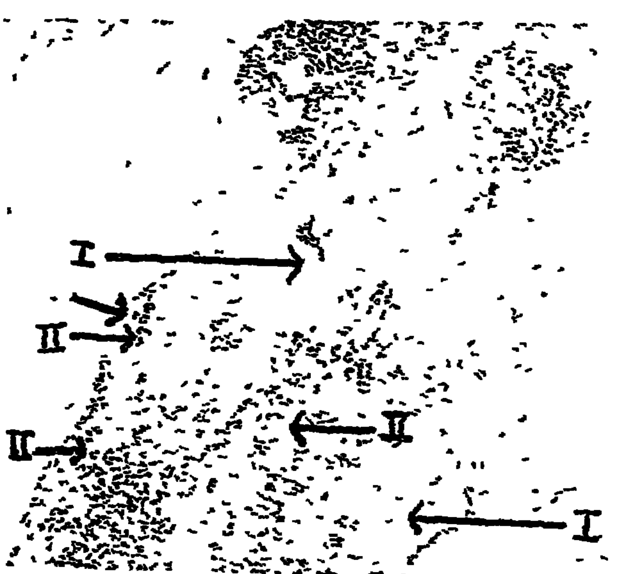


Fig 3 (case 3)—Upper part of pituitary stalk showing areas of hæmorrhage necroses (I), and plugging of portal vessels (II) (H and E. ×21) myelitis infects an individual in a family, nearly all of his susceptible household associates are concurrently infected It may well be that the antibody patterns found in the children in this survey are reflected at least in the older members of their families This seems likely from the epidemiology of poliomyelitis in Northern Ireland

The total numbers of confirmed paralytic cases in the boroughs and counties of Northern Ireland in 1950–55 are as follows

	1950	*1951*	*1952*	*1953*	*1954*	*1955*	*Total*
Belfast borough	110	15	19	31	14	1	190
Londonderry borough	0	0	1	34	4	0	39
Co Antrim	46	18	22	51	11	5	153
,, Armagh	24	2	5	3	1	18	53
,, Down	51	9	10	27	9	2	108
,, Fermanagh	2	0	2	8	3	4	19
,, Londonderry †	3	0	2	35	0	3	43
,, Tyrone	14	4	10	31	1	4	64
Total	250	48	71	220	43	37	669

The average annual age specific paralysis rate in the 0–9-year age group for 1950–55 is shown in fig 3

TABLE I—RESULTS OF POLIOVIRUS ANTIBODY SURVEY IN THE BOROUGHS OF BELFAST AND LONDONDERRY AND COUNTIES ANTRIM, DOWN, FERMANAGH, LONDONDERRY, AND TYRONE

Sample	Age (yr)	No tested	No with antibody to			Per cent † with antibody to	
			Type 1	Type 2	Type 3	Three types	None
Belfast borough Baby clinics	1	18	0	1	4	0	72 2
Nursery schools	2	3	3	3	3		
	3	32	29	22	30	65 6	3 1
	4	36	34	27	31	63 9	0
	5	2	2	2	2		
Primary schools	6	2	2	2	2		
	7	13	9	12	9	53 8	7 7
	8	27	25	23	25	77 8	3 7
	9	10	9	9	7	66 7	0
	10	3	1	1	1		
Private schools	4	8	5	1	1	0	37 5
	5	8	4	5	1	12 5	25
	6	6	2	6	0	0	0
	7–9*	3	1	3	0		
Londonderry borough	1	2	0	0	0		
	2	4	3	2	1		
	3	13	7	3	5	0	23 1
	4	7	6	6	5	42 9	0
	5	4	2	3	0		
Co Antrim	1	2	1	0	2		
	2	3	1	1	1		
	3	4	2	0	3		
	4	7	5	6	5	57 1	0
	5	11	7	11	8	63 6	0
	6	5	2	5	4	40	0
	7	1	0	1	0		
Co Down	1	3	1	0	2		
	3	5	3	4	1	20	20
	4	7	3	3	1	0	14 3
	5	2	1	2	1		
	14	1	0	0	0		
Co Fermanagh	1	7	1	0	1	0	85 7
	2	5	1	1	3	0	20
	3	10	5	5	8	30	0
	4	6	1	4	3	0	0
	5	1	1	0	1		
Co Londonderry	3	1	1	1	0		
	4	13	5	4	8	7 7	30 8
Co Tyrone	1	3	0	0	0		
	2	4	1	0	0		
	3	2	0	0	0		
	4	10	2	9	1	0	60
	5	4	2	1	2		
	6	1	0	0	0		

* 1 of each age
† In samples of 5 or more

TABLE II—ANTIBODY IN SIBLINGS

	Pairs of siblings		
Tested	With similar antibody pattern to all three types	With one additional type of antibody in older child	With on additional ty of antibody younger ch
29*	18	10	1

* Includes 3 siblings in one family

The highest paralysis rates were in the 0–4 year a group. Indeed of 669 confirmed paralytic cases in 1950-5 311 (46 5%) occurred in children aged less than 5 yea The small number of cases in older age groups sugg that they are relatively immune Unfortunately th were insufficient samples in the 5–9-year age group for to examine any possible relationship between antib and paralysis-rates If it is assumed that the samp tested from children aged less than 5 years were rep sentative of the recent poliomyelitis experience of t age group in Northern Ireland, some relationship mig be found between the antibody rate of the 0–4 ye age group and the incidence of paralysis in this a group in recent years That some such relationship m exist (in spite of the selected nature of the samples) seen from table III

Although the data for the 0–4-year age group in table do not merit statistical analysis, places with h paralysis-rates in the 0–4 year age group seem to ha high antibody rates in that age group, and low paraly rates seem to be associated with low antibody rat This apparent association is most noticeable in compar the paralysis-rates in table III with the proportion children with antibody to type 1 poliovirus

Of the thirty-four strains of poliovirus recovered Northern Ireland since August, 1955, twenty nine w type 1, and twenty six of these were from paralytic ca (Type 2 was isolated from 2 paralytic cases, and t other three strains—two of type 3 and one of type 2 were from non-paralytic cases) Furthermore the t strains of poliovirus isolated (at the Central Public Heal Laboratory, Colindale) from paralytic cases fr Northern Ireland in 1953 were also of type 1 All th

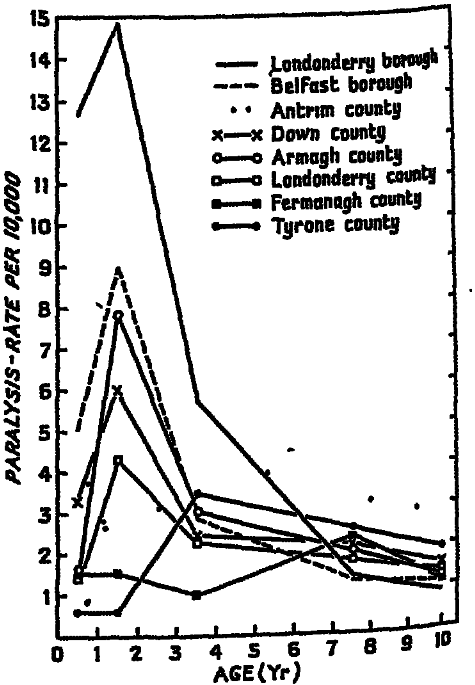


Fig 3—Annual age-specific paralysis-rate in 1950-55

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† There were 25 notified cases from co Londonderry in which no information was available about the presence or absence of paralysis A proportion of these patients may have had paralysis, and the paralysis rate for co Londonderry may therefore be slightly higher

REVIVAL OF STORED BLOOD WITH GUANOSINE

AND ITS SUCCESSFUL TRANSFUSION

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IN earlier papers (Prankerd and Altman 1954a and b) attention was drawn to the apparent benefit of two nucleosides, adenosine and guanosine, to red-cell metabolism during incubation of blood in vitro at 37°C In these experiments it was observed that, after twenty-four hours' incubation, red-cell metabolism continued in the presence of these nucleosides whereas it ceased if glucose alone was present This effect of these nucleosides was ascribed to their providing, after cleavage by cell enzymes, ribose phosphate; which could be utilised by the red cell for glycolysis, apparently when glucose could no longer be utilised

About the same time Finch and Gabrio (1954) briefly reported that adenosine improved the post-transfusion survival of stored blood, and they have since (Gabrio et al 1955) reported their observations in more detail Blood was stored, by these workers, with adenosine at 4°C and incubated at various times during its storage at 37°C, finally, the cells were labelled with ^{51}Cr, washed with saline solution, and transfused into healthy recipients Estimated cell survival showed great improvement with this treatment Adenosine, however, is very toxic when injected into man (Wedd 1931, Drury 1936) and it would prove unsuitable for adding routinely to stored blood unless the cells were washed before administration

I report here further observations on survival of blood stored in standard acid-citrate-dextrose preservative (A-C-D) at 4°C for periods up to eight weeks, and revived before transfusion with one of the two nucleosides Of these two compounds guanosine has been shown to be pharmacologically inactive, and blood revived with it has been transfused to man in routine manner without undesirable effects It should therefore prove to be a practical and simple means of increasing the optimal storage time of blood and eliminating waste

Methods

Blood collected in A-C D by the North London Blood Transfusion Service was used in these experiments after it had been discarded by the blood-bank as no longer serviceable This usually happens after three weeks' storage at 4°C

Two procedures were used to revive the cells

(i) At various times after three weeks storage 5 µmols of adenosine or of guanosine, in sterile isotonic saline solution, was added for each millilitre of stored blood, and 25 ml of the mixture was incubated for an hour at 37°C At the same time a further 25 ml of the same blood was incubated separately without the nucleoside

(ii) The nucleoside was added to blood in the same concentration at the end of three weeks' storage, and the mixture was incubated at 37°C for an hour and subsequently stored again at 4°C until required for transfusion The blood was then reincubated for an hour before transfusion

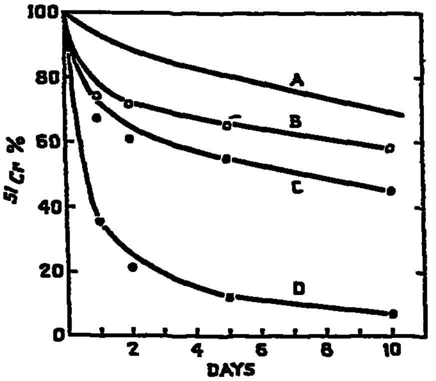

Fig 1—Survival curves for blood stored for six weeks in A C-D and revived immediately before transfusion A, fresh blood transfusion (mean of 5 normals) , B, 6-week stored blood incubated with adenosine C 6-week stored blood incubated with guanosine D, 6-week stored blood incubated with glucose

To estimate post-transfusion survival 30 µC of $Na_2{}^{51}CrO_4$ (15 µC per µg Cr) were added to 10 ml of revived blood and allowed to stand for an hour The blood was then centrifuged for ten minutes at 500 g and the supernatant plasma was removed The remaining cells were washed once with 20 ml of sterile saline solution, and recentrifuged the supernatant fluid was again removed, and the cells were finally suspended in 5 ml of saline solution and injected into a healthy recipient Samples of blood were taken at the end of ten minutes, twenty-four hours, forty-eight hours, about four days, and about ten days after injection, and the radioactivity in 10 ml. of these samples was estimated with an Ekco "pillar-type" scintillation counter The survival of cells was computed by standard methods taking the ten-minute sample as the 100% value The survival values at forty-eight hours were then expressed as per cent survival compared with freshly transfused cells

TABLE I—SURVIVAL AND CONTENT OF ADENOSINE TRIPHOSPHATE OF CELLS STORED FOR VARIOUS PERIODS AND INCUBATED WITH NUCLEOSIDES IMMEDIATELY BEFORE TRANSFUSION

Storage (days)	Nucleoside	% survival at 48 hr		Adenosine triphosphate (µg of phosphorus per ml of cells)		
				Before incubation	After incubation	
		Nucleoside	Glucose		Nucleoside	Glucose
38	Guanosine	75	54	25	41	30
	Adenosine	79	28	21	54	10
42	Guanosine	69	28	21	27	
	Adenosine	51	10	16	36	0
56	Guanosine	49	10	16	29	

To assess the relative toxicity of the two nucleosides, solutions of graded strength were injected into a narcotised cat, whose blood-pressure and electrocardiograms were continuously recorded

As a check on cell metabolism, samples of red cells were analysed chromatographically for phosphate esters as described previously (Prankerd and Altman 1954b) before and after revival with nucleoside

In a final experiment a pint of six-week-old blood, restored with the same quantity of guanosine (750 mg per 540 ml blood) in the manner described, was transfused to a recipient whose pulse, blood-pressure, electrocardiograms, temperature, hæmoglobin, blood-urea serum-bilirubin, and urinary urobilinogen were frequently recorded

Results

Fig 1 shows the survival after transfusion of labelled cells stored in A-C-D for six weeks and reincubated with one of the two nucleosides, or glucose alone before administration The increased survival of the nucleoside-treated cells at the end of forty-eight hours is obvious, and thereafter they survive normally

Table I summarises survival experiments on revived blood after various periods of storage and compares their survival with control samples The amounts of adenosine triphosphate in these cells before and after incubation are also shown Incubation with either of the two nucleosides persistently improves cell survival and is associated with resynthesis of intracellular adenosine triphosphate, which does not happen with glucose alone there was also intermittent diarrhœa The patient died on Nov 20, 1954, sixty days after admission to hospital

Necropsy Findings

The main findings 61 hours after death were those of congestive heart failure Several small recent infarcts were present in the right lung The heart was hypertrophied (22oz), mainly on the right side, its muscles and valves showed no lesion, and the coronary vessels were patent

Histology confirmed the macroscopic findings In an extensive search, including examination of more than a hundred sections of the heart, no toxoplasma was found Scattered throughout the heart muscle were a few foci of lymphocytes, plasma cells, and mononuclear cells, occasionally forming a perivascular cuff, or adjacent to vessels in the interstitial wall These were mainly in the left ventricle

Isolation of toxoplasma —A portion of heart muscle was forwarded to Dr Cathie at the Hospital for Sick Children, London, and toxoplasma was isolated by animal inoculation (Cathie 1955)

Discussion

Post mortem diagnosis of toxoplasmosis is difficult in the absence of animal inoculation because the toxoplasma may be very scanty and there are no specific histological stains

The degree of cardiac myohypertrophy was striking and, in the absence of other causes, must have been due to primary myocarditis Although scanty, it appears significant that histological lesions were found, particularly in the left ventricle

Paulley et al (1954) have pointed out that toxoplasmosis should be excluded in all obscure forms of myocarditis

Adams et al (1953) describe the changes in muscle as a focal disseminated myositis We were impressed with the scantiness of such lesions in the heart muscle in the present case, despite the well-marked clinical findings

Callahan et al (1946) pointed out two distinct forms of toxoplasmosis in the adult one they described as an acute exanthema with the most pronounced lesions in the lungs, and the other is a chronic asymptomatic disease, seen in mothers of infected children and revealed by the presence of neutralising antibodies in the blood Our case resembles Callahan's first type, except that the mode of death was cardiac

The effect of treatment is difficult to assess because the number of cases diagnosed appears to be small The various antibiotics, a sulpha drug, and pyrimethamine were all without effect in the present case

In some of the adult cases the infection has been acquired in a laboratory (Beverley et al 1955) In other cases the possibility of vectors—e g, ticks and mites—has been considered Toxoplasmosis is known to be widespread in the animal kingdom, with varying clinical manifestations

It appears relevant in the present case that, before the patient's illness, his dog was taken ill with diarrhœa and vomiting, was ill for six weeks, and died in July, 1954 A veterinary surgeon had advised destruction of the dog, but the owner had refused Olafson and Monlux (1942) found that, in dogs, toxoplasmosis produced granulomatous lesions in the intestines, lymph nodes, liver, and lungs, with *minimal* involvement of the nervous system, and there may be acute enterocolitis with focal ulceration of the mucosa Possibly the infection in the present case was acquired from the dog

Summary

A case of acute myocardial toxoplasmosis from which the organism was isolated is described

It is suggested that the source of infection in this case was from a dog

We wish to acknowledge the very considerable help and advice of Dr R Blowers of the Public Health Laboratory, Middlesbrough, and Dr I A B Cathie, of the Hospital for Sick Children, London

References at foot of next column

Preliminary Communication

HYDROCORTISONE IN THE PREVENTION OF TRANSFUSION THROMBOPHLEBITIS

THROMBOPHLEBITIS is a common troublesome complication of intravenous infusions,[1] especially when they are protracted or when hypertonic solutions are given[2] To avoid it Bolton Carter suggested[3] that no infusion should be continued longer than eight hours When it is essential to provide nutriment parenterally for several days—e g, in anuria and in hepatic coma—the use of fat emulsions, the catheterisation of the great veins, and the insertion of a cannula into the cephalic vein have been recommended

It was observed that patients receiving systemically large doses of cortisone or of hydrocortisone seemed less liable than others to develop phlebitis after protracted infusions—an effect which was attributed to the ability of these hormones to suppress inflammation Therefore, when hydrocortisone alcohol became available, it was decided to test the power of this steroid, added to an intravenous infusion, to prevent or to suppress phlebitis, advantage being taken of the fact that a very high local concentration of hydrocortisone could be produced in the vein receiving the infusion by a dose which would be without systemic effect Three patients were selected in whom there was an indication for the intravenous administration of hypertonic dextrose, and they were given 20% dextrose solution containing 0 001% (10 mg per litre) of hydrocortisone

The three patients, all of whom were in hepatic coma were given infusions through standard red rubber tubing into peripheral veins The infusions were continued for 32, 46¹/₂, and 63¹/₂ hours and discontinued 2 hours, 6 days, and 12 hours before death The fluids given to the first patient included 2 litres of the 20% dextrose hydrocortisone solution, the two other patients received 3 litres each In the third patient the solution was not begun until the fastest rate of flow obtainable had gradually fallen to 11 drops a minute and the vein was indurated for three inches proximal to the site of puncture, after 6 hours the rate had risen to 60 drops a minute, and after 12 hours no induration could be felt

No clinical evidence of thrombophlebitis developed in any of these patients during or after the 20% dextrose hydrocortisone infusions, and at necropsy Dr W G Spector found no abnormality in the peripheral vein either macroscopically or microscopically The first patient had a recent ante mortem thrombus in the portal vein

None of these infusions was very protracted, the longest lasting 63¹/₂ hours In each case, however, 20% dextrose was given into a peripheral vein without causing thrombophlebitis In one case signs of thrombophlebitis disappeared while the solution was being administered It seems likely that the addition of 0 001% hydrocortisone was responsible for the tolerance shown by the

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1 Richards H J *Med J Aust* 1955, ii, 7

2 Horwitz, A, Sachar L A Elman R *J Lab clin Med* 1943 28 842

3 Bolton Carter J F *Lancet*, 1951, ii 20

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ested in cats and found to be similarly non toxic hese would probably be active in reviving stored red ells, but, since guanosine is the cheapest of this group f substances, it is thought to be of most practical mportance

Further work is in progress to ascertain the practical value of reviving stored blood by these methods and to assess factors which influence cell revival, but, in view of the lack of complications observed here after transfusion to man, the value of these methods may well be considerable

Summary

Observations have been made on the effects of the nucleosides adenosine and guanosine in reviving stored blood

Using blood which has been stored in A-C D for periods up to eight weeks good survival-times of transfused red cells can be obtained

The ability of cells to survive after revival is related to their content of adenosine triphosphate

Unlike adenosine, guanosine is not toxic to man, and whole blood revived with guanosine has been successfully transfused

I am grateful to Dr R Moulton and Mr D Willoughby for performing the experiments on cats

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DIAGNOSIS OF SEX BEFORE BIRTH

C J DEWHURST
M B Manc, F R C S E, M R C O G
SENIOR LECTURER IN OBSTETRICS AND GYNÆCOLOGY IN THE UNIVERSITY OF SHEFFIELD

> " Another test for a woman who will bear or a woman that will not bear Wheat and spelt Let the woman water them daily with her urine If they both grow she will bear if the wheat grows it will be a boy if the spelt grows it will be a girl If neither grows she will not bear —*Egyptian Papyrus*

PROBABLY the commonest speculation on the outcome of any pregnancy concerns whether the baby will be a boy or a girl Many have professed their ability to foretell this by various criteria—e g, whether the baby is carried "all at the back" or "all at the front," whether a needle suspended over the abdomen rotates clockwise or widdershins, and when, in the menstrual cycle, the child is supposed to have been conceived More scientific methods have been based on the fœtal heart rate and the saliva test None of them, however, has stood the test of time and at present there is no alternative but to wait and see

The discovery, however, that genetic sex can be recognised by the different arrangement of chromatin according to sex in the nuclei in a biopsy specimen of skin (Moore et al 1953), an oral smear (Moore and Barr 1955), and a vaginal smear (Carpentier et al 1955) has suggested that the sex of a fœtus in utero might be diagnosed by examining the chromatin in the nuclei of desquamated skin cells in liquor amnii I report here the results of a short investigation of this matter

Principle

The nuclei of epidermal cells and other tissues of females contain a mass of chromatin which is rarely observed in male nuclei This aggregation of chromatin in female nuclei is located in different parts of the nucleus but is most definite and easiest to distinguish at the periphery, where Moore and Barr (1955) observed it in 40–60% of suitable nuclei in oral smears Most characteristically the chromatin is roughly triangular, with its apex towards the centre of the nucleus, but other shapes are found In male nuclei the chromatin is distributed in small particles throughout the nucleus and only rarely in aggregations Thus, with good nuclear detail, the sex can readily be distinguished

Technique

Liquor amnii was obtained by artificial rupture of the membranes for the induction of labour, or by paracentesis uteri, or at cæsarean section About 5 ml was centrifuged, and the supernatant fluid was poured away A thin smear, on a slide previously coated with egg albumin, was at once fixed in Papanicolaou fixative (equal parts of 95% ethyl alcohol and ether)

When liquor amnii obtained by paracentesis was prepared in this manner it was often washed off the slide during the subsequent staining, possibly owing to its low protein content This difficulty was partly overcome by adding 30% bovine albumin 0 25 ml to every 5 ml of liquor before centrifuging

The period of fixation was not critical and lasted 2–48 hours After fixation the slide was stained by a method similar to that described by Moore and Barr (1955)

The fixed smears were passed through absolute alcohol and 95% alcohol, two changes of about 2 minutes in each, then through distilled water for 5 minutes The smears were next stained with 1% fast cresyl violet for 10–15 minutes, differentiated in 95% alcohol (two changes) for about 1 minute and then absolute alcohol (two changes) for 1 minute, cleared in two changes of xylene, and mounted

Observations

Examination of the liquor amnii, obtained by artificial rupture of the membranes and prepared in this manner, soon showed that the typical arrangement of sex chromatin in female nuclei could be distinguished here as in other tissues Although many nuclei were found to be pyknotic and densely staining, and therefore unsuitable for study, as were others which were degenerate or distorted, a sufficient number were seen in which the nuclear detail was clear, to allow careful examination for sex differences In specimens from cases where females were subsequently born the female sex chromatin showed the typical arrangement described above in 25–40% of the nuclei suitable for study In specimens from cases where males were subsequently born less than 5% showed such an arrangement

Experiment I

In view of these differences, which were observed and confirmed in the earlier specimens examined, it was decided to test the accuracy of the method on liquor amnii obtained at cæsarean section or by artificial rupture of the membranes in cases where induction of labour was necessary 20 specimens were therefore examined which had been taken between the 36th and 42nd weeks of gestation, with one exception which was obtained at the 26th week from a severe case of pre-eclamptic toxæmia

Results—In 18 cases (10 male and 8 female) the sex of the fœtus was predicted correctly, and in 2 cases suitable nuclei were too few to permit any forecast These results seemed to indicate that, with care, a correct forecast of the sex of the fœtus is possible by this method, at least in so far as the sexing of nuclei in the liquor amnii is concerned

To test this hypothesis further and in circumstances more nearly resembling those in which it might be applicable, the study was extended to include liquor amnii obtained by abdominal paracentesis

In accordance with the changed policy of treating patients, most of the aggression was dealt with by social means (most commonly by removing the patient from the situation) rather than by physical methods of treatment Results suggested that a ward of chronically disturbed patients could be run without extensive use of sedation, E C T, or seclusion, if the frustrations and provocations leading to aggression were avoided by more individualised attention to patients The most important factors seemed to be the development of appropriate attitudes by nursing staff

Dr R K **Freudenberg** gave an account of an investigation conducted with Mr J P S Robertson into personal stresses in relation to psychiatric illness, the aim of which was to establish whether there are in fact statistically significant differences in the incidence of stresses in patients suffering from psychiatric illness as compared with a normal control group of non-psychiatric patients, and whether these influence diagnostic status and prognosis Only tentative conclusions were possible

100 consecutive psychiatric and 50 non-psychiatric admissions below the age of 60 were investigated according to a check-list of personal stresses covering ninety-one items grouped into questions on earliest childhood, childhood in general, school, occupation, sexual and marital life, and miscellaneous adult stresses 23 psychiatric patients were diagnosed as psychoneurotics, 19 as depressives, and 51 as schizophrenics

The incidence of personal stresses was highest in schizophrenics, while depressives did not differ significantly from controls, patients classed as psychoneurotic occupied an intermediary position but did not differ significantly from either of the other two groups Stresses found significant were present largely in the "childhood in general" section In schizophrenics there was a significantly higher incidence of discord between parents without actual separation, and objective occupational factors were more frequently frustrating Within the psychiatric group different stresses did not seem to be the main determinants for differences in diagnostic status Only the stresses of "childhood in general" had a suggestive differentiating influence on treatment response Abnormal birth or being an only child or an only child of that sex were more frequent in schizophrenics than in depressives, while orphans not brought up by parents were more frequent among psychoneurotics None of the separate stresses under occupation, sexual and marital, or miscellaneous adult stresses were of any significance Left handedness and late onset of voice change and menarche were commoner in schizophrenics who did not improve

In general, negative findings were more numerous than positive Among personal stresses in the three diagnostic groups of psychiatric patients in which there were no significant differences were some which had been frequently emphasised, including bottle feeding, weaning difficulties, lax or strict toilet training, over affection from the mother, early death of one parent, and early separation from the mother

Personal stresses in 100 consecutive female admissions over the age of 60 diagnosed as having senile dementia, arteriosclerotic dementia, paraphrenia, confusional states, or affective psychoses were compared with personal stresses in a control group of non-psychiatric patients over 60 The psychiatric group showed more frequent total stresses, among which were deterioration in financial situation, lack of occupation, and social isolation Senile dements had a distinctly lower incidence of stresses than patients with confusional states, the incidence approximating more closely to that in the control group The arteriosclerotic group showed most significant differentiating stresses Among patients with affective disorders, stresses concerned with domestic problems were probably the most important factors in prognosis

The results indicated that differences in diagnostic status were not due mainly to different personal stresses, although these might be slightly more important determinants than in the younger psychiatric sample

Dr Freudenberg felt that these findings were in agreement with the evolutionary theory of disease according to which illness is inherent in the nature of life itself and arises either from the universal preying of one species on another or from genetic variability or from environmental circumstances which the organism's inherited structure is unable to resist The complex relation of personal stress to illness could be further elucidated either by more refined methods which would yield more detailed and systematic knowledge of the existing social context and the particular person involved

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New Inventions

INFLATABLE POSTNASAL TAMPON

FOR CONTROL OF INACCESSIBLE HÆMORRHAGE

When bleeding from inaccessible regions of the nose or from the nasopharynx continues despite every encouragement to natural arrest, the choice lies between inserting some kind of tampon and more drastic intervention under anæsthesia When the latter course involves a second anæsthetic, as in reactionary hæmorrhage following adenoidectomy, the decision is serious; for, in addition to the risk of anæsthetic depression in an exsanguinated child, there is the grave hazard of blood inhalation during induction The alternative, often preferred, of inserting a postnasal pack via the mouth is most uncomfortable and disagreeable for the patient, and the pack, unless placed with skill and precision, cannot be relied on to be effective It is also not without danger in that downward displacement can cause acute respiratory obstruction

A similar problem arises in those 10% of epistaxes which arise, usually in the elderly, from invisible areas of the nasal passages and which are unamenable to arrest by direct pressure Control may be effected by nasal tampon, but it is generally effected by occluding the exit of blood via the posterior and anterior choanæ—in other words, by *indirect* pressure

Since nasal hæmorrhage can be arrested indirectly by preventing egress of blood from the nasal cavities, further means were sought to apply this principle without resource to general anæsthesia or undue discomfort to the patient The shape of the postnasal space seemed to lend itself to the use of an inflatable balloon, which could theoretically apply direct pressure to any bleeding point there, and at the same time block the posterior choanæ and palatal hiatus, while with the addition of a nose clip the nasal passages would be effectively isolated

With the helpful cooperation of Messrs Down Bros and Mayer & Phelps Ltd what is believed to be a new instrument has been devised, and has now been used successfully to control postadenoidectomy hæmorrhage in 11 consecutive cases during the past eighteen months With the confidence gained in the earlier cases the instrument has latterly been used at a stage in the bleeding when hope for natural arrest had not been abandoned but continued loss of blood was regarded as

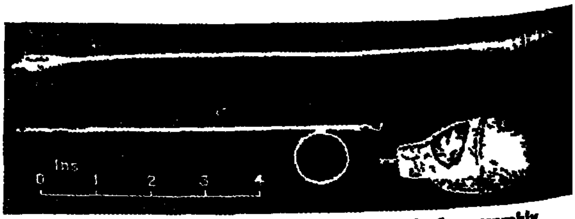

Fig 1—Balloon introducer, and bulb ready for assembly

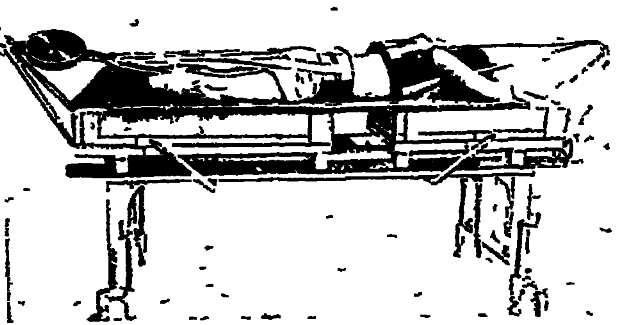
Fig 2—Traction has now been applied by turning wheel at head of couch platforms have separated, and spring balance registers 70 lb pull

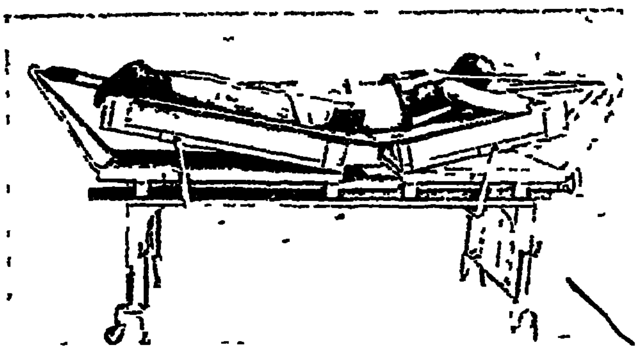
Fig 3—Ends of sections raised to cause hyperextension with traction still operating

Traction Couch

In the traction couch illustrated here (fig 1) the upper surface is divided into two sections, one for carrying the thorax, and the other for carrying the pelvis and the legs These can be raised at either end to elevate that end of the patient lying prone This enables variable and controlled hyperextension of the lumbar region to be obtained while traction is still being applied

The immediate application of a plastic support for the lumbar region while the patient is still lying on the couch is a safeguard against recurrence In doing this one can separate the two sections of the couch to create a gap which enables the plastic support to be wrapped round the patient and bandaged in position without removing the patient from the traction couch It is usual to apply this support without any hyperextension and with hardly any traction

The traction couch (figs 1–4) was originally made up for me from an old Bell's orthopædic table and is very satisfactory and easy to work The section carrying the pelvis and lower extremities is 41 inches long, and that carrying the head, neck, trunk, and arms is 29 inches long The two sections are mounted on runners and coupled together by a long coarse screw which causes them to separate from one another on rotation of the wheel at one end of the couch At both ends of the couch are stout brackets to which the harness is attached, one of these incorporating a spring balance The harness is made up of two belts of soft leather lined with 'Sorbo' rubber, the pelvic belt being 5½ inches wide and the one for the thorax 9 inches wide Adjustable webbing straps connect these belts to the brackets at either end of the couch

Lately I have used a specially designed table (fig 5) instead of that made up from a Bell's orthopædic table

Manipulation

The patient lies prone on the couch (fig 1), the harness is attached to the pelvis and thorax and the slack on the adjustable webbing belt taken up, and the wheel is turned causing the sections to separate until a pull of about 90–100 lb is registered (fig 2) Usually this pull immediately relieves the patient of pain After it has been maintained for 10–15 minutes, the ends of the couch are raised to produce hyperextension (fig 3) *Finally the couch is made horizontal again and the* traction discontinued

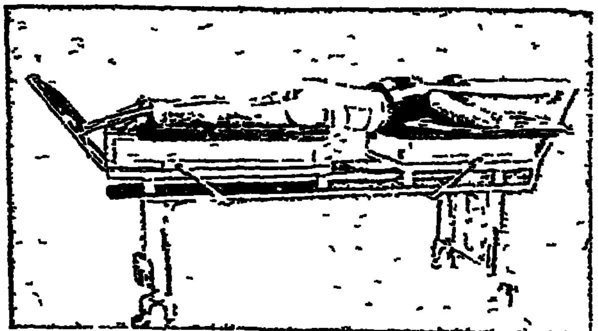
Fig 4—Application of plastic support for lumbar region with patient still prone with sections of couch separated

If at this stage it is considered advisable to make a plastic support, the patient remains prone on the couch with the thoracic harness in position, but ankle straps are *substituted for the pelvic harness* (fig 4) The sections of the couch are separated about 12 inches, and only just enough traction is applied to steady the patient and to prevent him from feeling uncomfortable because of the gap in front of his abdomen The whole of his lumbar region is now free for the plastic corset to be applied and moulded to him by bandaging

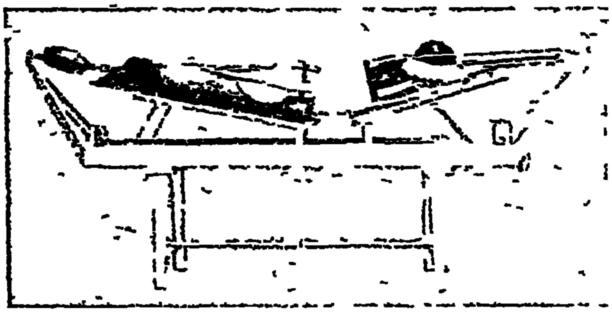
Fig 5—Specially designed couch ends of sections raised to cause hyperextension with traction still operating

Assessment of Effects of Traction-manipulation

The assessment of the results of any form of treatment of disc lesions in the lumbar spine is particularly difficult because of the large number of extremely variable features

Minor degrees of pain in the back and the leg are extremely common, they were formerly labelled lumbago or, sciatica, and few people of middle age have not experienced attacks of low back pain at some time or other There is a strong tendency to spontaneous cure, sometimes quite rapid, but a definite liability to recurrence The 50 patients reviewed here were in very severe and completely disabling pain, and required morphine to relieve them These patients have therefore been selected to some extent because the main symptom (pain) had been very severe Patients with less severe symptoms usually have a plaster or plastic support applied direct, and patients with minor symptoms are prescribed rest and physiotherapy

Results

The results are analysed in table I

Complete immediate relief of pain was obtained in 11 cases (22%), in 5 of these the pain returned to a slight the dissemination of *T saginata* eggs from sewage plants, for this probably explains the sporadic cases in Britain on farms where there is no evidence of a human carrier

The book will be useful to the human and veterinary pathologist and veterinary practitioner, but it is perhaps a little too detailed for the veterinary student There are many excellent illustrations and a comprehensive bibliography

Gynecology

Surgical Techniques Robert J Lowrie, m d , f a c s , associate clinical professor of obstetrics and gynecology, College of Medicine, New York University Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 523 £6 7*s* 6*d*

The companion volume to *Gynecology Diseases and Minor Surgery* is a massive book in which 60 contributors have written something for everyone—the undergraduate, the general practitioner, the postgraduate student, the obstetrician, and the general surgeon

The various surgical methods get full consideration for example, the authors give six different methods for the correction of stress urinary incontinence, four for urinary fistulas, and eight for hysterectomy

The book contains an enormous amount of information, nearly all of which is concerned with the practice of gynæcology in the United States, and in consequence many will think it of limited value to specialists and would be specialists in this country

For all the wisdom in its pages this is the kind of book that overwhelms by its complexity and by the very fact that it offers something for every reader As every contributor is an expert in his subject, then Rudyard Kipling must have been right "there are nine and sixty ways of constructing tribal lays, and—every—single—one—of—them—is—right!"

Modern Trends in Orthopædics

2nd series Editor Sir Harry Platt, m d , m s , f r c s , emeritus professor of orthopædic surgery, University of Manchester London Butterworth Pp 331 65*s*

In this first-rate collection of papers by experts, current views on a number of important conditions are summarised and analysed The writers give their considered opinions on what is sound and unsound in current practice There are chapters on reconstructive surgery, congenital dislocation, and fractures of the hip, traumatic and Pott's paraplegia, peripheral nerve injuries, antibiotics in bone and joint tuberculosis, muscle and tendon transplants in poliomyelitis, internal derangement of the knee, displacement of the upper femoral epiphysis, and contractures of the hand All are good, most of them excellent, and several brilliant Even the most accomplished orthopædic surgeon will gain from a study of these pages

L'art psychopathologique

Robert Volmat, chef de clinique à la Faculté de Médecine de Paris Paris Presses Universitaires de France 1956 Pp 325 Fr 1800

While the first world congress of psychiatry was meeting in Paris in 1950 an international exhibition of psychopathological art was held at the celebrated mental hospital of St Anne more than 2000 paintings by mental patients from 45 different institutions were on view In this book Dr Volmat commemorates that exhibition in a detailed manner suggestive of Germanic scholarship rather than French *esprit* His bibliography of 825 titles will be invaluable to students, but the text which precedes it is not easy reading

The first 135 pages set out the notes—translated, where necessary, but scrupulously unedited—which accompanied some hundreds of the pictures lent for this exhibition There follow three essays, on æsthetic form, on symbols, and on the expression of "archaic thinking" in art These open promisingly with a quotation from Malraux, to the effect that the psychotic, like the child artist, "à la maîtrise substitue le miracle"—a phrase which captures perfectly the unexpected quality of paintings by children and by schizophrenics But Dr Volmat's discussion of æsthetic philosophy is uninspiri Later he quotes Malraux again, to emphasise the paradox t in this age, when mass reproductions have made the beau of art generally accessible, the modern artist is more th ever repudiated In explanation, he advances Wittma view that modern art inflicts a narcissistic trauma on i observers, but Dr Volmat goes further and maintains th the public of today is incapable of understanding any co temporary ideas and trends Similar exaggerations mar t last chapter, on art as a means of group therapy few wou agree that patients' paintings are "as useful as all oth sources of clinical observation," or that the act of paint necessarily brings about a therapeutic abreaction

The book ends with 169 black-and-white reproductio —an eloquent, if muted, testimony to the comprehensiv ness of a remarkable exhibition

℞ for Medical Writing

Edwin P Jordan, m d , Willard C Shepard Phil delphia and London W B Saunders 1952 Pp 11 17*s* 6*d*

The first third of this book is a kindly and intima guide to the writing of medical articles The harde thing is to get started many people are familiar with t paralysis induced by a ream of blank paper to be fil by next Monday And when a start is at last made, t pen is apt to run away with the writer Dr Jord explains how to cope with these troubles

He begins with a chapter on preliminaries choosing t subject, reading it up, making notes, and suiting the style the reader Drafting and revision are then discussed length, and there is helpful advice about those importa points the title, the beginning, and the summary Tw thirds of the book is about illustrations and statistics T chapter on illustrations is technical, and though medi illustrators may find it interesting the ordinary medical wri needs something less involved The chapter on statistics also rather heavy going for those who are not statisticians and probably superfluous for those who are It would ha been better to have a much shorter and non technical accou of the subject

Diseases of the Thyroid Gland

Samuel L Gargill, m d , assistant clinical professor medicine, Harvard Medical School Mark Falc Lesses, m d , instructor in medicine at the School N York and London Oxford University Press 1955 9

Reprinted from Oxford Loose-Leaf Medicine, t book treats the subject in a conventional way Chapt on the anatomy, physiology, and biochemistry of thyroid are followed by detailed descriptions of diseases A reasonable balance has been struck betw the theoretical and the practical The authors' opini seem to be strictly orthodox, and it would be difficult find fault with them, although, like most Americ authorities, they may be unduly influenced by incidence of malignant change in nodular goitres T is a sound but not an exciting book, and the illustrati are good

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Medical Manual of Chemical Warfare (4th ed H Stationery Office 1955 Pp 88 4*s*) —For the new editi this manual, issued under the authority of the Admira War Office, and Air Ministry, has been extensively rev by a committee with Major General A Sachs as its chairm A new chapter on the nerve gases has been added, as wel a table showing the effects of war gases on food and wa A number of mainly industrial hazards, including hydro sulphide, ammonia, and corrosive acids, have been omit or dealt with only briefly, because they will be covered by *Handbook of Occupational Health* which is being prepared the Joint Services and Factory Department Committee Occupational Health Carbon monoxide, however, has b retained, and a new note has been added on gasoline A f section on Anoxia and Oxygen Therapy points out that Schafer method of artificial respiration has now given p to the back pressure/arm lift method of Holger Nielsen, w is clearly described and illustrated As an alternative, for when the arms or shoulder girdle have been injured, hip lift/back-pressure method is proposed

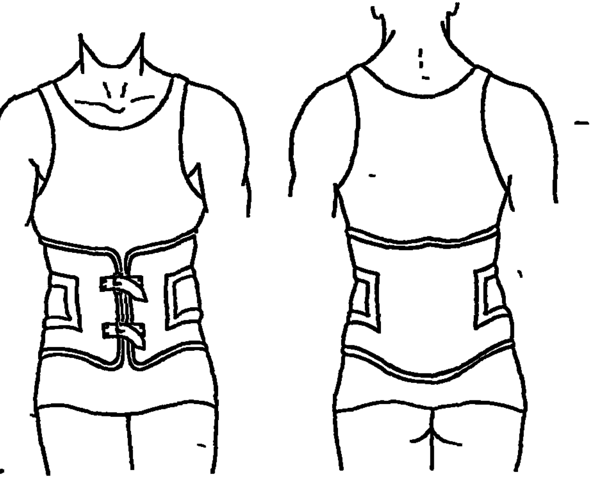

Fig 8—Application of plastic support to patient.

ugh position, a temperature of 120°C The corset is hen placed on the tray with the polyethylene side uppermost and is heated for about 15 minutes The whole of the polyethylene should become clear if it s at the correct temperature It must not be allowed to become too hot because it will then be too soft, like reacle Hence the need for a thermostat as well as a thermometer

Fitting

The corset can be applied with the patient lying prone on the traction couch with its two sections separated, but, if the patient is well enough to stand, this position is preferred because it leads to a better fit The patient then stands with his arms above his head, steadying himself by holding on to a bar He is covered with a layer of stockinet or a vest on which are marked the upper and lower positions for the corset and the midline at the back

The tray with the heated support on it is then removed and laid on top of the oven, and two strips of 2 inch calico bandage are placed on the upper and lower margins of the support These make it easier to hold and lift the support and can be held together in front of the patient so that they are useful in moulding the support They also prevent the material from stretching, which it is liable to do in the soft state The support is then applied to the patient posteriorly, the centre of the support must be made to coincide with the midline of the patient, it is then wrapped round to the front, held by the two calico strips, and bandaged on with two 4 inch openwove bandages It remains in position for a quarter of an hour, by which time it will be cool enough to have set, and is then removed The straps and buckles are applied by riveting in position as shown in figs 6 and 7 The corset is then fitted to the patient, and any minor adjustments are made so that it is absolutely comfortable in both standing and sitting positions Tapes can, if necessary, be attached to the lower bar to hold suspenders, and this is really a useful addition because it prevents the support from riding up

After-treatment

It is recommended that, as a general rule, these supports should be worn for at least six weeks after all symptoms have subsided, but they may be used for even longer periods They can in most cases be taken off when the patient lies down at night and when he wants to have a bath and to carry out hyperextension and straight-leg-raising exercises, and they take the place not only of the plaster corset but also of a Goldthwait's belt subsequently

Return to Work

Plastic supports for the lumbar discs have been most useful in getting the patients back to work, sometimes immediately after the application, provided the work does not entail much bending or lifting Farmers can get round the farm and supervise, bench workers can usually continue, and sedentary workers, such as insurance clerks, bank clerks, solicitors, teachers, and doctors, can do the greater part of their duties In this way many working-hours can be saved, and a man who works for himself does not need to miss much time, for he can be up and about with the lumbar spine supported in an upright position, so that healing can take place probably as rapidly as if he were recumbent

Conclusion

Traction-manipulation has a definite place in relieving a severe attack of pain in cases of prolapse of a lumbar intervertebral disc, and plastic corsets are a great improvement on plaster ones and help to maintain reduction and to prevent recurrences

There is, however, a hard core of patients with prolapsed lumbar intervertebral discs who are not relieved or suffer recurrence in spite of manipulation, supports, or prolonged rest in bed, and in these operation should not be unduly delayed

Every orthopædic surgeon must be familiar with the remark made by a patient after operation when relieved of the excruciating attacks of sciatica "Why didn't you operate sooner?"

Cost

The polyethylene ('Vitrathene') was obtained from Stanley Smith & Co Ltd, Worple Rd, Isleworth, Middlesex, in sheets measuring 7 ft × 3 ft × $^3/_{16}$ in costing £10 12*s* 3*d*, enough to make eight or nine corsets The polyurethane ('Moltopren') was obtained from Kay Bros Ltd, Reddish, Manchester, in sheets 6 ft × 3 ft × $^1/_4$ in costing 15*s* 4*d*, enough to make seven or eight corsets Rivets, buckles, and straps cost less than 2*s* 6*d* per corset, and the time taken by a skilled man to cut out the material is something less than an hour at 4*s* an hour, so the cost of materials used and the man's time for making up the corset come to just over £1 15*s*

I wish to thank the staff of the Norfolk and Norwich Hospital for their coöperation, Miss V Gibson, of the physiotherapy department for not only carrying out many of the manipulations but also for keeping careful record of the effect on the patients, Mr F Baker and the nurses of the orthopædic theatres for help in the application of the plastic supports, and Mr R Fox, the carpenter, for making the original traction couch The specially designed couch was made for me by Rowlands Bros, Aylsham, Norfolk

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THROMBOTIC THROMBOCYTOPENIC PURPURA

A HYPERERGIC MICRO-ANGIOPATHY

A Erskine Stuart
M B Glasg
OF THE DEPARTMENT OF PATHOLOGY,
DUNDEE ROYAL INFIRMARY

G MacGregor-Robertson
M B Glasg
MEDICAL REGISTRAR, WESTERN INFIRMARY, GLASGOW

Thrombotic micro angiopathy is characterised by pyrexia, hæmolytic anæmia, thrombocytopenia, and bizarre neurological symptoms It occurs more commonly in females and is of acute onset and fatal outcome At necropsy the gross appearances are neither specific nor striking, and it is usually only when microscopy reveals widespread intracapillary thrombosis that the correct diagnosis is reached

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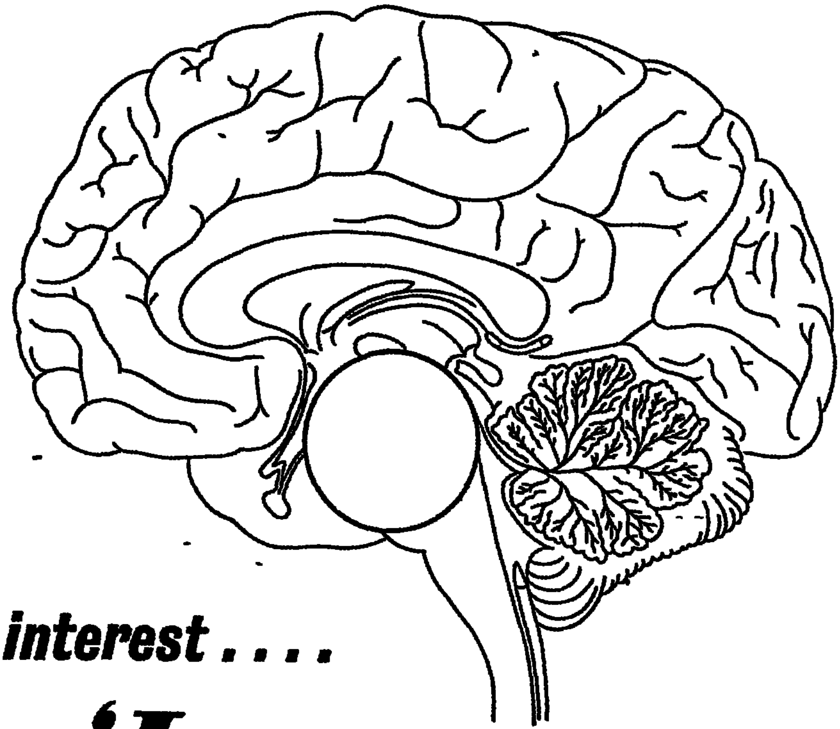

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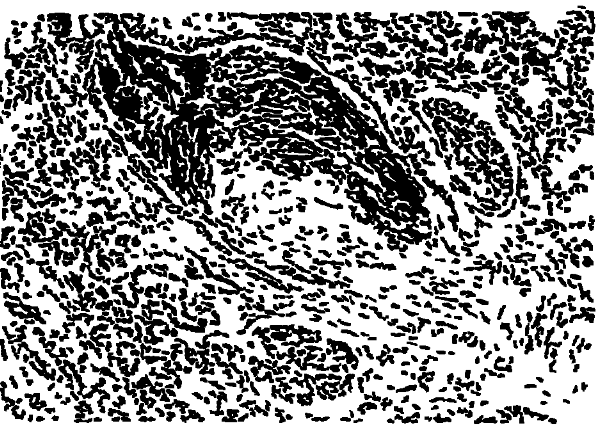

Fig 3—Partially organised thrombus in kidney

(June 11) and her pulse rate was 100 per min. Her blood sugar and blood-urea levels were normal. Her Hb was 51% (Haldane) (7.5 mg per 100 ml.) and reticulocytes 13%. On June 12 her temperature reached 102.4°F, and her pulse rate and respirations increased correspondingly. Fresh crops of petechiæ and numerous bruises appeared on her arms and body. She died in coma on June 14, without having recovered consciousness.

Necropsy findings.—The body showed numerous bruises and purpuric spots. It was very pale, and the conjunctivæ were slightly icteric. The *bone marrow* showed moderate erythroid hyperplasia red marrow occupying the upper two thirds of the medulla of the right femur. The vertebral marrow was uniformly red. The *lungs* were congested and œdematous at both bases, fluid being expressed from them with ease. The *trachea* and *bronchi* were healthy and the related lymph nodes not enlarged. The *pericardium* and pericardial sac appeared normal. The *myocardium* was pale and soft. The *endocardium*, valves, chambers, and arteries of the heart showed no noteworthy features. The *pulmonary and mesenteric vessels* appeared normal. The *œsophagus, stomach*, and *bowel* from duodenum to rectum appeared normal, and there was no hæmorrhage. The *liver* was of normal size and contained an increased amount of iron by the prussian blue reaction. The *gall bladder* and *bile-ducts* appeared normal. There were no pigment stones. The *spleen* was of normal size, dark red, and soft, with indistinct malpighian bodies, and contained an increased amount of iron by the prussian-blue reaction. The *pancreas* appeared normal. Both *kidneys* were smaller than usual (lt. 110 g., rt. 115 g.) Their capsules stripped easily, revealing a smooth surface. The cortex of both kidneys showed slight narrowing and considerable hæmosiderosis by the prussian blue reaction. The medulla was smooth and uniform. The vessels appeared normal. Both *ureters* and the *bladder* were normal. The *adrenal glands* were of usual size, but their cortex was deep-red and extremely congested. The *uterus* was of usual size and contained a small quantity of blood clot. The *skull bones* and *meninges* were normal. The *brain* was sectioned and showed no noteworthy abnormality.

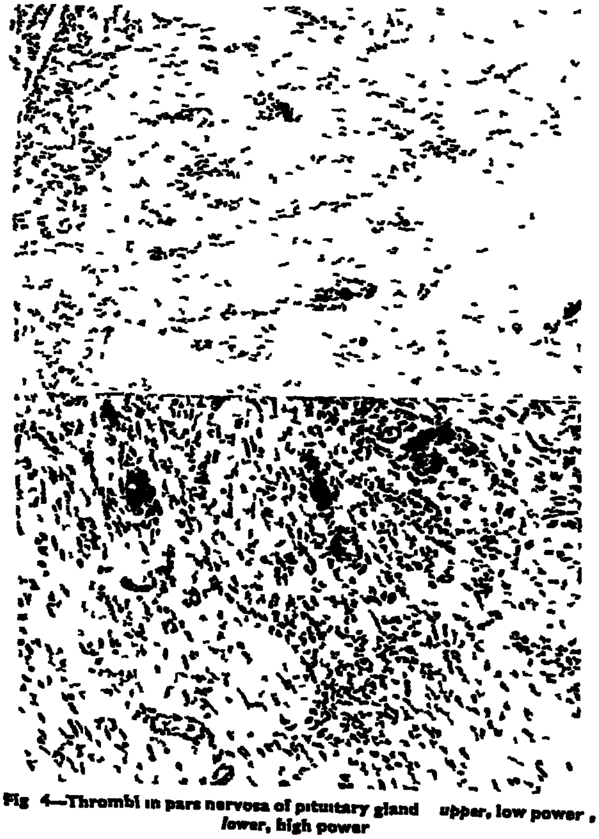

Fig 4—Thrombi in pars nervosa of pituitary gland: upper, low power; lower, high power.

STAINING PROPERTIES OF THROMBI

—	Platelet mass	Occlusive mass	Natural fibrin
Basic dyes			
Safranin	++	++	+−
Aniline blue (alcoholic)	−	−	−
Methyl violet	++	++	+
Bismarck brown	−	−	−
Celestine-blue	−	−	−
Acid dyes			
Light green	−−	++	−+
Chlorazol-black	−	−	−
Chromotrope 2R	−	−	−
Aniline blue (aqueous)	−+	++	−+
Other stains			
Sudan black	−	−	−
Heidenhain's iron hæmatoxylin	++	++	++
Picro-Mallory (Lendrum's modn)	Blue	Red	Red
van Gieson	Brown	Brown	Brown
Histochemical reactions			
Prussian blue	−	−	−
Acid polysaccharide	−	−	−
Periodic acid Schiff	++	−+	+−
Feulgen	−	−	−

Histology.—The lumina of many small vessels were partly or completely occluded by pink plugs, the so called thrombi (hæmatoxylin and eosin). Some of these were rather granular, whereas others, presumably older, were partially organised. The endothelium of the vessels containing the "thrombi" showed various degrees of swelling and proliferation, which sometimes encompassed the "thrombus". In some instances the vessels appeared dilated, and on occasion a segmental fibrinous deposition was seen in the wall adjacent to the occlusive mass, the fibrinous material lying immediately beneath the endothelium. Most of the affected vessels were of small calibre, arterioles, capillaries, and some venules. In the liver (fig. 1) the lesions were confined to the small vessels of the portal tracts. In the adrenal gland (fig. 2) the vessels in the capsular zone were much affected, and numerous microscopic hæmorrhages were present. "Thrombi" were numerous in the small vessels of the liver, the kidneys (fig. 3), the capsular zone of the adrenal glands, and the pars nervosa of the pituitary gland (fig. 4). They were scanty in the spleen and absent in sections of bone marrow, skin, lung, endometrium, uterus, and pars distalis of the pituitary gland.

Experimental Observations

The appearances and staining characters of the "thrombi" obtained in the present case were compared with pure platelets and fibrin.

Material and Methods

(1) A centrifuged deposit of human platelets was obtained by the method of Dillard et al. (1951). Smears from this deposit showed large numbers of well preserved platelets relatively little contaminated by leucocytes. This material, subsequently referred to as the platelet mass, was fixed in formol corrosive sublimate, and paraffin sections were prepared in the usual way.

ut sufficient evidence is accumulating to that pathologists should direct more attention to . Meanwhile, another aspect of cancer cytology, hardly appreciated in the clinical field as yet, but ultimately likely to affect clinical thought and practice more deeply than the diagnostic side, is advancing rapidly Malignant change can be maintained in successive generations of cancer cells belonging to one tumour by a persistent external stimulus, as may be provided by hormones in some breast cancers, but this phenomenon could also be explained by a transmissible, or hereditary, change within the cancer cell once it has been born Such a change must take place in those parts of the nucleus, chromosome, or cytoplasm responsible for inheritance The large size of the cancer cell's nucleus compared with its normal parent cell has long been noted[10] Furthermore, there is an increase in chromatin content, and the same is sometimes true of precancerous states[11] and cancer in situ This can readily be explained by an increased number of chromosomes, which are often found to be tetraploid or polyploid in cells from tumours of both man and mouse[12] Boivin et al[13] have shown a quantitative relationship between desoxyribonucleic acid (D N A) and the number of chromosomes in normal cells from the same species The work of Leuchtenberger et al[14] reveals an increase in D N A content of malignant cells, and this appears to correlate with the degree of polyploidy of those cells Is malignancy related to this increase in chromatin content and D N A ? It is significant that the nucleoprotein responsible for papillomata in cotton-tail rabbits contains D N A , but this infective agent finds its place in cytoplasm rather than nucleus Gigantism can be induced by chemical trauma, and advantage is taken of this by horticulturalists who induce polyploidy by painting seeds with colchicum in order to grow bigger and better plants But it is a far cry from gigantism to malignancy, and there are some growths, lymphoma in particular, which show few cells with more than diploid nuclei During a period of regression after irradiation, or treatment with nitrogen mustard, the morphological changes in the nuclei, which then show decreased mitosis, vary from pyknosis to enlargement sometimes associated with chromasia Similar changes induced by triethylene melamine in animals with experimental tumours have been accompanied by a greater increase than expected in the quantity of nucleic acids[15], Mellors[12] suggests that the nucleic acids accumulated because they were synthesised but not used when mitosis decreased In that case D N A could hardly be the chemical substance carrying the heredity of malignancy, unless its molecular arrangement had been altered, thus robbing it of this power It is theoretically possible that ribonucleic acid (R N A) may play a part since the organic mass of fat-free chromosomes, studied by interferometry, reveals in the mouse that D N A is linked with histone and R N A with non-histone protein The R N A complex seems to vary and the D N A complex remains constant, so it is conceivable that R N A provides the variation neede for differences in cell function within the body, whil D N A confers the characteristics of the individual If so, is malignancy carried with the variable factor The solution to these problems may turn the attentio of diagnostic cytologists to cytochemistry—and Leuchtenberger et al[14] have already suggeste D N A evaluations as a diagnostic cytochemical tes for malignancy

Infectivity of Nucleic Acids

During the past ten years or so advances in our knowledge of how viruses multiply have come mainl from intensive investigations of the bacteriophage Most bacteriophages seem to consist of a core o desoxyribonucleic acid with a protein overcoat, and one of the most exciting recent events was the demonstration by Hershey and Chase[16] that when bacteriophages infect their bacterial hosts the virus nucle acid enters the host cell while the greater part o the virus protein remains outside the bacteriu Evidently the chief function of the protein is to ac as a vehicle for the all-important nucleic acid, and once the protein has transported the nucleic acid t a new host bacterium, it can be dispensed with in th following stages of multiplication

At the moment, however, progress towards a bette understanding of virus multiplication seems to b coming mainly from studies of tobacco mosaic virus In this virus, the rod-shaped particles have a core o ribonucleic acid surrounded by a protein shell, an recently Fraenkel-Conrat and Williams[17] foun that the nucleic acid and protein could be separate from one another and then reconstituted Th reconstitution was shown convincingly by electro microscopy, and it was also found that some of th infectivity of the original preparation was restored Lately, Fraenkel-Conrat[18] recorded that when th nucleic acid of one strain of tobacco mosaic virus wa mixed with the protein of a second strain, recon stitution again occurred The reconstituted viru behaved serologically like the strain from which th protein was derived, but when the reconstituted viru multiplied, its progeny showed all the characters of th strain from which the nucleic acid was derived Fraenkel-Conrat also noticed some infectivit associated with the nucleic acid alone, this infectivit was unstable and it was susceptible to the action of th enzyme ribonuclease Both these characters differenti ate this infective behaviour from that of the intac virus and Fraenkel-Conrat suggested that it migh be a property of the nucleic acid itself Now, Giere and Schramm[19] have produced strong evidence tha the ribonucleic acid of tobacco-mosaic virus may b infective alone The basis of their evidence is that pure preparation of ribonucleic acid from which th protein was removed was still infective "th infectivity of the ribonucleic acid preparation is about 2 per cent of that of the native virus" Th infectivity of the nucleic acid was not neutralised b antiserum to the whole virus, since antibody effective against the protein part of the virus onl Like Fraenkel-Conrat, Gierer and Schra orm is interfered with, and a type of fibrin produced hose morphology differs from the classical fibrillar form may therefore be concluded that the occlusive material, ough it may contain platelets, is composed mainly of substance that could be compact fibrin Further riticism of the platelet composition of the occlusive ass is offered independently by Fisher and Creed (1955), who, using the staining technique of Glynn and Loewi 1952), believe the occlusive masses are "fibrinoid"

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Primary damage to the endothelium as the cause of he coagulum, suggested first by Altschule (1942), eemed to Engel et al (1947) and Trobaugh et al (1946) to e confirmed by their findings of endothelial swelling and roliferation in vessels without thrombi Similar changes were found in two cases by Fitzgerald et al (1947), who are not quite prepared to say that this endothelial change s the precursor of the coagulation Others have failed o find these endothelial changes (Baehr et al 1936, Bernheim 1943, Singer et al 1947) In the present case the overwhelming majority of non-thrombosed vessels appear normal

A different prethrombotic lesion is described by Gore (1950) and by Meacham et al (1951) a segmental accumulation of hyaline material lying below the intact endothelium Meacham et al suggest that increase in the amount of this material eventuates in the intraluminal mass, but they do not record any extension of the so called hyaline material outwards into the other structures of the vessel wall A similar focus of fibrinoid change in the vessel wall is thought by Allen (1951) to be the site of initiation of the thrombi, and he suggests that this disease, which he calls generalised arteriolocapillary thrombonecrosis, may be due to allergy

The hypothesis of primary damage to the terminal portion of the vascular tree has been favourably reviewed by March (1954), and in the present case a few vessels contained deposits of subendothelial material staining like fibrin and apparently in continuity with the intraluminal coagulum This hypothesis, however, is open to two criticisms

(1) "Thrombi" were commonly seen in vessels which otherwise appeared normal, but the "thrombi" may have propagated themselves along the vessel from a small focal point of mural damage

(2) Deposition of subendothelial fibrin, with a curious absence of accompanying thrombosis within the lumen, takes place in the three forms of fibrinous vasculosis described by Lendrum (1955) stagnant, hypertensive, and hyperergic

Thus some other factor, over and above the deposition of subendothelial fibrin, seems to be involved in the formation of the intraluminal thrombosis in this disease

The hyperergic basis of disseminated capillary fibrin thrombi is strongly supported by Pagel (1949, 1951), who suggests that the antigens act on the vessel walls, and the possibility that thrombotic thrombocytopenic purpura should be included in the group of diseases studied by Pagel (dermatomyositis and disseminated lupus erythematosus) is strengthened by Symmers and Gillett's (1951) description of a case showing features of lupus erythematosus, polyarteritis nodosa, and thrombotic thrombocytopenic purpura Moreover, Laszlo et al (1955) have published a case in which the features of thrombotic thrombocytopenic purpura were associated with disseminated lupus erythematosus Compared with polyarteritis nodosa, drug-induced arteritis, and disseminated lupus erythematosus, there is certainly little cellular reaction around the involved vessels of thrombotic thrombocytopenic purpura, but it is probably unjustifiable to make too much of this distinction This interpretation of the histological appearances, which suggest a hyperergic reaction of the vessel wall, is accepted by Dameshek (1955), who believes that this disease is a triple auto immune disorder affecting three tissues red cells, platelets, and small blood-vessels

It may be concluded that, in thrombotic thrombocytopenic purpura, there is some factor at work which determines the site of the "thrombi" in the precapillary arterioles, that the "thrombi" are largely composed of compact fibrin, and that there is some upset of the permeability of the vessels at these sites to explain the occasional presence of fibrin within the wall

From the clinical point of view it is rather galling to realise that, once again, this disease was unrecognised during life because of lack of knowledge of an established clinical entity We feel that this is the factor which maintains thrombotic thrombocytopenic purpura in its present position as a "rare" disease We wonder how many cases of "cerebral thrombosis," &c, have also had pyrexia, anæmia with slight icterus, and perhaps a few petechiæ We reiterate the suggestion of Symmers (1952) that either corticotrophin or cortisone might be used in the treatment of future cases Symmers (1952) gives an admirable survey of treatment used in the past

Summary

A case of thrombotic thrombocytopenic purpura is described

The staining reactions of the "thrombi" are compared with those of platelets and of naturally occurring fibrin. The results indicate a close similarity of the "thrombi" to fibrin rather than to platelets

The following conclusions are reached

(1) Some factor determines the site of the "thrombi" in the precapillary arterioles

(2) The "thrombi" are composed largely of compact fibrin

(3) Altered permeability of the vessels at these sites explains the occasional presence of fibrin within the wall

We wish to thank Prof D F Cappell for valuable assistance in the earlier part of this work, Prof A C Lendrum for his aid in Dundee, where the work was continued, Dr D K. Adams, in whose wards the patient was first seen, for encouragement and advice, and Dr H E Hutchison for interpreting the appearances of the biopsy specimen of bone marrow

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considerable, amounting, in terms of money, labour, and materials, to a value about half of what is spent by the government Important assistance has also been given by the United States government and the Ford Foundation, amounting to a quarter of the total cost Since its inception the main scheme has been supplemented by a preparatory one which, at the expense of restricting objectives, will provide some of the benefits for a greater number of people

For doctors, however, a noteworthy feature of the project is its comprehensiveness, which exceeds that of community development programmes in other countries Speaking at the conference, Dr JOHN B GRANT, of the Rockefeller Foundation, who is now professor of public health and medical care at the University of Puerto Rico, outlined principles for the development of backward areas

> The success of an attempt to eliminate poverty, disease, or ignorance depends, he said, on how far it is undertaken as part of "multi-purpose community development," and the project must be within the framework of a national plan for industry as well as welfare The programme must be based on practical economics—e g, on whether the number of doctors the country can afford is one per 1000 of the population, or one per 10,000, and whether the number of hospital beds is four per 1000 or only one per 1000 Each level of government—national, State, and district—requires, in Dr GRANT's view, a development organisation with coordinating and planning functions, designed to *act as a catalyst, not as an executive agency* The success of technical assistance depends on the degree to which it can mobilise voluntary self-help, and this in turn depends on the extent to which consciousness of local needs is generated in the community through its village councils The unit of organisation for community development must, he believes, be technically self-contained, providing its own services, supplies, and supervision empirically it has been found that the population it serves should not be less than 200,000 or more than 500,000, *and its area should coincide* with that of a previously existing administrative unit of government, with which it can be integrated No less important are the steps that must be taken to ensure local *initiation* of the plan according to the determined needs and it is similarly essential to provide for continuous representation from the village level to the highest organs of the State Finally, *a development programme must* provide for the training of personnel and for independent assessment and criticism of the project as a whole

Concluding his survey, Dr GRANT said that, by its adherence to essential precepts, the present plan seems to have placed India well in advance of other countries which have undertaken community development

But though the technique of village development, as he said, has been carefully studied and many schemes have been successful, it remains to be seen how such techniques will bear fruit on the historic soil of India The difficulties are immense, and it is not surprising that one can find, dotted about India, defunct small-scale schemes, with and without Evangelical backgrounds The Indian village has a remarkable capacity for absorbing (quite amiably) outside endeavour, and for having absolutely nothing to show for it ten years later Continuity of policy and adequate funds will thus be essential if the present project is to succeed and if India is to show how democratic methods can be applied in a field too often the preserve of the authoritarian theorist A five-year plan is a beginning, but what are five years among so many hundreds? If the slip back to old habits is to be avoided, the government must be prepared to extend the work in each block for a second, third, and even fourth five year period At present its exact intentions are not clear, but it evidently expects to cover the entire country with its community development programme during the second five-year plan (1956–57 to 1960–61)[1] This is a formidable task indeed, and it remains to be seen what will be the effects of the changing attitude of India towards American aid, and of the present internal unrest Certainly the financial burden will fall heavily on a country as poor as India, and we of the West ought to be prepared individually and nationally to do what we can to help For this vast and well-conceived experiment must not be allowed to fail for want of aid that we are able to offer

Annotations

TUBERCULOSIS IN THE TROPICS

THE waning of *tuberculosis* in Britain and other countries well supplied with hospital and other resources is not yet evident in less favoured areas, and there is no certainty that the methods which are proving effective here will be equally effective in different cultural, environmental, epidemiological, *and nutritional* conditions Even the causal bacillus may not be the one we know As Dr M G Candau, director general of W H O, remarks in his latest annual report[2] "There is increasing evidence that mycobacteria isolated from patients in tropical *areas* may differ, in type and in other particulars, from those which are defined at present as tubercle bacilli" Chemotherapy, without admission to hospital, may help to control tuberculosis in lands where the disease is rife, but we are not yet certain that it will, and meanwhile its use with imperfect supervision may be actually increasing the load of infection in communities by prolonging the lives of patients without rendering them non infective, and by promoting the spread of drug-resistant organisms

An important step *to solve* these problems has now been taken by W H O in conjunction with the Medical Research Council and the Indian Council for Medical Research An international research unit, selected by the M R C, is to conduct a five year survey *in* Madras In the first stage, which may take two years or more, a group of patients treated by various drug régime without being admitted to hospital will be studied for sputum conversion and compared with a reference group admitted to hospital If this stage goes well a second stage—probably an investigation of the community effects of widespread domiciliary chemotherapy—will be considered

Not the least important aspect of this venture may be the opportunity to train counterpart personnel with a view to establishing permanent cadres in clinical and bacteriological research The two vacancies on the unit announced in our advertisement columns this week comprise one for a bacteriologist, and one for a chest physician who will undertake some postgraduate teaching The unit's task will be difficult, but it should prove rewarding

NEW ANALGESICS

IN their continuous search for new analgesics with fewer side effects than those drugs in common use, pharmacologists commonly investigate the effect of variations in the basic molecule of one of the established analgesics Thus, Millar and Stephenson[3] have recently

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[1] The Second Five Year Plan Draft Plan Frame Mahalanobis P C March 17 1955 Indian Statistical Institute, Calcutta 35

[2] The Work of W H O 1955 Annual report of the director general to the World Health Assembly and to the United Nations H M Stationery Office Pp 211 10s

[3] Millar, R A Stephenson R P *Brit J Pharmacol* 1956 11 2

POLIOVIRUS ANTIBODY IN CHILDREN IN NORTHERN IRELAND

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In preparation for field and serological studies of poliomyelitis vaccine in Northern Ireland, investigations were started in the spring of 1955 to find children with little or no antibody to any of the three types of poliovirus

Arrangements were made with the borough and county medical officers of health to take samples of blood from some of the children in nursery or primary schools or from other children of similar age—i e, 2–9 years In addition a few samples of blood were obtained in some areas from children aged 1 year All the samples were selected, in that mothers were invited to give permission for their children to be bled, in the knowledge that they would be *offered* vaccination when a suitable vaccine became available Except the samples taken in September from the Belfast children aged 1 year, the sera were collected between May and July, 1955 *

Materials and Methods

Sera were stored at –20°C and inactivated at 56°C for 30 minutes before testing

Tissue cultures were either first or second pass monkey-kidney cell monolayers in roller tubes The methods described by Melnick (1955) for preparing these cultures were used, except that a simplified apparatus was used for the continuous digestion of monkey kidney and 6–12 oz medical flat bottles were substituted for Roux bottles in the preparation of second passage cells Lactalbumen medium (Melnick 1955) was used both for cultures and as a diluent for sera and virus suspensions

Virus strains, obtained from Dr A. Goffe, of the Wellcome Research Laboratories, were type 1, Brunhilde, type 2, Y-SK, and type 3, Leon

Tissue-culture Neutralisation Test—Sera were tested at a 1 in 4 dilution against an estimated 100 TCD$_{50}$ of virus Equal volumes of a 1 in 2 dilution of sera and virus suspensions containing 200 TCD$_{50}$ were mixed and allowed to stand at room-temperature for one hour Culture tubes containing 1 5 ml of medium were then inoculated with 0 5 ml of the virus serum mixtures and placed in roller drums at 37°C Two tubes were used in testing each serum against each type of virus Cultures were examined on the sixth day Only those sera which protected both duplicate tubes were considered positive In all the tests the virus suspensions and known positive control sera were titrated

Results

The detailed results of the survey are shown in table I, and figs 1 and 2 We do not claim that these results represent the serological pattern in all children of a particular age group in Northern Ireland.

Table I shows that antibody to each of the three types of poliovirus was present in children in all the areas studied In the Belfast sample the rates among children in private schools were much lower than in nursery and primary-school children—e g, only 1 of 25 (4%) in the former group had antibody to all three types of virus, compared with 83 of 128 (64 8%) of the nursery and primary school children (Social factors, which may be related to the antibody patterns found in the children in this survey, are being investigated by Dr E M Backett, of the department of social medicine, Queen's University, Belfast)

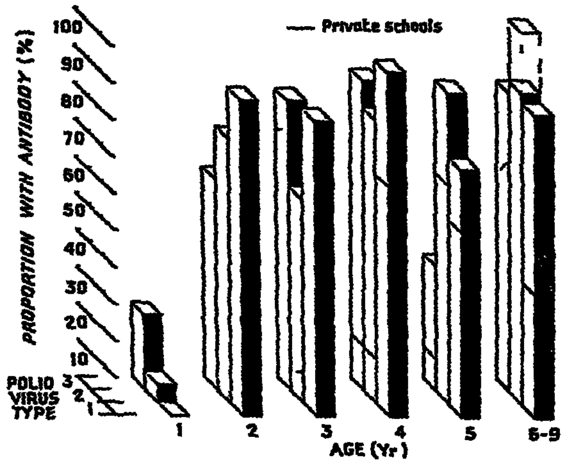

Fig 1—Percentages of children in Belfast and Londonderry boroughs with antibody to three poliovirus types in different age-groups. Interrupted line refers to children from private schools

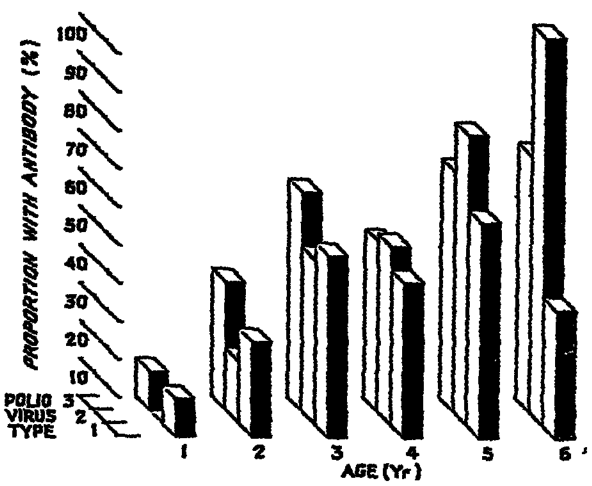

Fig 2—Percentages of children in counties of Northern Ireland with antibody to three poliovirus types in different age-groups

The antibody-rates in the boroughs of Belfast and Londonderry were usually higher than in the counties, of which co Tyrone had the lowest rates (table I)

It was incidentally observed that samples had been obtained from 28 pairs of siblings and from 3 siblings of one family

The results of tests on the sera from the siblings are shown in table II, which shows that both children in 18 pairs of siblings had the same antibody response, and the older child in 10 pairs of siblings had one additional type of antibody In only 1 pair of siblings had the younger child antibody not possessed by the older child This observation is in agreement with the evidence of Fox et al (1955), Brown et al (1954), and others, that when polio-the electron microscope The symptoms of panniculitis —the *peau d'orange* and the paræsthesia—Baker attributes to the tension which arises when normal subcutaneous fat increases rapidly beneath a thickened and largely inextensible corium How the skin changes, and what the change signifies, we do not know The clinical condition is usually self-limiting, and improves if weight is reduced and sodium intake restricted Its appearance at the time of the menopause suggests some hormonal factor, and it may be worth recalling that at other times of rapid change of hormonal activity—pregnancy and the puerperium—there are striking changes in collagen content in, for example, the uterus.

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* Sera from co Armagh, which were received during January, 1956 have not been tested

SPLEENS THAT ARE LEFT

THE indications for the removal of enlarged spleens and the results of the operation are subjects which have provoked much discussion It is often difficult, however, to assess the value of the operation because we do not know what happens to patients with similarly obtrusive viscera who, for one reason or another, retain their spleens The need for this sort of information was pointed out in 1938 by Howells [1] He compared the results in 53 patients with Banti's disease who had their spleens removed with a similar series of 43 patients who retained their spleens, so far as expectation of life and anæmia were concerned, there was no significant difference between the two groups Jordan and Heck,[2] of the Mayo Clinic, have recently tackled this question again and their results are valuable and interesting

They reviewed the records of all patients seen at the clinic between 1930 and 1945 who were diagnosed as Banti's disease or syndrome, splenic anæmia, or congestive splenomegaly, and who did *not* have their spleens removed They concede that it is likely that some of these patients would today be diagnosed as hypersplenism—or more specifically as splenic neutropenia or splenic pancytopenia Nor is it always clear from the records how many of the cases listed as Banti's disease had primary cirrhosis of the liver Jordan and Heck have not attempted to make retrospective diagnoses, they give the details so that the reader can form his own opinion In the selected period there were 98 patients who had been followed for five years or more and whose records were therefore worth studying These 98 patients are divided into three groups in group 1 are 34 patients who declined to follow their physician's advice to have their spleen removed, in group 2 are 28 patients with a definite diagnosis but who for some reason were advised not to have a splenectomy (in 11 the risk was said to be too great, and in 3 the disease was not thought to be sufficiently severe), group 3 includes 36 patients with similar clinical and laboratory findings to the other groups, but for some reason the clinician was not sure about the diagnosis and therefore did not recommend removal of the spleen

The records show that 49 patients (exactly half) survived for more than five years after they were first seen in the clinic, and the five year survival-rate of 50% applies also to each of the three groups separately The list of causes of death shows that more patients in group 1 died of gastro intestinal hæmorrhage than in the other groups, and this reflects current opinion that such bleeding is a good indication for splenectomy For comparison with this group, there have been several reports on survival in Banti's disease after splenectomy, and, on the whole, results are no better For example, Pemberton and Kiernan,[3] also working in the Mayo Clinic, had a five year survival rate of 54 8%, though it has to be remembered that more of their patients had bleeding œsophageal varices than those who kept their spleens Jordan and Heck also found that the only reliable guide to prognosis was the bromsulphalein retention test for liver function, and there was a direct correlation between the degree of retention of the dye and the five-year survival, thus, 72% of the patients with normal excretion of the dye (i e, less than 6% retention after one hour) survived, whereas in those who retained 6–11% of the dye in the blood after one hour, the survival was 54%, and so on Some surprising stories are included to illustrate what may happen to these patients A man of 42 was first seen in 1908 with spleen and liver enlarged to the level of the umbilicus, hæmoglobin 40%, and white cells 8280 per c mm A diagnosis of splenic anæmia was made and no treatment was given In 1950, at the age of 84, he was reported in good health, having survived a gastroenterostomy for obstructing duodenal ulcer at the age of 66, the spleen was found to be enlarged then A physician of 56 was seen in 1935 with spleen enlarged to umbilical level normal hæmoglobin, white cells 3500 per c mm, and platelets reduced to 73,000–90,000 per c mm Splenectomy was advised but declined, and fifteen years later he felt fine and had successfully undergone a prostatectomy

Jordan and Heck reasonably conclude that splenomegaly with hypersplenism is not alone a firm indication for splenectomy The operation should be advised "only for those patients whose symptoms are severe enough to justify the surgical risk, it should not be advised simply to correct some deficiency of the cellular elements With this opinion most physicians who see such cases will agree, the signs, symptoms, or complications in addition to the splenomegaly must be taken into account when deciding whether or not to operate Of course such retrospective surveys can give only a rough comparison because nowadays a much more precise diagnosis is possible, and "Banti's disease or syndrome" is much less of an omnibus diagnosis than it was The leukæmias the reticuloses, and conditions like myelosclerosis can all be distinguished, and the presence of gastro intestinal hæmorrhages with signs of portal hypertension should lead to careful consideration of the value of a portacaval shunt

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[1] Howells, L *Lancet* 1938 i 1320

[2] Jordan, G L jun Heck, F J *Ann Surg* 1956, 143, 29

[3] Pemberton J de J, Kiernan P *Surg Clin N Amer* 1945 25 880

FULL MILITARY HONOURS

SIX years ago we announced,[1] with great regret, that the *Index-Catalogue* of the United States Army Medical Library at Washington would have to end with the eleventh volume of its fourth series This elegiac volume (Mh–Mn) has now appeared, and medical workers in libraries, laboratories, and lecture rooms all over the world will receive it sadly

For the past 35 years the *Index* has been vainly struggling to keep pace with the rising tide of monographs and papers Each year it fell further behind, and by 1950 it had a file of 1¹/₄ million unpublished items which was growing at the rate of 200,000 items a year Publication was at the rate of a volume of 80,000 references every three years By 1958, it was estimated, there would be an unpublished backlog of over 3 million references—more than all the *Index Catalogue* had been able to publish since it first appeared in 1880 A surfeit can be more embarrassing than a deficit, and the Surgeon-General's Library has had to admit defeat, but it is publishing "selected monographic material" from the backlog, and it has revised the form of its monthly *Current List of Medical Literature*, which now includes 100,000 items annually and semi annual cumulations of author and subject indexes The library now also publishes an annual catalogue of monographs and this year the first five year cumulation has appeared

The 3 million references contained in the 58 volumes of the *Index-Catalogue* will be a permanent memorial to ndings suggest that type 1 virus may have been of most importance in producing paralysis in Northern reland in recent years.

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[1] *Lancet* 1950 i 426

It is emphasised that our samples were taken not as part of an epidemiological investigation but to define a population group with low levels of antibody. Nevertheless the epidemiological data from Northern Ireland show that low antibody-rates were found in young children in the areas with the lowest paralysis rates in that age group.

It is generally accepted that the age distribution of paralytic poliomyelitis in any population indicates the state of immunity of the different age groups, and this appears to be the case in Northern Ireland, if the selected samples were representative.

We conclude from the results (tables I and III) that the serological responses to vaccination might best be studied in the 0–4-year age-group in co. Londonderry, co. Fermanagh, or co. Tyrone, and it appears that a similar conclusion might have been reached by examining the paralysis-rates in that age group (table III).

Summary

A survey was made to find a group of children in Northern Ireland with low rates of antibody to the three types of poliovirus, in preparation for serological and field studies with poliomyelitis vaccine.

A high incidence of naturally acquired immunity to all three types of poliovirus occurs at an early age in the children of most areas studied in Northern Ireland. In Belfast the incidence was highest in children attending nursery and primary schools but was lower in children attending private schools. In general there was a lower incidence in the counties, of which co. Tyrone had the lowest rates.

The results of tests on sera from siblings agree with previous observations on the concurrent infections of family associates.

Provided that the groups of children examined were representative of all children in their age group, it appears that the paralysis-rate in a given age group in Northern Ireland is a good index of the immune status of that age group.

TABLE III—COMPARISON OF AVERAGE ANNUAL AGE SPECIFIC PARALYSIS RATE IN CHILDREN AGED 0–4 YEARS (1950–55) AND PERCENTAGE OF THAT AGE GROUP WITH ANTIBODIES

Place	Paralysis rate (per 10,000)	Percentage of sample with antibody to type		
		1	2	3
Belfast Borough	4·47	73·2	55·7	71·1
Londonderry Borough	8·85	61·5	42·3	42·3
Co. Antrim	3·87	56·2	43·7	68·7
„ Armagh	3·68	?	?	?
„ Down	3·28	50·0	50·0	28·6
„ Londonderry *	2·55	43·8	35·7	57·1
„ Fermanagh	1·19	28·6	35·7	53·6
Tyrone	2·31	15·8	10·5	5·3

* Among the notified cases in this age group were 9 in which no information was available about the presence or absence of paralysis. Since some of these children might have had paralysis, the paralysis rate for co. Londonderry may be slightly higher.

We wish to thank all the borough, county, and divisional medical officers in Northern Ireland for assistance in collecting the samples of blood and for providing epidemiological data; and the medical superintendent and staff of the Northern Ireland Fever Hospital for data on Belfast cases. Before this laboratory was equipped, sera were kindly tested by Dr. W. Wood, of Glaxo Laboratories Ltd., and at the Virus Reference Laboratory, Colindale; we are most grateful to them for their assistance. This investigation was aided by grants from the National Fund for Poliomyelitis Research and the Northern Ireland Hospitals' Authority. Much of the basic equipment for virus research in the department of microbiology of the Queen's University, Belfast, was provided by a grant from the Rockefeller Foundation.

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Melnick, J. L. (1955) *Ibid.* p. 754.

ACUTE MYOCARDIAL TOXOPLASMOSIS

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TEES SIDE HOSPITALS

TOXOPLASMOSIS, both congenital and acquired, is still regarded as a rarity. Most of the cases reported in this country have been of the congenital variety in children. Paulley et al. (1954) reported 3 cases of myocardial toxoplasmosis in adults, in which the diagnosis was based on a positive dye test and a positive complement-fixation test. They believed their cases to be chronic acquired myocardial toxoplasmosis.

The acquired form has also been known to take an acute course resembling typhus (Pinkerton and Henderson 1941), often with electrocardiographic changes.

Siim (1951) has reported a more benign syndrome associated with generalised lymphadenopathy and resembling glandular fever. Cathie (1954) has isolated toxoplasma from such cases.

We report here an acute fatal case, predominantly myocardial, in an adult.

Case-report

A male police detective, aged 30, was admitted to hospital on Sept. 21, 1954, complaining of bronchial symptoms of two weeks' duration. For the previous two months he had had vague malaise associated with a persistent head cold. The cough was productive of purulent sputum, but there had been no hæmoptysis. Before admission penicillin and erythromycin had been prescribed by the family doctor. There was no history of any previous illness. In his youth the patient had worked on a farm but he for many years had not been associated with farming. His family history was unremarkable.

On admission his temperature was 101°F, and he had gross tachycardia (pulse rate 128) with a systolic murmur at the apex of the heart. Blood pressure 85/60 mm. Hg. There were signs of acute pulmonary œdema but no evidence of congestive heart failure. The other systems were normal. Radiography of the chest showed severe pulmonary congestion with moderate enlargement of the heart to the left. Electrocardiography showed a left bundle branch block. A blood-count showed Hb 96%, and white cells 9700 per c.mm. (differential count normal).

Treatment and course.—After investigation it was considered that he had a myocarditis of undetermined origin, possibly of the Fiedler type. The tachycardia was only partially controlled by digoxin 1 mg. daily. Further courses of penicillin and aureomycin were given. Theophylline mono ethanolamine and 'Neptal' relieved the pulmonary symptoms a little. Further electrocardiography during the illness showed left bundle branch block. The patient's temperature was undulating, rising to 102°F. The patient became very confused. Examination of the cerebrospinal fluid on Nov. 8, 1954, showed cells less than 1 per c.mm., protein 15 mg. per 100 ml., no increased amount of globulin, and a negative Wassermann reaction. The dye test for toxoplasmosis on Oct. 7, 1954, was positive 1 : 32 and the complement fixation test positive 1 : 8. Dr. I. A. B. Cathie (personal communication) considered these results significant and advised the administration of pyrimethamine and a sulpha drug. A course of pyrimethamine 50 mg. daily and sulphamethazine 1 g. six-hourly was started on Oct. 29, 1954, and continued for seven days, but there was no response to treatment. By Nov. 10, 1954, sacral œdema and enlargement of the liver had developed. The mental confusion was now more obvious. A week before death a transient erythema appeared on the trunk, with a few petechial hæmorrhages on the left lower chest. During this period

Special Articles

TYPES OF STEALING

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THIS paper describes an attempt to validate, by statistical methods, some of the concepts used by psychiatrists in their reports to juvenile courts The hypothesis to be tested was that "syndromes" of stealing can be recognised, each of which is shown by a boy with a particular predisposition and each of which has a characteristic age of onset and course A basic assumption was that in children the motives for stealing are largely unconscious and that, even where there are other superficial factors, these unconscious motives will determine the form of the theft In other words, whether or not a boy steals may be determined by training, opportunity and so on , but if he does steal, then the way in which he steals will reflect his unconscious drives These drives are not necessarily neurotic or abnormal simply because they are unconscious On the other hand, in some boys the drive is undoubtedly neurotic

Material and Methods

The study was made in three parts The first, involving about 200 boys, was descriptive, for the purpose of clarifying concepts Information on the next 100 boys was quantified and allowed a further modification of ideas The final study, on 200 boys, is the one reported here

These 200 boys, so far as was administratively possible, were consecutive admissions to Stamford House remand home, who had been charged with theft, and remanded *for psychiatric report* *No control group was needed, for* types within this sample are compared with each other and not with an assumed normality As about a fifth of the boys who appear in the London courts are referred for psychiatric examination , as there are six courts with changing benches , and as magistrates differ on the points which call for a report, the sample is more representative than might be supposed It is certainly more representative than the samples drawn from child *guidance clinics*

The offence with which the boy was charged was placed in one of five categories, which were derived from descriptions in the literature modified by the first two parts of the study Various items of information about the boy were recorded, and the type of offence was then compared with this information

Marauding Offences

These are carried out by three or more boys They are unplanned or "semi-planned" Semi-planned means that the boys have not formally agreed to carry out a particular theft, but if the opportunity arises (such as an open window) they take it for granted that they will pick up whatever is accessible They may be wandering around a big store, not wanting anything in particular, but stealing attractive goods which they often throw away again afterwards There is often a considerable and deliberately chosen risk in these escapades, but this element *did not have to* be present for the offence to be classified as marauding

Proving Offences

This name was chosen because these offences are usually attempts to prove one's toughness or manhood They were thought to be more in the nature of self-reassurance than an attempt to achieve "peer status" as in the marauding offences These offences were arranged in the following subdivisions

(*a*) Breaking and entering alone (but not including the "secondary" offence defined below) *These offences, it was* later decided, should not have been included among the proving offences

(*b*) Any form of theft carried out alone *if the stolen* goods are exhibited, if a symbol of dominance is stolen (such as a gun, or a racing bike if the boy uses it in an ostentatious way), or if the boy is obviously showing off to *one* less experienced or younger

(*c*) Taking and driving away a motor vehicle

Comforting Offences

These offences fell into two groups

(*a*) Stealing from parents
(*b*) Impulsive pilfering alone or with one other boy

Secondary Offences

Planned theft of any sort, alone or with others of similar type, with a definite idea of what can be stolen, with reasonable precautions against detection

Other Offences

Any offence which could not be placed in one of the above categories, including doubtful cases Examples were—stealing under instructions from father, stealing food after having run away from home, and stealing coke to help a sick mother

The following information was collected about the boy his age , his height, weight physical condition sexual development, and intelligence (all transformed into standard deviations) , the socio economic level of his home , the age of his first known theft , whether he had stolen from home at any time , details of separation from mother before the age of 5 , length of breast feeding, and—an essential feature—his parents' attitude towards him

The *information* was *collected* from an interview with the boy, the probation officer's report, the London County Council education department's records including a school report, the case record or a report from any child guidance clinic the boy attended, and *a full social* history taken by the psychiatric social worker at Stamford *House*, Mrs McConville *The parent's* attitude was assessed independently by the probation officer, by the psychiatric social worker, and by myself It was not always possible to make three assessments but unle there were two in agreement on a given variable, the attitude was recorded as unknown On democracy, acceptance, and indulgence—the definitions of these terms being derived from the paper by Baldwin, Kalhorn and Breese (1945) working with the Fels scale—the *attitudes* were recorded as high, medium, low, inconsistent, or "not applicable" Each parent was rated independently of the other

Discussion

Many writers, from Healy (1915) onwards, have pointed out that delinquents cannot be considered a homogeneous group, though some speak of "the delinquent" as if all young offenders were hardened *antisocial* characters Friedlander (1947) takes this latter view, while the Gluecks (1950) finally conclude that "the delinquent group is a composite of several sub types" The proponents of the "typical young delinquent" school of thought are often psychiatrists working in a clinic, and it is reasonable to suppose that the material they see there is highly selected, and consists largely of children with whom simpler methods have consistently failed

TABLE I—AGE GROUPS OF PRESENT *OFFENCES*

Type of offence	Age (years)			Total
	8–11	12–14	15–17	
Marauding	20	30	15	65
Proving	1	6	18	25
Comforting	13	22	18	53
Secondary	0	6	16	22
Other	3	16	16	35
Total	*37*	*80*	83	200

$\chi^2 = 30\ 54$ n = 8 P < 0 001

ans If this is so, it will be useful in preventing and ring transfusion thrombophlebitis and will provide a ife way of nourishing patients with intravenous hyper-nic dextrose Further evidence is now being sought, nd an attempt will be made to determine the lowest oncentration of the steroid which will prove reliable for his purpose

These three patients were under the care of Dr J F Stokes t University College Hospital I am grateful to him for advice nd encouragement, and to Dr Spector for the pathology eports

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A POLAK
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Medical Societies

ROYAL SOCIETY OF MEDICINE

Function of the Mental Hospital

THE section of psychiatry met on April 10, with Dr W D NICOL, the president, in the chair, to discuss the Changing Conception of the Function of the Mental Hospital

Dr A R MAY outlined the changing pattern of psychiatric treatment by comparing two groups of patients admitted to Netherne Hospital in two three-year periods, 1935–37 and 1945–48 He stressed that results must be assessed against the changing background due to altered attitudes to mental illness as a whole In the hospital this was shown by the number of patients on parole, which was 5% in 1932 and 60% in 1955 Outside the hospital the running of outpatient clinics by hospital staff resulted in the admission of earlier and milder cases with a correspondingly better prognosis

The use of different physical methods of treatment had varied since their introduction on a large scale in 1942 Thus patients treated by prolonged narcosis numbered 175 in 1945, but only 19 in 1955 The number of patients receiving electroconvulsive therapy (E C T) rose from 380 in 1942 to 1216 out of 1900 patients in 1955 50 leucotomy operations were performed in 1942, 79 in 1949, and 19 in 1955 Deep insulin treatment was used in 133 patients in 1951, but in only 95 in 1955 In 1955 the number of patients receiving paraldehyde averaged 122, and sodium amylobarbitone 106, and there had been a sharp increase in the use of chlorpromazine

The method of sampling was chosen to produce numerically comparable groups for the two three year periods every other consecutive male and female admission was used in the period 1935–37, and every sixth admission in the second period covering 1945–48 600 cases fell into each of the two sample groups, and a comparison was made between patients with schizophrenia or affective psychosis treated without (sample 1) and treated with (sample 2) physical treatments Five-year follow-up was achieved in about 80% In sample 1 there were 173 schizophrenics and 120 with affective psychosis, in sample 2 the figures were 125 and 83 Although the total death-rate fell, deaths due to exhaustion and suicide remained fairly constant

The number of symptoms among patients with schizophrenia and affective disorders was significantly higher in sample 1 36 4% of schizophrenics were hallucinated, compared with only 14 4% of sample 2 Among patients with affective disorders there were major symptoms in addition to depression or mania in 62 5% of sample 1, but only 45 7% of sample 2 These figures suggested that the increase in admissions during the second period was largely due to the admission of milder cases

Hallucinated and non-hallucinated schizophrenics and complicated and uncomplicated affective states were examined separately Among hallucinated schizophrenics there were no significant differences in improvement or recovery-rate between sample 1 and sample 2 Among non-hallucinated schizophrenics significantly more patients in sample 2 were at home after one and five years, although among these too the proportion of recoveries remained about the same The evidence suggested that physical methods of treatment had increased the number of patients discharged and reduced the total time spent in hospital, without however increasing the proportion of recoveries

Among patients with affective psychoses, those with more than one main symptom showed significant improvement in the treated sample on all items of comparison Here the greatly increased discharge and recovery rates might be attributed to the advent of physical treatments, which however did not materially improve the prognosis of patients whose only main symptom was either depression or mania

Dr MAY concluded that physical treatments appeared to have a pronounced effect in certain cases of schizophrenia and affective disorders, but results should be evaluated in relation to parallel improvement in the therapeutic atmosphere of the hospital There was no definite evidence as to which factor was causal and which consequential, but together these constituted the significant alteration in the pattern of care of the psychiatric patient during the past twenty years

Mr M S FOLKARD gave an account of a sociological investigation into the origin, prevention, and treatment of aggressive behaviour in a ward of 50 disturbed female patients

While the investigation was being conducted in the early part of 1955, considerable changes were taking place in therapeutic policy and ward organisation Patients were increasingly engaged in occupational and social activities, and more attention was given to individual patients, more liberal procedures were introduced for deviant behaviour previously controlled by rigid discipline and frequent sedation and E C T Ten weeks were spent making observations on the ward, the rôle of a relatively non-participant observer could not be maintained because the observer's presence itself tended to improve patients' behaviour

During the investigation two hundred and ninety eight acts of aggression were committed by 32 patients, a hundred and five of these created only a mild disturbance Statistical analysis showed that poorer cooperation with nursing staff and lack of parole were characteristics associated with aggressive patients Of 14 very aggressive patients 12 were unmarried, a higher proportion of patients who had been in hospital six or more years were aggressive There were more good workers among non aggressive patients, perhaps because employment provided an outlet Of 15 patients who had been leucotomised, 7 were still fairly aggressive and 5 very aggressive Of 23 patients who had received up to fifty electrical treatments 12 were aggressive, compared with 20 out of 27 who had received more than fifty treatments, suggesting that electrical treatment played no part in its prevention More acts of aggression occurred at meal times than in any other single situation

Ninety-one aggressive acts were related to patient-staff interaction, where personality differences among the staff were found to be important factors Eighty-eight aggressive acts arose from patient-patient interaction, mostly related to food, drink, sweets, and cigarettes, and response to interference and abuse A hundred and eighty aggressive acts lasted less than ten minutes, eighty-seven lasted between ten minutes and an hour, and thirty-one more than a hour

TABLE VI—TYPE OF THEFT AND SOCIO-ECONOMIC LEVEL ACCORDING TO FATHER'S WORK

Types of offence	Professional and skilled	Semi-skilled	Unskilled	Institution	Total
Marauding	12	18	35	0	65
Proving	10	8	6	1	25
Comforting	12	20	19	2	53
Secondary	3	7	8	4	22
Other	7	11	16	1	35
Total	44	64	84	8	200

$\chi^2 = 25.34$ n = 12 P < 0.015

in the upper levels, while marauding thefts tend to occur in the lower levels. The association between economic level and proving thefts is largely due to the fact that car-stealing is commoner in boys from upper levels (Wattenberg and Balistrieri 1952). The link between marauding stealing and underprivileged areas confirms observations of many writers (Mays 1954) that this type of offence is normal behaviour in boys of that class.

Study of physical condition, height, and weight did not yield clear-cut information, though there were hints that marauders have a high proportion of short boys.

The statistical findings were elaborated by study of boys making up each type. Most of those in the comforting group were obviously unhappy, but a distinction appeared between the two subtypes: the parents of those who stole from home seemed to be actively hostile, whereas the parents of those who stole impulsively and alone, from outside the home, were, although rejecting, casual in their attitude. In this latter group there were also three mothers whose earlier good relationship with the boy had been disturbed by illness and several parents who partially rejected the boy after the birth of a sibling.

The secondary stealers showed a family background of emotional instability and insecurity, and over a third of them had a sharp sense of grievance. They were impulsive and immature.

The background of the provers showed psychosexual difficulties usually due to a possessive, over-protective mother. The subtype which was originally placed in this group—the boys who committed breaking and entering offences alone—was found to be composed mainly of severely disturbed boys with no common problem.

No follow-up study was undertaken, but earlier studies based on similar concepts (Healy and Bronner 1939, Glueck and Glueck 1940) show that most young offenders reform. It seems likely that comforters, who begin early in life, continue to steal, whereas marauders give it up early in adolescence. Provers, who begin in adolescence, continue until early adult life. All this would be expected from the emotional drives which give rise to the offences. The secondary stealers are apparently rejected boys grown up, and they form the bulk of adult criminals. But to describe them as "typical" young delinquents is incorrect, for they are in the minority among juvenile delinquents.

Delinquents should not be thought of as a homogeneous group, and the present findings suggest inferences about the motivations which should be a guide towards treatment. Ideally, every offender should have treatment bespoke to his own requirements, but this is seldom practicable, and magistrates or others have to make a broad decision based on general impressions. With this in view I should suggest that boys who commit comforting offences need affection and not further deprivation, for this is probably the cause of the theft. Proving offenders are humiliated and unsure of themselves: they need reassurance and not further authoritarianism. Marauders, on the other hand, seem to be psychologically normal. They need alternative outlets for their drive and gang tendencies.

Summary

A statistical and clinical study of 200 young
thieves shows a firm association between pare
rejection and stealing from home, and a more cor
relation between unhappiness and impulsive soli
pilfering away from home. Boys who have been separ
from their parents early tend to commit these typ
offence.

Gang depredations begin in the prepubertal years a
are not associated with any clear pathogenic pare
attitude, but with a lower socio-economic background

Stealing, involving any form of bravado, such as th
of motor vehicles, is associated with adolescence. T
boy usually has a protective and affectionate mot
and an authoritarian father.

The rejected child has a poor prognosis and is lik
to become more deliberate in his offences. The oth
tend to reform, but their delinquent years cover so
what different age ranges.

Broad lines of treatment based on these findings a
suggested.

I carried out this research, under the supervision of Pr
A J Lewis, as part of the requirements for the PH D Lo

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ADDICTION TO METHYLATED SPIRIT

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THE special feature of the addiction dealt with he
is that the addicts drink products usually regarded
undrinkable.

Methylated spirit and surgical spirit, of which meth
lated spirit is the main constituent, are the more co
monly used "beverages" of these drinkers. Ma
however, develop skill in recovering methylated sp
from various commercial products. Thus boot pol
shellac, paints, and liquid brass polish have been t
sources for our patients. The brass polish is sometim
taken neat. Two of our patients report having consum
embalming-spirit.

All our patients addicted to methylated spirit h
been people whose original preference was for the usu
alcoholic drinks presumed to contain only ethyl alcohol
(ethanol), and they began to drink methylated spirit for
an exclusively economic reason.

Addiction to alcohol is always to ethyl alcohol, never
to methyl alcohol or the higher alcohols—amyl, butyl

ndesirable. It has not yet been used for epistaxis in dults since a suitable occasion has not arisen but its eliability in children is sufficiently encouraging to ustify trial in older patients

The balloon, made from latex rubber, has a capacity f about 30 ml, and is inflated by means of a fine tube ome 7 in long running to a standard 'Record' syringe nount The balloon is kept blown up by fitting a small ubber cap over the mount The introducer is basically a $8^1/_2$-in stainless-steel tube open on one side with a ring andle near the proximal end One end has a narrow rough in which the stretched tip of the balloon can be etained The other has a similar notch to grip the balloon tubing (fig 1) To assemble for use, the tip of the balloon is stretched until it slips into the trough, where it is held by virtue of its own expansion when the tension is released. The deflated balloon and tube are laid in the body of the introducer, the latter being retained in position by the notch provided (fig 2)

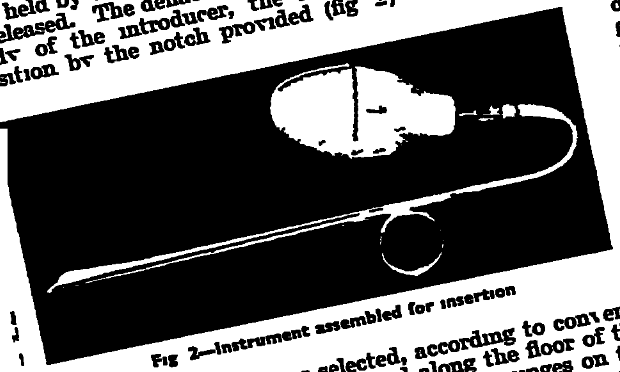

Fig 2—Instrument assembled for insertion

Either nasal passage is selected, according to convenience, and the introducer is passed along the floor of the nose, close to the septum, until the tip impinges on the posterior wall of the nasopharynx When the ring of the introducer lies vertically downwards the balloon will face the roof of the postnasal space and is inflated by a steady, single, complete squeeze of the 20-ml rubber ball fig 3) The tube may be kinked while a cross-action spring-clip is temporarily applied to prevent escape of air While steady traction is exerted on the tube the introducer, which has hitherto prevented the balloon slipping downwards into the oropharynx is withdrawn from the nose The tube is then strapped to the opposite cheek, still under slight tension, across the fulcrum of the columella, and the spring-clip, if desired, may be discarded after the nozzle of the tube has been occluded by a rubber cap Removal of the balloon is easily effected by allowing it to deflate

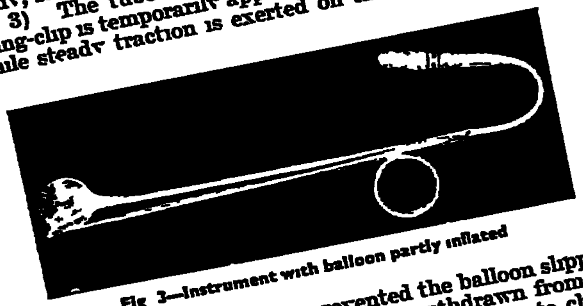

Fig 3—Instrument with balloon partly inflated

20 ml has proved a satisfactory amount of air for the balloon in children under 12 years of age In adults 30 ml would probably suffice, and a 30-ml bulb may be included in the outfit In all 11 cases introduction and emoval have been tolerated with little protest and have aused no difficulty to house-surgeons The balloon has generally been left in overnight and no ill effect, such as otitis media, has ensued

The apparatus, obtainable from Messrs Down Bros and Mayer & Phelps Ltd may be conveniently sealed in an airtight tin, together with a formalin tablet, the balloon having been dusted with glove-powder and wrapped in lint Before use the balloon and introducer may be rinsed in normal saline

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Reviews of Books

Biology of Senescence

ALEX COMFORT, M B Camb London Routledge & Kegan Paul 1956 Pp 257 25s

ATTEMPTS to explain the process of senescence have never passed the stage of multiple hypotheses, and this, as Dr Comfort shows, is first because the basic facts are not known even of the distribution of senescence in animal populations, or of its dependence upon growth, reproductive activity, or ecology Secondly we may have been looking for the wrong thing for it seems very probable that there is no single factor, hormonal or other, whose presence or absence determines senescence

Senescence is a potential part of the life-cycle of many vertebrates, though it is rarely reached in the wild state, but some fish seem to show no evidence of it, and it may be, as Bidder thought, related to the migration of vertebrates to dry land, when a specific size, and therefore cessation of growth, became a factor in the survival of swiftly moving animals It is perhaps only because of the development of speech and the social habits of man that he has come to live commonly into the senescent period, for in a primitive social community a few elder statesmen who form the teachers, judges, and historians of the group are advantageous—perhaps more so than in our present society of small family groups—and may thus escape the pressure of selection in the post reproductive age

Dr Comfort discusses all these questions and many more He does not claim to answer the fascinating questions that he asks, but leans towards the view that 'many organisms are provided by evolutionary selection with a 'programme' of development and function which is directional and finite" As the programme runs out, the organism develops "a continuously self-aggravating disequilibrium" and mechanisms of homœostasis begin to fail Although he concludes that "all theories of senescence are at present based on unwarrantable assumptions in the absence of concrete answers to essential questions of fact," this does not preclude an interesting discussion of the manner in which the period of adult vigour might be prolonged and senility postponed in man, and on the ways in which further biological research might be directed towards relieving some of the present ignorance Although enlivened by some attractive similes and concepts and an occasional quotation from Belloc's lighter poetry, this is a serious work and not easy to read but those who are interested will find it rewarding, and it should be intelligible to any doctor, even if he has forgotten much of his early biological training This book also contains an assemblage of biological facts and references which must be of unique importance to serious students of the subject

Veterinary Parasitology

GEOFFREY LAPAGE M D M SC late lecturer in animal pathology and pathologist to the Institute of Animal Pathology University of Cambridge Edinburgh Oliver & Boyd 1956 Pp 964 £3 3s

THE control of parasitic infections in farm stock has received increasing attention in recent years but it would be difficult to find a book in the English language which covers the subject in such an authoritative and comprehensive way as does this

Dr Lapage s book is divided into four parts which embrace a study of the Nemahelminthes Platyhelminthes Arthropoda, and Protozoa and he has given a zoological description of the phyla to which the various species belong This is followed by detailed consideration of the individual species including its life history effects on its hosts symptoms of disease that may be caused and treatment and methods of control There is little in the subject matter which calls for criticism In his excellent description of liver fluke disease Dr Lapage remarks that acute liver rot may possibly be commoner in sheep than is generally supposed—a statement with which those who have examined numbers of sheep livers in slaughterhouses will fully agree In dealing with the life history of *Tænia saginata* he might have mentioned the observation of Götzsche, Silverman, and others that seagulls may be responsible for of this hospital and that addicts to alcohol now form a majority of our male admissions from July 1, 1954, to June 30, 1955, 199 addicts to alcohol were admitted in the total of 320 male admissions

Case-reports

At the time of writing our inpatients include 8 drinkers of methylated spirit (all males) We append some points from the histories of each All are voluntary patients except case 2

CASE 1—An unmarried labourer, aged 51, of no fixed abode, had been addicted to alcohol for 21 years and to methylated spirit for $19^1/_2$ years, and had 24 convictions for drunkenness He was quiet, well behaved, above average intelligence, sociable and a good worker in hospital, and had no psychotic features

CASE 2—A labourer, aged 37, lived with his wife and 6 children when not in hospital or in prison Addicted to alcohol for 13 years and to methylated spirit for 6 years Convictions 15 for drunkenness and 2 for breach of peace Usually quiet and pleasant but has periods of manic excitement, has been 15 months in hospital and is certified, good worker when well, of average intelligence, has escaped 3 times from hospital during present admission, was twice previously admitted here

CASE 3—A seaman, aged 49, married but separated from his wife and 1 child, of no fixed abode, has not worked since 1950, when right leg was amputated above knee, after accident while drunk Addicted to alcohol for 28 years, and methylated spirit for 26 years Convictions for drunkenness over 200 Euphoric, friendly, of average intelligence, since accident has status of cripple—i e, walks with crutches and not expected to work

CASE 4—An unmarried labourer, aged 44, of no fixed abode, addicted to alcohol for 23 years, and to methylated spirit for 9 years Convictions for drunkenness over 50 Quiet, solitary, of more than average intelligence, with good vocabulary, sensitive, pessimistic, well behaved in hospital, and works well but believes himself irrecoverable

CASE 5—An unmarried labourer, aged 30, a sporadic vagrant living for periods at his parents' home, addicted to alcohol for 8 years, and to methylated spirit for $2^1/_2$ years Convictions for drunkenness 7 Schizoid features prominent, shy, solitary, emotionally blunted, but hopeful and coöperative regarding treatment and recovery Intelligence above average, and good rapport exists but from intellectual acceptance more than emotional response

CASE 6—A married fireman, aged 47, of no fixed abode, separated from his wife and 2 children for 8 years Addicted to alcohol for 27 years and to methylated spirit for 11 years Convictions for drunkenness over 40 Has general paralysis of the insane well arrested by treatment, seems unimpaired intellectually and of average intelligence, an exemplary patient who works well in hospital and now has good prospect of being reconciled with wife and family

CASE 7—An unmarried tool setter, aged 41, of no fixed abode, addicted to alcohol for 16 years, and to methylated spirit for 5 months Convictions for drunkenness 4 Euphoric, extraverted, but with strong sense of shame at having become "depraved" drinker, coöperative and optimistic regarding prospects of recovery, sociable and works well in hospital

CASE 8—A miner, aged 58, married but childless and separated from his wife for 5 years, but visited by and reconciled with her since admission, lived as vagrant for 8 months before admission Addicted to alcohol for 31 years, and to methylated spirit for 3 years Convictions for drunkenness 23 A pleasant quiet man, who has worked very well in hospital as builder's labourer, is about to be discharged to live with wife and is felt to have good prospect of sustained recovery

Prognosis

We have only recently—i e, in the last year—come to believe that sustained recovery is possible in some of these cases 3 people at present, including our only female, have periods of 3–7 months' sobriety behind them and are working and keeping in touch with the A A organisation We believe that if we continue to work hopefully and sympathetically on these patients we can obtain as good results as with other addicts to alcohol

Treatment

The general principles of detoxication, sedation a rest in the early stages are observed as with other ad to alcohol Preparations of vitamin B complex w vitamin C and potassium bromide gr 60 b d are g in most cases because this salt can replace the l sodium chloride, and in addition has a sedative act- Depletion of sodium chloride from tissue fluids is bel to be the chief factor causing craving

A special feature in the physical treatment of addict methylated spirit is that disulfiram ('Antabuse') unsafe Despite the low content of methyl alcoh methylated spirit, if the spirit were taken in the disulfiram- sensitised patient, the chemical linkage might liberate a dangerous amount of formic acid in the blood

Individual psychotherapy and group therapy, provi by membership of Alcoholics Anonymous, together w hospital routine are the most valuable therap- weapons and used with enthusiasm, should recoveries

Summary

Addiction to methylated spirit and its derivatives is a secondary or substitute addiction developing on the basis of an established addiction to ordinary form of ethyl alcohol

It is caused by poverty

Addicts to methylated spirit are more hopeful material than has been supposed for treatment and rehabilitation in hospital

We are grateful to Dr J W MacPherson for help and encouragement

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In the Mental Hospital *

CHANGES OF SOCIAL ENVIRONMENT THEIR EFFECT ON MENTALLY DETERIORATED PATIENTS

A R MAY

M B Lond, D P M

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Now that emphasis is placed on the desirability of treating psychiatric patients outside hospital whenever possible, we may expect the mental-hospital population to consist increasingly of patients whose illness is chronic and who are mentally deteriorated The likelihood that physical methods of treatment will do much for these patients is now discounted, and it is realised that any advance in their management must depend upon reorientation of the attitude of the staff, who must understand and accept the difficulties yet maintain their interest and enthusiasm Apathy among the staff is a factor which must be acknowledged and faced if the problem is to be tackled at all

In this article I shall describe how such a change of attitude influenced the behaviour of a ward of chronic deteriorated patients

THE BACKGROUND

The Patients—The ward was a closed male ward holding up to 70 patients (never less than 65) To it were sent all the most deteriorated patients in the hospital and there was no significant change in the characteristics of those admitted during our investigation (January

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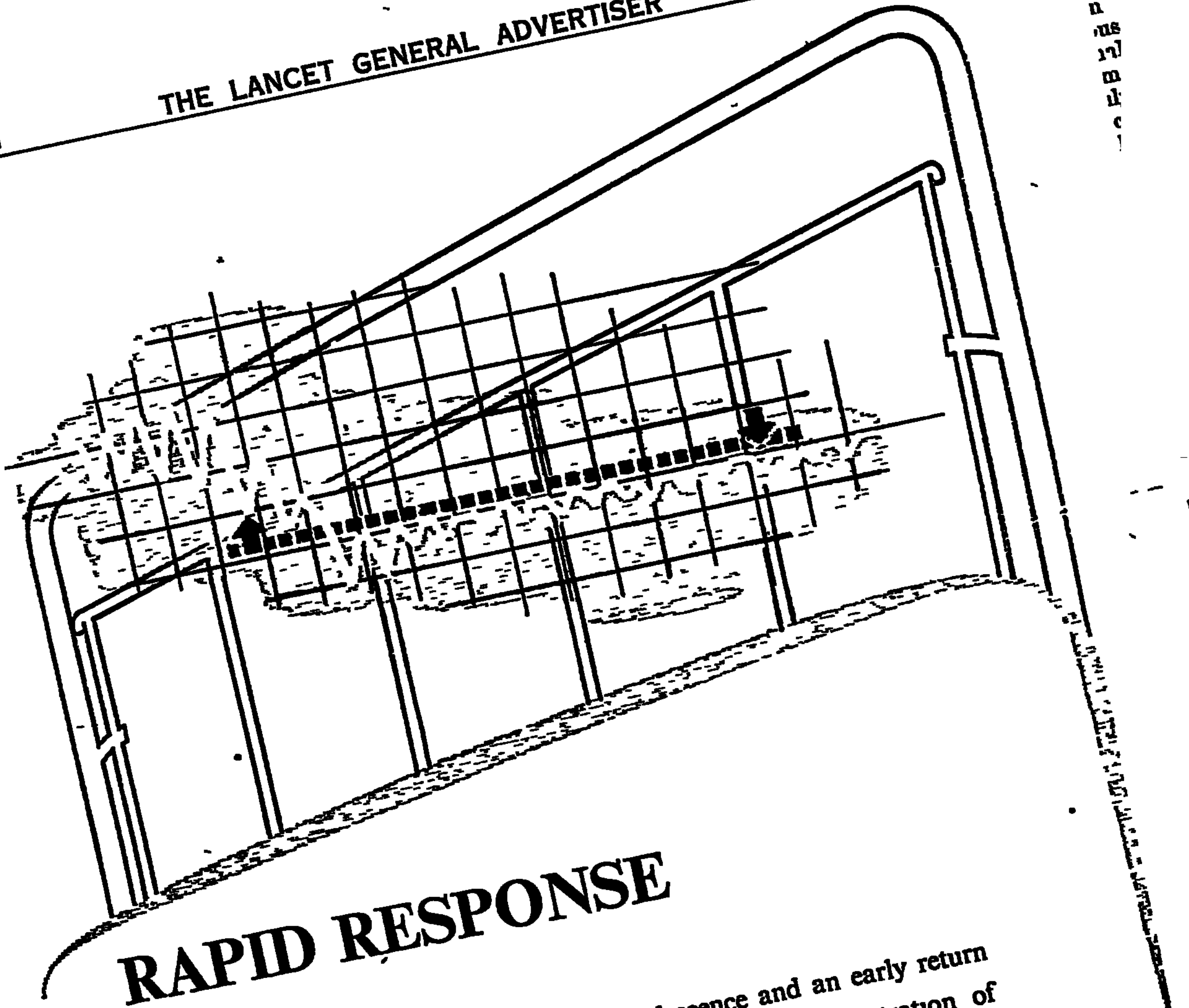
* A group of articles chiefly concerned with the value of active occupation and work for mental patients, and the means whereby it is best provided



RAPID RESPONSE

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TABLE II—COMPARISON OF FACTORS REFLECTING BEHAVIOUR AND SOCIALISATION

—	1954		1955	
	Jan – June	July – Dec	Jan – June	July – Dec
Electroconvulsion therapy				
No of treatments	292	318	151	81
No of patients	29	32	19	13
Ratio	10 1	9 9	8 1	6 2
Incidents reported				
Total no	43	42	28	15
Glass breakage	14	10	8	1
Between patients	15	25	13	8
Involving staff	8	7	5	2
Incontinence (night)				
No of patients	22	27	18	5
Destruction of property				
No of incidents reported	10	12	8	4
Destruction of clothing				
No of incidents reported	14	11	8	5
Patients absconding				
Incidents	8	2	1	0
No of patients involved	5	2	1	0
Patients employed				
Departments	4	4	5	3
Occupational therapy	8	8	8	16
Working parties	8	8	8	43 (8+35)
Ward work	40	35	35	6
Patients on sedatives				
Day	6	5	7	2
Night	11	7	13	5
Ground parole				
No of patients	8	10	13	20

no similar ward that could be used as an independent control Many of the patients shown as ward workers in the records of 1954 did in fact do no more than sit about in the ward

DISCUSSION

Assessment of behavioural changes is difficult despite the introduction of Behaviour Rating Scales[1,2] One cannot measure directly the difference in the staff's attitude, or the change in the social environment or atmosphere of the ward Nevertheless the evolution of a group attitude brings with it alterations in activity, which can be measured or counted, and table II is good evidence of increased cooperation and tolerance among staff and patients alike

Instances of improvement in individual patients are numerous At least 10 patients who were formerly mute and solitary have become spontaneous both in expressing their wishes and in offering to work The number of those unable to converse rationally has fallen from around 40 to 20 Over 50 patients now attend the social functions in the main hall, compared with 20 in January, 1955 The interest taken by staff in patients is now obvious and it is a matter of pride when a patient begins to show increased social awareness

The nursing staff as a whole has become conscious of a change for the better Junior nurses now look forward to working on the ward, and several have asked for a further period of duty there From being a source of embarrassment, the ward is now considered suitable for inclusion in any visitors' itinerary of the hospital

All members of the ward staff have been encouraged by the response to their efforts They see the problem in a more realistic light, and have proved for themselves that given a therapeutic atmosphere even the most deteriorated patient is capable of some improvement This is no new discovery, but the sense of achievement that has accompanied its verification has had a profound effect on morale

My thanks are due to Dr R K Freudenberg for his encouragement and advice, to Dr J P S Robertson for his help and criticism, to Mr J N Long for his loyal support, and to Charge Nurse R Brass and Charge Nurse W Neary, who so clearly saw what was wanted

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2 Shattin L Freed E X *J ment Sci* 1955 101 644

Symposia

HYPOTENSIVE DRUGS

A SYMPOSIUM on hypotensive drugs and the control of vascular tone in hypertension was held under the auspices of the Biological Council on April 5 and 6 at the Wellcome Building, London A gathering of about 250 chemists, biochemists, physiologists, pharmacologists, and clinicians attended The speakers included several well-known visitors from abroad

Chemical and Biochemical Aspects

Dr H R **Ing** (Oxford) dealt with the structure-activity relationships of the veratrum and rauwolfia alkaloids, of the hydrallazine group, anti-adrenaline drugs, and of ganglion-blocking agents Certain simple amidines share with the veratrum alkaloids the property of a reflex fall of blood-pressure by stimulating afferent endings in the heart and lungs He suggested that 'Dibenyline' and its congeners were reversibly adsorbed at particular sites before irreversible combination with tissue constituents occurred—a view supported by the enhancement of activity in phentolamine, which contained the phenoxyethyl group, characteristic of reversible anti-adrenaline drugs such as piperoxan He pointed out that replacement of the three methyl groups attached to the nitrogen in mono quaternary ganglion stimulators by larger alkyl radicals invariably converted the molecule into a pure blocking agent, and he suggested that the more powerful the stimulating action of the original compound, the more potent would be the blocking action obtained by this replacement Dr Ing thought that a promising field for future research would be the study of tertiary bases as ganglion-blocking agents since, unlike the quaternary drugs (hexamethonium, pentolinium, &c), they would be readily absorbed after oral administration He cited 'Mecamylamine,' a secondary base, and two tertiary bases as examples of purely blocking agents He also stressed the need to study the selective activity of blocking agents on sympathetic and parasympathetic ganglia Examples of drugs which blocked parasympathetic ganglia preferentially were known—for example, 'Elvetil'—and he thought that drugs blocking sympathetic ganglia preferentially might be discovered

Mr J W **Billinghurst** (Beckenham) said that from over a hundred compounds that he had synthesised, two did appear to have some preferential blocking effect, they were diquaternaryamino benzhydryl compounds Their pharmacology was described by Mr A F **Green** (Beckenham) They have a ganglion blocking effect resembling that of the methonium compounds but they have the advantage of greater potency, greater selectivity, and much longer action This was confirmed clinically by Dr S **Locket** (Romford) who had tested them on about 60 patients They were potent hypotensive agents, producing when given subcutaneously in a dose of 5–20 mg a satisfactory lowering of blood pressure that lasted all day Dry mouth, constipation, ocular changes, and postural hypotension seldom caused any trouble They were absorbed orally, although the dose needed to be higher than the subcutaneous one

Dr H **Blaschko** (Oxford) distinguished between hypotensive drugs which interfered with the reaction between receptors and hormones (or neurohormones) and those which altered the amount of active hormone available to the receptors The first group included blocking agents The second group interfered with biosynthesis, release, or inactivation He regarded dopamine dehydrogenase, a newly discovered enzyme which forms noradrenaline, as the catalyst of the rate limiting step in pressor amine formation Amine *oxidase* might regulate noradrenaline formation by removing excess dopamine

THE LANCET
LONDON SATURDAY, APRIL 21, 1956

Cancer Cytology

Incredulity has delayed the development of exfoliative cytology in this country Many people have felt that the method must be one of hit and miss, for how can one be sure that a malignant cell will conveniently present itself at the moment and site at which a sample is taken ? Indeed how can the malignant cell be recognised with certainty as it lies alone, shorn of its recognisable surroundings ? It is also argued that where a growth is so accessible that there is a reasonable chance of obtaining an exfoliated cell, biopsy may be undertaken with more certain results it seems better to scrape the uterus than to take a smear from the vagina or cervix Wilcox et al[1] who "screened" 9815 patients for uterine or cervical growth by means of routine smears, found, out of a total of 233 cases of cancer, 33 in which suspicions raised by cytology were confirmed by clinical review and in 17 of these detection was possible only by cytology False positives bedevil results, and they affected 7% of the findings recorded by Wilcox et al Guerriero[2] found much the same proportion of misleading results, and eroded and infected cervices were the commonest source of a false positive Sometimes the hyperplastic changes in cells from the pregnant cervix simulated carcinoma For these reasons Guerriero recommended biopsy for the abnormal cervix, cytology being reserved for the apparently normal McDonald et al[2] would prefer to restrict uterine cytology to the detection of cancer in situ

Diagnostic cytology supplies only circumstantial evidence which must be weighed with other factors If the malignant cell can be caught just a little more than occasionally, then cytology's greatest application will be to those remote sites inaccessible to biopsy For example, bronchial washings examined by Clerf and Herbut[3] revealed malignant cells in 88% of 540 patients with growth in the lung, whereas biopsy was positive in only 31% of the same group There are, however, dangers in the procedure at this particular site biopsy may be impossible, and once suspicions are aroused by cytology thoracotomy may be the only means of further investigation It would be unfortunate if a major operation was undertaken on the evidence of a false positive Moreover, it may be impossible to determine from a positive result where the primary tumour lies, and a metastasis can pass as a primary lesion while the real source remains undetected, thus leading to an unnecessary thoracotomy and resection On the other hand, the work of Foot[4] is promising He examined smears from pleural, peritoneal, and pericardial effusions due to metastatic deposits, by studying the number of cells, their nuclei and cytoplasm, and their arrangement into "proliferation spheres," he was able to classify the primary site of the tumour correctly in approximately 70% of samples for mammary, bronchial, and gastric carcinoma Diagnosis of ovarian lesions proved elusive and reduced the over-all accuracy to roughly 50% Nevertheless, increasing experience on these lines might make it possible to identify the primary lesion from bronchial washings

The colon is another site where cytology might be a great help, though the important cells are sometimes out of reach Wisseman et al[5] and Bader and Papanicolaou[6] have shown that diagnosis by this method is feasible when the lesion lies in or distal to the descending colon Fæcal detritus is an obvious hindrance which can be eliminated only by preliminary purgation and enemata The method of collection is again by washings rather than by direct smears from secretions Rubin et al[7] have shown that cytology can determine the significance of a filling defect seen on barium enema which may be either a Crohn s lesion, diverticulitis, or carcinoma Galambos and Klayman[8] have had similar experiences, moreover, their negative findings were significant for cancer was ultimately excluded in 32 patients with colonic symptoms, though in 5 a radiological diagnosis of cancer had been made Cytological examination showed no malignant cells in any of the 32 Having had no false positives, they state categorically that the presence of malignant cells is conclusive evidence of a malignant lesion, and from their positive results in 26 patients they were even able to diagnose correctly a metastatic ovarian deposit Cytology would have special application in ulcerative colitis since malignant change may be hard to detect either clinically or radiologically, a positive cytological report in the long-standing case would tip the scale in favour of surgery despite the absence of other indications of malignancy—and carcinomatous degeneration in this disease is by no means inevitably fatal if taken early There is, however, one difficulty for the diagnostic cytologist in this disease, since large columnar cells are sometimes seen which simulate certain types of malignant cells The presence of undifferentiated malignant cells, however, may, according to Galambos et al,[9] be regarded as reliable evidence of cancer Galambos and his co-workers also indicate that these large columnar cells are worth further study because of their similarity to the large gastric cells of addisonian anæmia, which like ulcerative colitis carries an increased incidence of malignant degeneration Could these cells therefore represent a metaplastic reflection of the malignancy to come ?

Though diagnostic cytology is a difficult and time-consuming method requiring an expert hand, it must eventually become widely used in this country It may be confined, however, to centres where smears, properly obtained and fixed, may be sent for scanning by trained technicians under the supervision of a pathologist The subject is still in the exploratory

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[1] Wilcox H R Pederson E S Kischer C W *Surg Gynec Obstet* 1956 102 215

[2] McDonald J R Andujar J Lee Clark R Collins V P Guerriero W F, Hartman A W *Amer J clin Path* 1954, 24 688

[3] Clerf L H, Herbut, P A *J Amer med Ass* 1952, 150, 793

[4] Foot N C *Amer J Path* 1954 30 661

[5] Wisseman, C L Lemon H M, Lawrence, K B *Surg Gynec Obstet* 1949, 89, 24

[6] Bader, G, Papanicolaou, G N *Cancer*, N Y 1952 5, 307

[7] Rubin, C E, Klayman, M I, Kirsner, J B *Med Clin N Amer* 1955, 39 261

[8] Galambos J T Klayman, M I *Surg Gynec Obstet* 1955, 101, 673

[9] Galambos J T Massey B W, Klayman, M I Kirsner, J B *Cancer*, N Y 1956, 9 152

Dr G A **Perera** (New York) was not so optimistic as the two previous speakers He described his personal experience in evaluation of hypotensive drugs In his view the rauwolfia alkaloids not only failed to produce an adequate fall in blood-pressure in many patients, but were also liable to produce mental depression He had not found the veratrum alkaloids of any value whatever unless pushed to the limit, when they produced nausea and vomiting Hydrallazine modified the blood-pressure only slightly and needed to be combined with other drugs Pentolinium lowered the blood-pressure to normal or near normal, but was without effect on the renal complications of hypertension In the malignant phase of hypertension symptoms were ameliorated, retinopathy improved, and congestive failure relieved more consistently than by rest or sedation Side-effects and difficulties of regulation had prevented Dr Perera and his colleagues from using the ganglion blocking drugs successfully in patients with advanced disease except those who were cooperative Administration of hypotensive drugs was not justified in uncomplicated hypertension without symptoms The results obtained with any drugs in the treatment of hypertension were suppressive and not curative

The results of trials with combinations of hypotensive agents in Sweden were described by Dr B **Hood** (Gothenburg) He stressed that a high proportion of hypertensive patients were admitted to hospital in too advanced a stage of their disease for effective treatment to be possible In a series of 66 adequately treated patients with hypertension in grades IV (malignant) and III, 11 were dead and 55 living, 36 of them working full time Dr Hood said that at present he used oral pentolinium, combined with one of the rauwolfia alkaloids and also hydrallazine In his view the use of this triple combination was a considerable advance on sympathectomy

Prof C **Bartorelli** (Milan) gave an account of his experience with hexamethonium and reserpine in hypertension He also described experiments with the ganglion-blocking agent, ecolid, this was found to increase greatly the blood flow to the lower limbs but not the upper limbs

In the discussion Dr E L **McDonald** said that he gave anticoagulants before hypotensive drugs to diminish the risk of thrombo-embolic phenomena which might result from a fall in blood-pressure

Dr R W D **Turner** (Edinburgh) deprecated the use of hypotensive drugs in symptom-free patients. He said that the lives of patients with symptomless hypertension were being made miserable by the administration of potent drugs

In reply to a question Professor **McMichael** said that the chance of the malignant form developing in a patient with hypertension was about 1 in 200

Control of Vascular Tone in Hypertension

Prof **Clifford Wilson** said that the clinical and pathological features of established hypertension were the same whether or not there was a manifest cause such as phæochromocytoma or renal disease In the malignant phase of hypertension there was a qualitative change in vascular behaviour—namely, regional vasoconstriction followed by paralytic vasodilatation This might be the cause of fibrinoid necrosis of the arterioles

Dr M A **Floyer** and Dr J M **Ledingham** showed that both renal and extrarenal factors were involved in experimental hypertension in rats The extrarenal factor was probably of adrenal origin and could be neutralised by the normal kidney Changes in intracellular and extracellular electrolytes accompanied the experimental procedures These were difficult to interpret, but possibly they might affect the reactivity of the arteriolar muscle

Dr B **Folkow** (Gothenburg) produced evidence t the resistance of the limb vessels in full ischaemia d tion was raised in hypertensive patients He sugg that this might be due to some structural change, a pointed out that mild thickening of the arteriolar would greatly shift the range of resistance over wh nervous and humoral control could operate

Dr J **Conway** demonstrated that the barore reflexes of hypertensive rabbits were fully active stabilising the blood-pressure at its abnormal level. H thought that the logical use of ganglion blocking dr was as adjuvants to direct vasodilators

Prof C **Heymans** (Ghent) said that the barorecep reflexes could be set to new levels by local action o vasoactive substances on the carotid sinus

Dr J H **Green** showed records from the carotid se nerves in hypertensive dogs which confirmed that th resetting of the reflexes took place on the affer side

Dr R S **Duff** said that hypertensive patients had, o the average, a normal hand blood flow Their ves were, however, more than normally sensitive to adren line, though not to noradrenaline Patients treated with ganglion-blocking drugs became hypersensitive to noradrenaline as well

Dr **Peart** described work indicating that the increased vascular resistance in the hands of hypertensive patient persisted after inhibition of sympathetic constrictor tone

In winding up the discussion, Professor **Wilson** said that the regularity with which experimental hypertension was reversible argued against structural changes in the arterioles being important in its maintenance He had suggested that persistence of hypertension after removal of a clipped kidney was due to hypertensive lesions in the remaining kidney, but he did not think that the functional abnormality could be closely correlated with histological changes On the whole he thought the rat experiments provided some close analogies with hypertensive disease in man, but he welcomed the increasing amount of work on the vascular responses of hypertensive patients The discussion had shown that there was at the moment less interest than formerly in the search for circulating vasoconstrictors as the cause of hypertension, and greater emphasis on the local conditions affecting arteriolar reactivity

Public Health

Infectious Diseases in England and Wales

Disease	Week ended March				
	3	10	17	24	31*
Diphtheria	6	4	7	6	6
Dysentery	1752	2071	2133	2571	191[illegible]
Encephalitis					
Infective	1	5	2	2	[illegible]
Postinfectious		1	3	1	[illegible]
Food poisoning	158	189	117	246	115
Measles excluding rubella	2815	2665	2891	2804	[illegible]666
Meningococcal infection	40	32	34	41	30
Ophthalmia neonatorum	25	45	38	15	25
Paratyphoid fever	5	6	13	7	3
Pneumonia primary or influenzal	1339	1153	947	817	560
Poliomyelitis					
Paralytic	14	13	11	9	11
Non paralytic	3	0	8	3	3
Puerperal pyrexia	237	267	274	285	180
Scarlet fever	841	909	889	982	6[illegible]6
Smallpox					
Tuberculosis					
Respiratory	593	696	680	671	[illegible]1
Meninges and C N S	12	10	14	13	5
Other	66	67	80	77	70
Typhoid fever	2	2			4
Whooping cough	1182	1131	1320	1416	11[illegible]9

* Not including late returns

ound that the infectivity of their nucleic-acid preparation was unstable, and was abolished by treatment with ribonuclease It is possible that some of the infectivity of the reconstituted virus prepared by FRAENKEL-CONRAT may have been due to the nucleic acid present, the protein acting mainly as a stabilising factor, further experiments will be required to settle this point

We have become familiar with the fact that pure preparations of desoxyribonucleic acid can, under certain conditions, transform pneumococci and other organisms into the serological variety of organism from which the nucleic acid was derived Now comes the idea that a ribonucleic acid alone can induce an infected cell to produce intact virus particles More and more problems in biology seem to be gravitating towards the chemistry of the nucleic acids

The Indian Village

IF today we seem to hear less about the theory of preventive medicine, this is partly because, in so many parts of the world, theory has passed into practice Under the auspices of the United Nations, of governments, of philanthropic foundations, and of private agencies, schemes which a few years ago would have seemed visionary have brought together teams of medical and other experts for joint action against poverty and disease

Of such schemes, one of the most interesting is the Indian Community Development Project, described by Mr T SWAMINATHAN, of the Indian Civil Service, at the Conference on Regional Planning and Development held in London last September This project, started in 1952 under the Indian government's first five-year plan, is intended eventually to raise the standards of living of a population of no fewer than 310 million, most of whom have hitherto existed at subsistence level Naturally its achievement must take many years, but the progress already made shows with what energy and foresight the Indian leaders are tackling some of their problems In this they owe much to Mahatma GANDHI, and it is because he saw clearly the limitations of welfare schemes imposed from above that the I C D P is primarily a movement to enlist the cooperation of the people in their own betterment the government, through its central agencies, supplies the means, but the momentum is to be supplied by the villagers, working through their village organisations During the British tenure of India the peasants got the benefit of sound systems of justice and taxation, and a skeletal rural medical service, but otherwise no great effort had been made for their social advancement indeed, the policy was, on the whole, to tamper with rural institutions as little as possible Only now, therefore, is the village population (83% of the total) beginning really to emerge from the two or three millennia during which its intricate customs and beliefs seem to have changed very little So far new ideas have not made much impact, though bicycles, cinemas, sewing-machines, and alarm clocks have been fully accepted by those few who have means to enjoy them But the government of free India, activated by GANDHI, the threat of Communism, and universal franchise, has set to work to narrow the great gulf between itself and the overwhelming majority of its citizens

The programme began in 1952 with 55 " project areas," each consisting of 500 villages with a total population of about 200,000 These areas are divided into " development blocks " which cover about 100 villages and are themselves divided into " circles " containing 5–10 villages In each village there is a development council through which the villagers themselves operate the projects and seek the specialised help and advice they require Projects are planned in agriculture, communications, education, health, cottage industries and subsidiary employment housing, and social welfare the health projects centre mainly upon the protection of water supply, proper disposal of human and animal wastes, the control of epidemic diseases, and the provision of midwifery and medical services Such work demands complex administrative machinery, but the Indian scheme differs from many others in that this machinery revolves round the all-important " village-level worker,"—who, with the individual village councils is responsible for each circle This vital man has to cope with the forces of reaction as represented in almost every village by the big landowner, the money-lender, the priest, and even the council of elders, all of whom fear that the influx of new ideas and equipment may reduce their power and prestige (Perhaps no other institution anywhere is more truly conservative than the Indian Hindu village, where one self, one's children, and one's children's children forever, are destined to follow the narrow caste rules—working, marrying, and conforming in all respects, on pain of social excommunication) With the villagers' confidence and cooperation, the village-level worker can do great things without them he does nothing except deepen the villagers' inherent suspicion of " government " and all its representatives Hence one of the question marks behind this great effort is whether enough of the " right " men will be prepared to forsake the bright lights of the big city for the mud hut and humble fare of the village Medical workers, too, have always proved hard to attract to the countryside

Though the project is too big for detailed description, some idea of the scale is given by the fact that on the medical side alone the personnel requirements of the first five-year plan are 620 doctors, 2480 midwives, and 620 each of health visitors and sanitary inspectors—figures which, it is hoped, will be trebled in the second five-year plan The problems meeting these medical workers are great, for it is no medical vacuum into which they move, and they inevitably come into competition with the local " veds " or practitioners of the Ayurvedic system (which has given us rauwolfia among other things), to be found in most villages Their task is not made lighter by the (to most Western eyes) misguided government support to schools of Ayurvedic and homœopathic medicine To the average Indian, Western medicine (known as " allopathic ") is but one alternative of a number, to be considered if the " ved," " hakim," or " homœopath " fail to cure the condition quickly, with their very much cheaper medicines Public health measures also, are not made easier in circumstances where successful opposition can be made to B C G on the grounds that it means " Birth Control General "

Though the I C D P is primarily financed by the Indian government, the people's contribution is

Letters to the Editor

STAPHYLOCOCCAL ENTERITIS

SIR,—I have read with great interest the article by Dr Todd and Mr Hopps[1]

The two cases which they report under the title "staphylococcal enteritis" were actually pseudomembranous enterocolitis Although there is much resemblance in their clinical manifestations, pseudomembranous enterocolitis and staphylococcal enteritis apparently are two separate and distinct entities

The relationship between pseudomembranous enterocolitis, antibiotic therapy, and antibiotic resistant staphylococci is probably not causal but coincidental A review of the necropsy records at the Mayo Clinic showed that from 1927 to 1936, inclusive, when no antibiotics were used, 42 patients died of pseudomembranous enterocolitis, whereas from 1943 to 1952, inclusive, in the antibiotic era, only 37 patients died of pseudomembranous enterocolitis[2] In staphylococcal enteritis the enteric mucosa remains intact, whereas in pseudomembranous enterocolitis the mucosa is denuded In staphylococcal enteritis the early administration of an antibiotic effective against the staphylococci found in the stool usually leads to recovery Such therapy is usually ineffective in pseudomembranous enterocolitis

The pathogenesis of pseudomembranous enterocolitis is not clear It usually follows operations on the bowel, but has been seen in patients with bowel lesions who had not undergone operation, or who had an entirely different type of illness It is conceivable, in this antibiotic era, that some of these patients may also show resistant staphylococci in the stool The presence of these organisms in large numbers may aggravate the underlying pseudomembranous enterocolitis

Staphylococcal enteritis is a different pathological entity It appears that the victims of this complication either harbour or contract from carriers staphylococci which are resistant to the administered antibiotic agent These organisms then invade the intestinal tract, where an opposing normal flora has already been substantially suppressed by antibiotic therapy In the intestinal tract the staphylococci grow in pure culture and most probably produce a toxin which causes the gastro intestinal and systemic symptoms—namely, diarrhœa, vomiting, fever, confusion, shock, oliguria, and azotæmia Not all of these symptoms are necessarily present in every case In overwhelming toxæmia the patient may die in a few hours, even before the onset of diarrhœa Staphylococcal enteritis has followed the administration of various antibiotics, and has occurred in both surgical and non surgical patients, and in patients who received the drug orally or parenterally This entity may be treated successfully if (a) it is recognised early, (b) the offending antibiotic is immediately withdrawn, (c) this is replaced by erythromycin, and (d) the necessary supportive therapy (to maintain or restore fluid and electrolyte balance, blood pressure, &c) is instituted Today erythromycin is generally recommended as the antibiotic of choice in this situation However, sensitivity of the isolated pathogen should always be determined because of the possibility of an erythromycin resistant staphylococcal strain

Diarrhœa during a course of antibiotic is not always due to resistant staphylococci The mild diarrhœa without systemic reaction that so commonly arises during oral administration of the so called broad-spectrum antibiotics is probably produced by chemical irritation, sensitivity to the drug, or disturbed intestinal milieu Possibly in some such cases one may find an abundance of antibiotic-resistant staphylococci in the stool Mild diarrhœa without systemic symptoms will respond to the discontinuance of the offending antibiotic medication, without any further measures

Veterans Administration Hospital
Montrose New York U S A

ALLEN E HUSSAR

DEFICIENCY OF ESSENTIAL FATTY ACIDS

SIR,—After the gentle reprimand which Dr Sinclair has given me (April 7) for daring to comment on matters in which I have not worked experimentally, it is good to see that he himself has not hesitated to refer to the work of others In building his house, he has used as his cards some twenty-five reports of original work, in which he has himself been associated with four Of the diseases of which he speaks, his work has been on atherosclero not on carcinoma or leukæmia or peptic ulcer or disseminated sclerosis or any of the other parts of his "etcetera"

My purpose, however, is not merely to say *tu quoque* to Dr Sinclair It is to give one tiny warning to his readers, and one tiny suggestion to Dr Sinclair The warning is that the decorations on the edifice—terms like tetraenoic and trans fatty acid—are bright and glittering but they may well dazzle the eyes of those who are viewing it from the non-specialists' enclosure As a result, it may be that the cards look like real bricks and that the stability of the edifice is assumed to be much greater than it really is

The suggestion is that Dr Sinclair himself removes one of the crumpled cards in his foundation If his gentle hands remove it, they may inadvertently tumble down the whole pretty building, which at this stage does not perhaps deserve so cruel a fate I refer to the statement made by Dr Sinclair, and previously by Dr Nyrop that margarine is deficient in E F A Irrespective of any "unnatural" trans acids which margarine may contain and which *may* (according to Sinclair) act as "anti vitamins" for E F A, the plain fact is that margarine contains more E F A than butter *when tested biologically* That is to say, whatever the relative amounts of linoleic and *arachidonic acids*, or whether there are substances which may increase or decrease their potencies, the final result in the animal is that the substitution of margarine for butter in the diet increases the *effective* amount of E F A

I might add that in my previous letter[1] I referred to the work of Dr H J Deuel in which he had found that the biological E F A activity of margarine was some two to four times that of butter Since then, Dr Deuel has personally informed me that refinements in his methods of testing suggest that this is an underestimate, and that *margarine may have five times the amount of E.F.A or even more*

Truly the problem of the association of fatty acid deficiency with the conditions mentioned by Dr Sinclair requires a great deal more work It is for the future to show whether the resulting evidence becomes a strong wind which destroys his beautiful edifice, or a gentle breeze which settles it into a stable permanent structure

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London, W 8

JOHN YUDKIN

THE BASE DEGREES BY WHICH WE RISE

SIR,—In his letter to Barbara (April 7) Dr "Peter Davey" (or could it be Professor Peter Davey ?) discusses the position of pathologists in regard to the lack of higher examinations and of a representative organisation. May I, as another private individual, comment ?

If I have appreciated the troubles of the clinical pathologists correctly, they are concerned because they do not know what advice to give to their registrars who ask which higher qualification should be sought Dr Peter Davey asks what purpose these exams serve and seems to dismiss them as unnecessary Unfortunately—and the more intelligent registrars in clinical pathology appear to have recognised this—hospital pathologists have to live in the same world as the rest of us and the competition for consultant posts is now becoming such that the young man (or his sister) without a higher qualification is likely to wait a very long time for an appointment He might be more successful, of course, in the less competitive field of university pathology It is becoming increasingly obvious that if hospital pathologists wish to keep the pay of consultants, they will have to fill their ranks with holders of higher qualifications, or their medical brethren in other specialties and the lay administrators will demote them—and this notwithstanding the truth that a good pathologist always acts as a consultants' consultant eported an inquiry into the analgesic action of a series f compounds in which the N-methyl group of pethidine s replaced by a tertiary amino alkyl group. Experi- nentally one of this series, morpholinoethylnorpethidine, s somewhere between three and seven times more potent han the parent substance, yet without equivalent increase n toxicity. This analgesic seems well worth further nvestigation, but experimental findings are not always substantiated in clinical practice. In 1949 a piperidyl analogue of iso amidone was found under experimental conditions in both animals and man to be less depressant to respiration than morphine, pethidine, and amidone[4 5] Clinical trial as an adjunct to nitrous oxide anæsthesia, however, now suggests that it is not a satisfactory substitute for pethidine because of the severe respiratory depression that it may cause, and there is also some doubt about the adequacy of analgesia[6]

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[1] Todd A S, Hopps P O D *Lancet* 1955, ii 719
[2] Dealing W H, Hellman, F R *Proc Mayo Clin* 1953 28, 121

[1] *Lancet*, 1955 i 46

PROTECTION AGAINST TETANUS

NDEPENDENCE Day celebrations in the United States ed to be responsible for many deaths from tetanus, at the use of tetanus antitoxin in the treatment of the juries reduced the number of deaths from 100 per 1000 njuries on Independence Day, 1903, to 3 deaths per 1000 n 1913. In the early months of the 1914–18 war not enough tetanus antitoxin was available, largely because the incidence of tetanus had been negligible on South African soil during the Boer war. The incidence of tetanus in 1914 was about 8 cases per 1000 wounded—a similar figure to that recorded during the Franco-Prussian war of 1870. But ample supplies of tetanus antitoxin were soon produced, and the incidence fell to 1 per 1000 wounded. Yet, despite the way in which antitetanus serum has been used more and more freely since those days, some 50 or more people still die from tetanus in this country each year. Most of these infections probably arise as the result of injuries so trivial that they are not seen by a doctor, so that the injured have no chance of protection by passive immunity. It seems therefore that this annual loss of life can be substantially reduced only by the wider use of active immunisation.

The protection afforded by tetanus antitoxin lasts only about two weeks, and in persons who have had antitoxin on a previous occasion it may be eliminated om the body abnormally rapidly and no appreciable rotection may be conferred. Fortunately, we can give much more lasting protection by active immunisation. Since whole armies can be immunised before facing considerable risks of injury, it is natural that much of our information about active immunisation should come from military sources[7] It is largely as the result of war experience that successful methods have been established. Two doses of tetanus toxoid, at an interval of six weeks, followed by a third dose six months later, confer adequate immunity for five years. Booster doses are best given every four years. After an injury a further dose of toxoid stimulates the defences sufficiently to make the administration of antitoxin unnecessary unless treatment has been delayed for more than twenty-four hours after injury[8] Both the British and United States armies used routine immunisation during the late war, and immunisation was compulsory for American soldiers. The incidence of tetanus was reduced to $^{1}/_{25}$ of the 1914–18 rate in the British Army, and among American troops there was only 1 case of tetanus among all battle casualties. Tetanus antitoxin was given to British wounded, but the Americans used no antitoxin, giving their injured a booster dose of tetanus toxoid. After a break from 1945 to 1949, active immunisation has been a routine procedure in the British Army, so that there is a section of the community—men who have done their National Service—with an adequate basal immunity. But the rest of the civilian population are poorly defended. Most deaths from tetanus occur in the 5–14 age group and there is therefore much to be said for immunising children when they go to school. Combined diphtheria-tetanus immunisation of children has been compulsory in France since 1940, and nearly all Danish children are similarly treated[9] In the United States and Canada diphtheria-tetanus immunisation, often combined with whooping-cough vaccination, is widespread. The child entering school at 5 might well receive a booster dose of diphtheria prophylactic combined with the initial dose of tetanus toxoid. But, since basic immunity to diphtheria will already have been established in many of these children, the secondary response to the diphtheria toxoid might well swamp the antigenic response to tetanus toxoid unless the composition of the combined prophylactic were suitable, so careful inquiry into the effect of various prophylactic combinations would be needed before such a scheme could be adopted.

It is not easy to envisage immunisation of the whole adult population, although those most at risk might well be offered protection. Agricultural workers, especially those in eastern and south western England, labourers, stable hands, and mechanics are all prone to injuries contaminated with earth. But so are pedestrians, cyclists, and drivers on our roads, and that includes almost everybody. Nevertheless, in a generation's time the toll of tetanus would be much reduced if expectant mothers and children entering school were added to National Servicemen as priority candidates for tetanus immunisation.

MENOPAUSAL PANNICULOSIS

A FEW years ago Copeman and his colleagues[10 11] gathered evidence to show that “the fat tissues of the body are subject to pathological variations which cause pain.” They were investigating the common syndromes of “fibrositis” and “rheumatic” pain, and they suggested that, in certain cases at least, the characteristic pain originates in areas of local œdema of the fibro fatty subcutaneous tissues, particularly in the residual fat areas of the back. Their post mortem dissections and biopsy studies of the back in fibrositis showed that the palpable painful nodules were often identifiable as œdematous fat lobules. Their view of the origin of the pain as a local tension œdema was supported by their finding that induction of a state of clinical dehydration (again in selected patients) brought relief of pain to a significant proportion. Copeman[10 12] has suggested a similar cause for the type of fibrositic pain that occurs in panniculitis, a condition frequent at the age of the menopause, in which the panniculus adiposus increases in bulk in certain characteristic regions of the limbs and back, producing pain and tenderness. He believes that also in this syndrome the underlying mechanism is a shift of extracellular fluid into the fatty tissue cells.

Baker[13] has recently studied panniculitis (she prefers the term “panniculosis”) by means of skin biopsies in 49 cases. The biopsies showed no apparent abnormality of the subcutaneous fat, apart from increased bulk, but 80% of them showed an increased depth and density of the collagen layer of the skin, though the fibres themselves were mature, acellular, and morphologically normal under

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[6] Masson A H B Anæsthesia 1956 11 59

[7] Barr M Sachs A Army Pathology Advisory Committee Report on the Investigation into the Prevention of Tetanus in the British Army 1955 W O code no 11262

[8] Looney J M Edsall, G Ipsen J, Chasen, W H New Engl J Med 1956, 254 6

[9] Scheibel I Bull World Hlth Org 1955 13 381

[10] Copeman, W S C, Ackerman, W L Quart J Med 1944, 13, 37

[11] Copeman, W S C, Pugh, L G C Lancet, 1945, ii, 553

[12] Copeman, W S C Brit med J 1949 ii 191

[13] Baker, D M Ann rheum Dis 1955, 14, 385

been steady and is still continuing Both women were originally unable to carry out their duties as housewives and were even unable to look after themselves fully They have now for some time been able to run their own houses again

These cases are described in the hope that others will try this method, which, it seems, may arrest the progress of the disease and enable the patient to lead an active life

Winchester C B S FULLER

PROGRESSIVE EXOPHTHALMOS TREATED BY ORBITAL DECOMPRESSION

SIR,—Effective as the approach described last week by Mr Rowbotham and Mr Clarke would appear, a simpler and satisfactory approach in my experience is through the ethmoids and the roof of the antrum by a short incision medial to the inner canthus

Market Rasen,
Lincs M SPENCER HARRISON

ELECTROPHORESIS OF PLASMA-PROTEINS

SIR,—Dr Gero and his colleagues (Dec 31) mention that their electrophoretic findings support the hypothesis that splitting of the β band may be caused by some change in the lipoprotein pattern of the serum

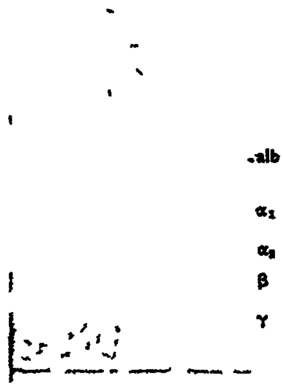

Fig 1—Example of 4-hour run

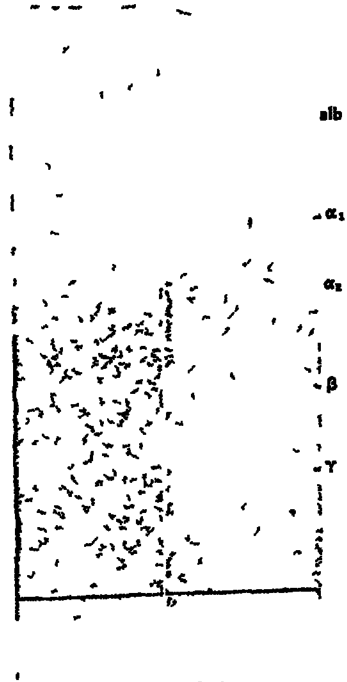

Fig 2—Example of 16-hour run

I was able to illustrate by paper electrophoresis the effect of heparin injection on lipoproteins After 24 hours' refrigeration at 0°C, fasting serum and serum taken 30 minutes after injection of 25 mg of heparin are added to one third part of homogenised and sterilised, undiluted milk The milky sera are then incubated at 37°C for $2^1/_2$ hours Next, 0 08 ml of each serum sample is brought upon a strip of filter paper with a median split and electrophoretically run for 16 hours using a barbitone buffer pH 8 6 After staining with sudan black, three features can be seen (*a*) In almost all paper-strips the right side (post heparin milky serum) is less stained than the left side (fasting milky serum), indicating a disappearance of lipids This corresponds with the clearing effect (*b*) Nearly all strips show a shift of the β globulin lipoprotein band towards the space between β and α_2 bands, sometimes even towards the α_1 and α_2 bands This occurs only on the right side of the strip (*c*) Sometimes a more or less clear band appears between the β and γ globulins, which suggests a splitting of the β globulin band into two components—namely a more rapid (see [*b*]) and a slower one This too is only seen on the right side of the strip

We are trying to ascertain whether this third feature appears only when the patient has symptoms of duodenal ulcer I could not demonstrate that atherosclerotic patients form an exceptional group in show features (*a*) and (*b*) It is noteworthy that feature (and (*b*) are also seen in a four hour run electrophor with smaller strips and 0 02 ml of serum The featu described here are shown in figs 1 and 2

Department of Internal Medicine,
University of Utrecht Holland J VI

HYDROCORTISONE IN SEVERE TETANUS

SIR,—Despite the introduction of potent antitox penicillin, various relaxants, general anæsthesia, tracheotomy, and intermittent positive pressure respirat in the management of tetanus, the problem of prevent death in severe cases is still unsolved We have shown controlled studies [1–3] that corticotrophin, oral cortiso, and oral hydrocortisone can effectively suppress the manifestations of severe tetanus in man, modifying the course and reducing the mortality Corticotrophin takes about 48 hours before exerting its full effe Injected cortisone suppresses pyrexia quite well b aggravates spasms and has an adverse effect on the whole We report here the results in five cases of severe tetanus treated with parenteral hydrocortisone

All five cases (see accompanying table) were "severe" according to the criteria previously laid down by us The patients were given hydrocortisone in addition to the bas therapy, which included antitoxin, penicillin, paraldehyde supportive measures, and wound hygiene Each of them received on admission an infusion of 50 mg hydrocortisone over about 4 hours (case 3 received two such infusions) Intramuscular injections of hydrocortisone suspension were started at the same time, 25–50 mg being administered every 6 hours at first If hormone was still required after 10 days the patient was switched to oral cortisone to conserve the supply of hydrocortisone The basic therapy, apart from hormones, was essentially the same as we applied in previous trials

DATA ON 5 CASES OF SEVERE TETANUS

Case no	Age (yr)	Sex	Mode of infection	Incubation period (days)	Period of onset (hr)
1	35	F	Dog bite of rt leg	6	48
2	12	M	Puncture by rusted nail of rt foot	5	36
3	10	M	Otorrhœa lt ear	6	24
4	40	*F*	*Furuncle of lt ear*	5	30
5	60	M	Puncture by thorn of lt foot	6	24

Case 2 died of circulatory failure 64 hours, and cases 3 and 5 died of respiratory failure 38 and 60 hours respectively, after admission

Cases 1 and 4 survived

CASE 1 needed hormones for 20 days, the dose was tapered off after 12 days Lockjaw was complete from the 2nd to the 4th day, improved gradually thereafter, and disappeared on the 25th day Spasms were frequent up to the 7th day and occasional up to the 13th day Paraldehyde requirements were only moderate The temperature, which fluctuated around 100°F, went above 101°F on four occasions in the first week and was normal on the 16th day Her stay was prolonged because in the 4th week, during convalescence, she developed pneumonia requiring additional streptomycin, and in the 5th week an abscess in her left thigh at the site of previous paraldehyde injections, requiring drainage We have occasionally seen such abscesses even in cases not treated by hormones, especially where some paraldehyde has got into the subcutaneous tissue In this case we do not think that the abscess was related to previous hormone therapy, because it developed long after the withdrawal of hormones

CASE 4 received hormones for 14 days, the dose being tapered off from the 6th day Trismus, which was never

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1 Lewis, R A, Satoskar, R S, Joag, G G, Dave B T, Patel J C *Indian J med Sci* 1954, 8, 1
2 Lewis R A, Satoskar R S, Joag, G G, Dave, B T, Patel J C *J Amer med Ass* 1954, 156, 479
3 Dave, B T, Satoskar, R S, Joag, G G Patel, J C, Lewis R A *J postgrad Med*, *Bombay*, 1955, 1, 4

ts four editors—Fletcher, Garrison, Alleman, and Dr Claudius F Mayer Nobody will miss it more than those keen writers who have overwhelmed it with their industry

MYASTHENIA GRAVIS

THE Myasthenia Gravis Foundation, established in New York in 1952, is a charity which collects funds for research into the disease Considerable sums have already been allocated to this work in the United States, but the most notable achievement of the Foundation so far was the conference organised by their medical board of advisers, and held in Philadelphia in December, 1954 Eighteen of the papers read at the conference have now been published in the *American Journal of Medicine* [1]

Viets reviews the work on the ætiology and treatment of myasthenia gravis carried out since 1934, the year in which Mary Walker's description of the action of neostigmine stimulated interest so strongly Koelle describes recent knowledge of the structure of the motor endplate, gained by new techniques which, he points out, have not yet been used in investigating possible structural defects in myasthenia Van Maanen, in his study of neuromuscular blocking agents, notes that the paralysing dose of decamethonium (C10) is smaller for the tibialis than for the soleus of the cat, the opposite is true for tubocurarine This high selectivity of a blocking agent for different muscles in the same species is in line with the affection of certain muscles—such as the ocular, facial, and pharyngeal muscles—in myasthenia

Electromyographic studies led Johns and his colleagues at the Johns Hopkins Hospital to the conclusion that the myasthenic block was of the competitive curare-like type They also compared the effects of acetylcholine in normal subjects and patients with myasthenia, and they obtained results which they felt could be best explained by a competitive block produced by choline, "released in a normal manner during neuromuscular transmission following hydrolysis of endogenous acetylcholine" Churchill-Davidson and Richardson, on the other hand, have found that patients with mild and localised myasthenic weakness showed diminished sensitivity to decamethonium, while those with generalised weakness did not have this tolerance They also found that the block produced by decamethonium in myasthenic patients is of the dual type and not a simple depolarisation, as in the normal subject—a conclusion opposed to that of Johns et al. Churchill-Davidson and Richardson believe that the underlying dysfunction in myasthenia is an alteration in the way in which the endplate responds to acetylcholine, rather than any change in the amount liberated at the nerve ending The work of Botelho suggests yet another possibility From simultaneous studies of electrical and mechanical activity in myasthenia, she finds that tension changes at stimulation rates of 3 per sec and 30 per sec are a closer reflection of muscle weakness than are changes in action potential Botelho suggests that myasthenia may be at least partly due to changes in the contractale ability of the muscle, neostigmine being capable of restoring contractility when no alteration in neuromuscular transmission can be shown

Andrew and Harold Wilson have continued their ork on thymic extracts from myasthenic patients, ormal adults, and fœtal whales The blocking effects ey obtained with thymic extracts were not found in milar preparations of lymph nodes and voluntary uscles They feel that an increased thymic secretion xplains the cure of myasthenia by thymectomy, but might in time lead to irreversible changes at, or near, the neuromuscular junction, and this would account for the failure of thymectomy in some cases of long-standing myasthenia Eaton and Clagett give an extensive critical review of the results of thymectomy in the United States, and they also refer to Keynes's British series, the largest of all. They had been sceptical of their own results in 1949, but when they later re-examined them, excluding the patients with thymomas and dividing the remaining patients into groups according to sex and age, they found that surgery was significantly better in young women, in whom 53% of results were "very good," compared with 25% in a similar series treated medically In men the advantage of surgery was slight—35% of good remissions as opposed to 30% with medical treatment They agree with Keynes that the prognosis is much worse with thymomas and that operation should be preceded by irradiation

Discussing the influence of pregnancy in myasthenia, Schlezinger finds that equal numbers of cases improve, get worse, or remain stationary during pregnancy The behaviour of the disease during one pregnancy is no guide to what may happen to the patient during a subsequent pregnancy Schlezinger draws attention to previous reports of transient myasthenia in the newborn offspring of an affected mother The recognition of this possibility by the obstetrician and the treatment of the infant with neostigmine may be life-saving

Schwab has treated 60 patients with the new drug WIN 8077 ('Mysuran') This drug has a stronger anti-curare effect than neostigmine and its action lasts about twice as long It produces the same undesirable side effects which, because of its prolonged action, may be more serious, calling for caution and very gradual increase in dosage when stabilising a patient Schwab et al [2] have since reported that 59 out of 75 patients were being satisfactorily maintained on this drug

Osserman describes further results with pyridostigmine ('Mestinon') He confirms that many patients get fewer side-effects than with neostigmine and like pyridostigmine, especially because its slightly longer action often makes a night dose unnecessary Tether [3] has lately recorded further experiences which reinforce earlier encouraging findings with this drug [4]

At the Philadelphia conference Tether dealt in detail with the management of myasthenic crises He gave examples of patients who were treated too energetically and carried from a myasthenic crisis to a cholinergic crisis One of his patients had reached the astonishing dose of 215 tablets (3225 mg) of neostigmine daily towards the end of pregnancy Patients requiring such large doses are more safely managed by frequent injections, since uneven absorption is a serious and uncontrollable hazard when tablets are given in large numbers

INDEX OF THE LANCET

OUR Index for the second half of last year should have been issued many weeks ago, but the recent interruption in the work of our printers has prevented their completing it We hope next week we shall be able to say when it will appear

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DR ÉDOUARD RIST, chief physician to the Laennec Hospital, Paris, has died at the age of 85 He was a past president of the French Tuberculosis Society and was elected a fellow of the Royal College of Physicians o London in 1940

DR MATTHIEU PIERRE WEIL, the news of whose deat has reached us, was for many years head of Fernan Bezançon's clinic in the Hôpital St Antoine in Pari His great intelligence, his warm heart, and his orator made him for many years a well-known and well-love figure at international congresses on rheumatology.

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[1] *Amer J Med* 1955, 19, 655

[2] Schwab R S Marshall, C K, Timberlake, W J *Amer m* *Ass* 1955 158 625

[3] Tether, J E *Ibid* 1956, 160, 156

[4] See *Lancet*, 1954, ii, 800

to have a semitransparent tube, although the present tube size is not ideal and a thinner walled tube would be better

Silicone rubber's excellent heat-resisting properties would allow it to be sterilised at a temperature high enough to destroy any protein contaminants

The disadvantages of this tubing are its high initial price (offset by its durability) and its unsuitability for use in the operating theatre with explosive anæsthetics, or by an oxygen tent It may be possible in the future to produce silicone rubber with better conducting properties

The silicone rubber tubing was prepared by Midland Silicones Ltd, London, and the sets were assembled and sterilised by the courtesy of Dr W Weiner, Birmingham Regional Blood Transfusion Service The electrical properties of silicone rubber tubing were examined by Mr A Quinton, principal physicist to the Queen Elizabeth Hospital, Birmingham

Metabolic Research Unit,
Little Bromwich General Hospital,
Birmingham 9
R. F Fletcher

TREATMENT OF NEPHROSIS WITH PREDNISOLONE

SIR,—It has been pointed out to me that in seeking brevity some ambiguity as to the dosage of prednisolone used by me in the treatment of nephrosis may have been introduced into table I of my paper published in last week's issue

The dosage recommended in the form of oral tablets of prednisolone was

60 mg daily for 10 days
40 mg daily for 10 days
20 mg daily for 10 days
10 mg daily for 10 days

Royal Hospital for Sick Children,
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GAVIN C ARNEIL

FAMILIAL HEMIPLEGIC MIGRAINE

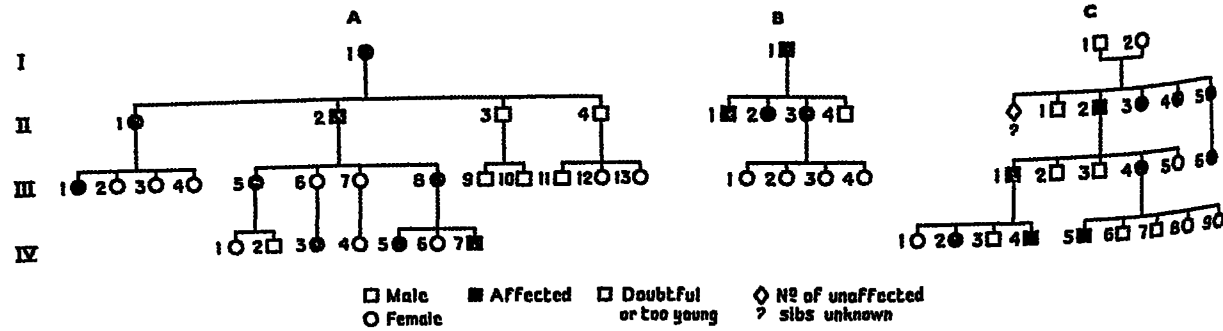
SIR,—Many people with headache do not have migraine, and some people with undoubted migraine (who have the typical visual attacks) do not have headache There is general agreement that environmental factors in the form of digestive or metabolic disturbances and psychological upsets play a part in firing off the migraine attack, but there is little agreement as to what those factors are For these reasons the compilation and interpretation of family histories of migraine over several generations is difficult Migraine is frequently noted in two successive generations, but it may be sufficiently common in the population for it to behave in this way whether the innate tendency were conveyed as a mendelian dominant or recessive character

The peculiar form of migraine known as hemiplegic migraine does not share all these genealogical disadvantages, however It is very rare, and the nature of the attacks is so striking that a fairly accurate, if secondhand, account of them should be obtained even when the affected person is no longer living The attacks are usually very similar in different members of the family Several workers have recorded cases in more than one member of a family, and the most recent account, by Blau and Whitty,[1] concludes "The condition appears to be inherited through a recessive gene and is not sex linked" Of these two conclusions the first seems to be untenable, and Dr Blau and Dr Whitty have since amended it (Feb 11) by stating that the condition is apparently inherited through an irregular dominant gene Their second conclusion is unproven from the data provided

Good descriptions of the disorder are given by Symonds[2] and by Blau and Whitty[1] In the accompanying figure A is the family tree from the latter paper This shows direct transmission through three, and in one instance four generations This in a rare condition is by itself practically proof of a dominant inheritance, the only exception to this mode of inheritance in this family being the individual III 6, who transmitted the disorder though escaping herself Presumably this exception led the authors to postulate a recessive heredity, but for this to be the case, no less than 4 individuals in this small family group must have married persons heterozygous for the complaint, which, in the absence of a series of consanguineous marriages, would in such a rare condition be beyond any likelihood It is quite common for a dominant condition to skip a generation (the phenomenon known as incomplete penetrance) Assuming that the individual III 6 carried this dominant gene, the offspring of affected individuals are exactly as they should be for dominant transmission 8 inheriting the gene and 9 unaffected None of the unaffected members (except III 6) had affected children

Other records, as far as they go, support a dominant transmission Dynes[3] recorded hemiplegic migraine in a mother and daughter, and Symonds[2] in two families—father and son in one, grandfather father, and son in the other Whitty[4] recorded three families, consisting of mother and daughter, father and daughter (in which the father only had ordinary migraine), and the family illustrated in the accompanying figure, B Clarke[5] recorded in detail the extraordinary family illustrated in the accompanying figure, C In this family the individuals I 1 and 2 were said to be free from the complaint, but as they were probably born about 1810 the information may not be complete Perhaps the environmental stimulus for firing off the attack did not occur in those days They had a "very large family" of whom 4 certainly, and a 5th probably, had hemiplegic migraine As the number of sibs in this generation is not recorded and as 4 of the children in generation IV were still very young when the family was investigated, there is not much to be gained by calculating the ratio of affected to unaffected offspring

With regard to sex linkage, indications of the well known form (a recessive gene on the X chromosome) are of course lacking A dominant gene on the Y chromosome is also ruled out, but there is nothing in Blau and Whitty's family to exclude a dominant gene on the X chromosome It is, however, ruled out by pedigrees B and C in which affected males have transmitted the disorder to male offspring A dominant gene on the homologous portion of the sex chromosomes is more difficult to rule out but pedigrees B and C



Hemiplegic Migraine A, Blau and Whitty, B, Whitty, C, Clarke

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1 Blau, J N Whitty, C W M *Lancet*, 1955, ii 1115
2 Symonds, C *Trans med Soc Lond* 1952 67 [illegible]
3 Dynes, J B *Brit med J* 1939 ii 116
4 Whitty, C W M *J Neurol Psychiat* 1953, 16, 1[illegible]
5 Clarke, J M *Brit med J* 1910, i, 1534

ABLE II—AGE OF SEPARATION AND AGE OF FIRST THEFT

—	Separated before 2 years old	Separated after 2 years old	Not separated	Total
ore 7	12	4	9	25
er 7	22	18	125	165
Total	34	22	134	190*

$\chi^2=43\ 68 \quad n=2 \quad P<0\ 001$

* Information was unreliable in 10 cases

The importance of unconscious symbolism in many efts by children has been described by many writers, cluding Schmideberg (1935), Bowlby (1946), Fenichel 946), and Gardner (1947), but opinions vary on inter etation Some workers emphasise that the stolen ods represent affection, of which the child has had less an normal, others hold that the theft is predominantly gressive—the main motive being to injure the victim he present study suggests that in different offences oth these motives, and others, are present Whatever e motivation of an offence, however, clinical examina on repeatedly confirms the truth of Healy and Bronner's 1936) remark

> “ Young people enter into delinquency commonly not with ny deliberate rejection of ethical standards nor as a rational nterprise Later on in life, when criminalistic skills are cquired and material gains result the story may be lifferent delinquency in these early years represents mainly a welling up of blindly active responses ”

Results

I observed no connection between type of offence and intelligence But there was a clear association between type of offence and age (table I) It is arguable that only older boys would commit secondary offences or steal motor vehicles, but, even with these groups removed, the distribution is statistically significant Table IV shows that proving stealing is not merely the offence of an older and previously delinquent boy

TABLE III—AGE OF SEPARATION AND STEALING FROM HOME AT ANY TIME

—	Before 2 years old	After 2 years old	Not separated	Total
From home	17	12	20	49
Not from home	17	10	114	141
Total	34	22	134	190*

$\chi^2=21\ 55 \quad n=2 \quad P<0\ 001$

* Information was unreliable in 10 cases

The effect of maternal separation in infancy has been stressed in recent years I could find no clear relation between age at, or length of, separation and type of present offence, but a clear association between early separation and early stealing (table II) There was also a clear association between early separation and stealing from home at any time (table III) In other words, children who are separated early tend to begin their stealing early and tend to steal from home An interesting finding, which was, however, not definite enough to be statistically significant, was a positive correlation between maternal rejection and a history of early separation In other words, the history of early separation may be associated with present behaviour because it is also associated with present rejection—this point is often overlooked No importance could be attached to length of breast feeding

The age at which stealing began was related to the type of theft As shown in table IV, boys now committing marauding thefts began to steal between the ages of 8 and 14 This age has been neglected by psycho analysts, who regard it as part of the latency period, but other workers (Hall 1908, Ackerson 1931, Piaget 1932) have shown that it is an active and important age, for boys at least It is the gang age, and marauding offences are gang offences Most of the provers, on the other hand, began rather later, while a large proportion of the comforters and secondary offenders began early in life

The most important part of the study dealt with parental relationships (table V) The clearest association was between maternal rejection and the comforting type of offence, especially stealing from home Some offences are not due to both parents acting together, but to a conflict of attitudes between the parents In both subdivisions of the proving offences there is a similar combination of “ good ” mother and “ bad ” father Father's failing is to be authoritarian (low in democracy) and often inconsistent, while good mothers are often too affectionate An over-protective mother or an authoritarian father may cause rebellion in adolescence—an age at which self-consciousness about masculinity reaches a crisis (Alexander and Healy 1935, Blos 1941, Selling 1942, Elkin 1946) In the marauding group study of the parental attitudes does not show a definite background Compared with the other groups it gives the impression that the parents are reasonably affectionate, but rather inconsistent in their discipline Without a control group it is impossible to say whether this combination is a likely cause of this type of offence or whether it is merely the predominant pattern at this cultural level Experience suggests the latter

TABLE IV—AGE OF FIRST KNOWN THEFT AND TYPE OF PRESENT THEFT

Type of offence	Age				Total
	Before 7	8–11	12–14	15–17	
Marauding	2	32	26	5	65
Proving	0	5	10	10	25
Comforting	15	18	14	6	53
Secondary	7	10	3	2	22
Other	2	14	15	4	35
Total	26	79	68	27	200

$\chi^2=50\ 28 \quad n=12 \quad P<0\ 001$

Consideration of the socio economic level showed further differences (table VI) Comforting offences spread over the whole range, proving offences are commoner

TABLE V—TYPE OF THEFT AND PARENTAL ATTITUDES

—	Democracy				Acceptance				Indulgence				Total
	Maternal		Paternal		Maternal		Paternal		Maternal		Paternal		
	Good	Bad	Good	Bad	Good	Bad	Good	Bad	Good	Bad	Good	Bad	
Marauding	30	26	22	30	31	24	27	25	26	30	21	28	320
Proving (*b*)	12	2	2	9	8	2	4	4	10	4	2	7	66
(*c*)	7	3	2	7	7	0	5	1	7	2	2	4	46
Comforting (*a*)	7	12	2	12	3	23	4	13	5	14	4	10	109
(*b*)	10	10	4	15	8	15	8	13	10	10	5	12	120
Secondary	7	7	2	11	9	8	4	8	7	7	3	9	82
Other	19	9	11	13	25	8	13	9	17	11	7	13	155
Total	92	68	45	97	91	80	65	73	82	78	44	83	898

“ Good ’ is a combination of ‘ high and medium ’ in acceptance and democracy, and ‘ Medium ” alone in indulgence (as “ high ’ indulgence from the working definition would be considered to be ‘ over ’ indulgence)

A rating of “ *high* ” in acceptance should also probably be considered bad, because it includes the over affectionate mother but if it had been rated “ bad ” it would have masked an interesting finding in the proving group

TABLE II—RESULTS OF DUAL READING

Classification	Both observers	Observer A	Observer B	Action*
Active primary	6 (*66 6%*)	6 +2 (*88 8%*)	6 +1 (*77 7%*)	9
Active post primary unilateral	31 (*72%*)	31 +7 (*88 4%*)	31 +5 (*83 7%*)	43
Active post primary bilateral	15 (*100%*)	15 +0 (*100%*)	15 +0 (*100%*)	15
Total	52 (*77 5%*)	52 +9 (*91 5%*)	52 +6 (*86 5%*)	67

* Sent to chest clinic for full investigation and treatment

films was prepared Those persons were then re-examined radiographically Meanwhile, the miniature films were read again by the director of the other unit, and the persons he wished to recall whose names and numbers did not appear on the first list were recalled in addition

A register was kept, which showed the numbers and names of those persons recalled by observer A on the left-hand page and by observer B on the right hand side It was thus easy to see which persons had been recalled by both observers During the course of several months the results from 10,000 people were collected

All the large films were read and reported on independently by both observers and classified for tuberculosis under the old mass X ray classification

20 active primary
22 active post primary unilateral
23 active post primary bilateral

We are concerned here only with cases which were considered to be active by one or both observers (although this does not necessarily mean they were clinically active) and with the efficiency of miniature film reading

The survey revealed a total of 67 cases which were agreed by both observers to require further clinical investigation The results of the dual reading of the miniature film of these cases are shown in table II

It is clear that in many of the observer-error trials, opinions are expressed on figures which are far too small Thus the much quoted American figures of one series were based on 30 subjects out of 1800 students, Stradling and Johnston's figures [5] on 198 out of 1000, and our own on only 67 out of 10,000

Both observers recalled only 77 5% of the total, but each separately did better A recalled 91 5% and B 86 5% In other words, under-reading of agreed abnormals was 8 5% by A and 13·5% by B These figures are in close accord with those of Stradling and Johnston, who stated that "It will be seen that our under-reading error when viewing single postero anterior films alone is 9 11%"

Other American figures, quoted by Birkelo and Yerushalmy in 1947, were that for 1256 persons, 131 films were called "positive" by one or more readers and for different readers, the number varied from 56–100

Stradling and Johnston in considering the under-reading error, which appears lower than that found by the American workers, quote factors which may be of importance

(1) The American figures relate to minimal tuberculous lesions, whereas theirs contain the mixed abnormalities observed in routine practice

(2) The agreed abnormals in the American series are relatively small groups, 30 out of 1790 Their English group contained a higher proportion of abnormals—198 out of 1000

In our results, so similar to theirs, these factors do not obtain, for most of our cases involved minimal lesions occurring in National Service recruits, and, moreover, they were diluted, not at the rate of 30 out of 1790, but 67 out of 10,000

As far as the mass X-ray cases are concerned, it would appear that there is greater difficulty in recognising active primary lesions and the least difficulty from *bilateral lesions—but it is clear that far more extensive* trials would be necessary to elucidate these points

It must be borne in mind that these 67 cases labelled "active" are not by any means necessarily so In fact, in mass surveys, the majority are reported on by the chest clinics as inactive and not requiring treatment If half the cases were active, which may be so in this series since most were found in National Service recruits, then the number of truly active cases missed by A was around 5% and by B 7%

We have discussed this problem with Dr Peter Kerley and he agrees with us that observer error is significantly increased (*a*) by indifferent technique, (*b*) by inexperience and lack of training, and (*c*) by attempting to read too many films too quickly All these factors could readily be eliminated Many people are using X-ray apparatus without any training in technique and they lack experience of the quality of film required In addition, many readers have insufficient experience of minimal lesions and are apt to miss them or fail to appreciate their significance

A J Eley
London T G Paxon

VISITING IN MENTAL HOSPITALS

Sir,—Dr Salfield is right when he states that mental disorder, though sometimes treatable by physical means, remains *mental*, right again, when he suggests that no problems of life can be solved by physical treatment, but he is wrong in not agreeing that unrestricted visits is the first essential It is simply because the illness is *mental* that we must never lose sight of the fact that the sole objective of psychiatry is to ease the minds of the mentally ill

Although we like to pretend otherwise, the fact is that by far the greatest number of admissions are those admitted against their will, and it is only natural that these frightened and bewildered persons should seek that sympathy, comfort, hope, and assurance that *only* relatives and friends can give Moreover—apart from the fact that my opinion is based on a point-blank study carried out continuously for seventeen years—I should like to remind Dr Salfield that the Royal Medico Psychological Association represents the great majority of our psychiatrists, and that it was their representative committee who proudly informed the Royal Commission of their unanimous desire for unrestricted visits

That there is a shortage of nursing and medical staff is true, it is to be regretted and deplored, but it is, however, beside the point

Edzell, Angus H G Woodley

RESIN-REINFORCED PLASTER CASTS

Sir,—In 1953 I reported the results of a trial of plaster casts using bandages soaked in a freshly prepared solution of melamine resin with ammonium chloride as catalyst [1] At that time I suggested that it would be helpful if the resin and catalyst were incorporated in plaster bandages Such bandages have been produced, and I have tried them with similar results to those reported previously

The casts made from them are lighter, stronger, and more durable than those made from ordinary plaster bandages Moreover, it is noted that when one has finished making a plaster cast, hardly any plaster has *fallen out of the bandage into the basin containing the* water used to moisten the bandage This is in sharp contrast to the heavy deposit found when bandages are home made and to a lesser extent when machine made Sayle Creer [2] confirms this The cost of these bandages is slightly greater than that of the ordinary plaster bandage, but in practice fewer bandages are needed, thus in the end effecting a saving For example, a satisfactory wrist cock-up splint was made using only one bandage as an anterior slab, and fixing it with a gauze bandage It weighed 107 g when dry, compared with 184 g when

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[5] Stradling P Johnston R N *Ibid* p 1247

[1] *Lancet*, 1953, ii 1317

[2] Sayle Creer W *J Bone Jt Surg* 1955 37B, 640

All of these are extremely dangerous to life ldiction to methylated spirit is explained by the fact at the spirit consists mainly of ethyl alcohol

In our addiction unit we discourage the notion that e drinker of methylated spirit is a lower type than her addicts to alcohol We find he is almost equally pable of rehabilitation Indeed drinkers of methylated rit show some favourable qualities · for the most part ey live quietly and cheaply, often sleep rough, and rgely keep out of the way of other people Most of em do casual work and live and drink at a very low ost Among our patients the incidence of theft petty aud, begging, and all crimes other than drunkenness, , remarkably low We know of no type of patient who esponds with such warmth to sympathetic interest and riendliness

Methylated Spirit

The official name is industrial methylated spirit It sold mainly for use in industry, but certain domestic ises—e g , as fuel for spirit-lamps—are also recognised The Methylated Spirit (Sale by Retail) Scotland Act, 1937, secures that the purchaser enters in a register his name, address, the quantity obtained, and the purpose or which the spirit is to be used. Sellers have to be registered with the local authority, and a label on the bottle must indicate the name and address of the seller ere is no similar restriction to the sale of surgical irit, which by volume is just over 95% methylated spirit

The *British Pharmaceutical Codex* (1954) defines methylated spirit as " a mixture, made by a legally authorised methylator of 19 volumes of alcohol (95 per cent) with 1 volume of approved wood naphtha " The latter substance consists mainly of methyl alcohol and gives to the mixture its 4% of that substance The *B P C* describes the spirit as " a colourless mobile volatile liquid with an odour of alcohol and wood naphtha and a burning taste "

The taste is so repulsive that aversion to it is never ercome, but when it is highly diluted with water, all soned drinkers find it potable When occasionally ey can afford cheap wine or beer, however, they prefer fortify these drinks with methylated spirit Sometimes hey will add the spirit to tea or to sugared water

Methylated spirit is less dangerous to life than is often supposed We have never found the specific lesions of poisoning with methyl alcohol—i e , optic neuritis or atrophy—in any of these patients The findings are the same as in cases of prolonged overdosage with ethyl alcohol For instance, polyneuritis is often present Addicts to methylated spirit show a slightly higher incidence of this condition than do addicts to other alcoholic drinks, but this may be wholly due to the fact that they tend more than the others to neglect their general nutrition while drinking

That the effects of these two types of drinking differ so little from one another is probably because methylated spirit contains only 4% or less of methyl alcohol, and the overwhelming preponderance of ethyl alcohol tends to prevent the oxidation and conversion of the methyl alcohol to formic acid Indeed ethyl alcohol can be used effectively in the treatment of poisoning by methyl alcohol

In Great Britain, fortunately, methylated spirit and its derivatives are the only liquids containing methyl alcohol that are used widely or regularly The drinking of concoctions containing a high percentage of methyl alcohol has been rare and almost limited to the latter period of the late war and the immediate post-war years in which whisky remained scarce In all such cases the victims obtained " whisky," &c , from irregular sources, thinking that they were buying good drink In the U S A during the prohibition period wood alcohol with a high content of methyl alcohol was sold by some bootleggers, and 444 deaths due to poisoning by methyl alcohol from this source were recorded in 1931.

The Addicts

Weeks (1938) states

" Methylated Spirit drinking is the last stage of alcoholic excess , no one ever starts to drink such stuff, but when the appetite has been whetted by other forms of alcohol, when means to buy decent drink are not available and craving comes, these unfortunate victims turn to anything "

Weeks showed, perhaps, a little less than his usual sympathetic understanding in this summing up We cannot agree that the drinking of methylated spirit is " the last stage of alcoholic excess " Addicts to ordinary alcohol can and do go to hell as effectively and more devastatingly than the drinker of methylated spirit when having used up their normal resources, they insist on still drinking brandy or whisky at the expense of selling their furniture, realising on life policies, mortgaging houses, " borrowing " from relations and friends, &c Also the " whetting of the appetite by other forms of alcohol " is not our experience of drinkers of methylated spirit Not, one of them developed a *preference* for methylated spirit . all would have preferred to continue drinking whisky

Emotional blunting, a tendency to vagrancy, pessimism of outlook and depression are characteristic of typical drinkers of methylated spirit They are also poorly socialised but nevertheless show a pseudo gregariousness by sharing sleeping-out places—e g in yards and lofts of brick-works Their drinking too is often communal because it is more economical to share a bottle among a group This description closely resembles the classical picture of simple schizophrenia We do not however, find that these people are actively psychotic Their auto sedation, their self-exclusion from friction with society, and the leaning on each other of the group life they evolve seem, in combination to save them from psychotic breakdown They are not solitary, bearded, and almost wordless tramps like the schizophrenics of the type they resemble They may be down-at-heel and shabby, but they retain an interest in washing and shaving

Of the 21 male drinkers of methylated spirit who were inpatients in 1955 all but 3 showed the personality features outlined above Cases 3 and 7 (see below) are 2 of the 3 atypical cases Both of these men are hearty hypomanic extraverts

Not one of our drinkers of methylated spirit has been a dullard or mentally defective All have been average or above average in intelligence

Admissions

The Addiction Unit was started at Gartloch Hospital in March, 1950 An Alcoholics Anonymous (A A) group was founded at the hospital in January, 1951 This was the first hospital A A group, affiliated to the parent body, to be founded in Europe From the patients drinkers of methylated spirit were among the first admitted, the first, a man with over 200 convictions, arriving in May, 1950 The following are the figures

Year	*Addicts to alcohol*	*Drinkers of methylated spirit*
1950	30 (3 F)	3 (10 0%)
1951	44 (6 F)	3 (6 8%)
1952	97 (7 F)	5 (5 1%)
1953	113 (4 F)	12 (10 6%)
1954	133 (6 F)	15 (11 3%)
1955 (to end of July)	134 (4 F)	22 (1 F) (16 4%)

F, female

The 60 drinkers of methylated spirit include only 1 female, and the 549 addicts of alcohol include only 30 females In each case our figures give a misleading impression of the sex-distribution nationally, which is probably about 9 males to 2 females The explanation is that the Addiction Unit has grown up on the male side

I wish to thank Prof J Rutkowski and Prof R Pakula for their valuable advice, and Dr B Marzinek, Dr M Brzeziński, Dr M Baranski, and Dr L Landowski for their help in the investigations I administered to these patients 'Distreptase,' containing both enzymes, and sometimes either streptokinase or streptodornase In all these cases I used only the products of the Polish Institute of Hygiene

Surgical Ambulatorium
of the Health Department,
Warsaw

HENRYK RYKOWSKI

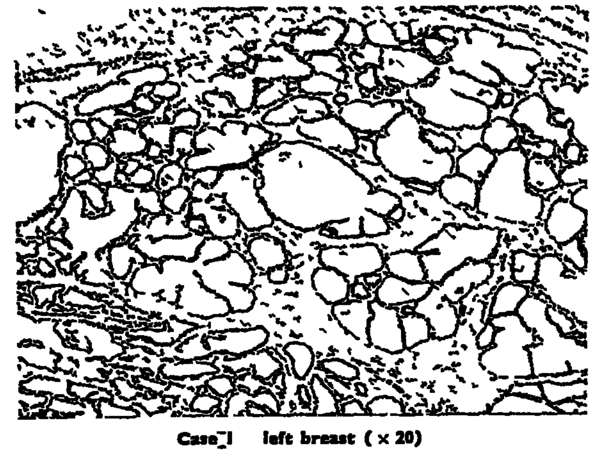
BREAST CHANGES IN FIBROCYSTIC DISEASE OF THE PANCREAS

SIR,—In raising the question of the relation of breast enlargement to fibrocystic disease of the pancreas, Dr Jolly[1] referred to three cases in which these conditions coexisted One of these cases has now come to necropsy and we report here the clinical and histological findings The clinical aspects of a second case, still alive, are also presented

CASE 1, a female, was first seen at 2 weeks of age, when mucoviscidosis was diagnosed Both breasts were much enlarged Subsequently treatment consisted in administration of oxygen and, at different times, penicillin, oxytetracycline, chloramphenicol, and erythromycin but not aureomycin The breasts remained in the same state till death at the age of 6 weeks Necropsy revealed cystic fibrosis of the pancreas and suppurative bronchopneumonia, from the lungs *Pseudomonas pyocyanea*, an anthracoid bacillus, *Staphylococcus albus*, and a non hæmolytic streptococcus were isolated From the enlarged breasts a thin opaque secretion could be expressed, and on section (see figure) greatly dilated ducts and acini, lined by a flattened epithelium, were set in a dense fibrous stroma, there was little secretion in the cystic spaces Mucin stains (mucicarmine and periodic acid/Schiff reaction) of breast and pancreas gave indefinite results

CASE 2 is a female, aged 2 years, in whom mucoviscidosis was diagnosed at the age of 1 month, when the breasts were not enlarged Enlargement was observed by one of us (C E S) between the ages of 5 and 14 months, when aureomycin was administered intermittently Subsequently aureomycin therapy was stopped, and the breast enlargement subsided and has not recurred This child's elder sister also has mucoviscidosis and treatment included aureomycin, but no enlargement of the breasts was observed

Since the breast is essentially a serous gland, Lightwood[2] felt that it was unlikely to be involved in fibrocystic disease of the pancreas, but di Sant' Agnese et al[3] found that the electrolyte composition of the sweat was abnormal in this disease and suggested that all exocrine glands, whether mucus producing or not, are affected We know of no reference to morphological changes in the breast or sweat-glands in pancreatic fibrocystic disease, and accordingly in case 1 the alternative diagnosis of "neonatal mastitis" was considered Forssell[4] described 92 cases of this condition and showed that secretion of "witch's milk" and the associated histological changes not infrequently persisted for several months In the light of Forssell's observations we conclude that case 1 is an example of "mastitis neonatorum"



Case 1 left breast (× 20)

Our experience and that of others[1 2 5] might suggest that there is more than one cause of breast enlargement in mucoviscidosis Enlargement soon after birth almost certainly represents "mastitis neonatorum," but in other cases the swelling occurs later and may be related to antibiotic therapy "Mastitis neonatorum" is ascribed by Forssell to maternal œstrogens If certain antibiotics augment the circulating œstrogens by reducing vitamin B intake,[5 6] then breast enlargement after their administration, whether in mucoviscidosis or not, has a fundamentally similar pathogenesis to that of "mastitis neonatorum" We have not yet had the opportunity of studying the histology of enlarged breasts following aureomycin or oxytetracycline therapy, but on this hypothesis the structural changes should be similar to those in case 1 In Dr Jolly's cases of fibrocystic disease, enlargement of the breasts was not apparently related to aureomycin treatment, but aureomycin is not the only drug associated with breast enlargement,[5] and it would therefore be of value to know if his cases received any other antibiotics If aureomycin and oxytetracycline act by interfering with assimilation of vitamin B the response to vitamin-B therapy would be worth knowing It is difficult at this stage to explain why breast enlargement affects only some patients who receive aureomycin

Department of Child Health
C E STROUD

Department of Pathology
Welsh National School of
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A G HEPPLESTON

ORDEAL BY TREATMENT

SIR,—In recent visits to a friend in a surgical ward, I have been shocked by the changes that seem to have taken place in the ten years since I myself had several major operations Perhaps it may be useful to doctors to know how this transformation strikes a layman

Starting before operation, the passage of a nasal tube is presented to the patient as a great modern boon which prevents postoperative pneumonia But this "boon" can be a humiliating and painful affair I myself saw patients coughing, choking, and struggling as the young nurse tried and tried again to work the long tube up the nose and down the throat

As soon as possible after recovering from the anæsthetic, the patient is made to do exercises with the hands, later with the arms and head Vigorous young women come round and pommel him on the back saying, "now please cough," again and again One can hear patients swearing and groaning under this treatment

Beds being still scarce, there is a strong desire to get rid of the patient quickly There is also immense pride in getting him up and walking within a few days of the operation To the layman it seems little short of lunacy that, seven days after big abdominal operations, the patients who were so recently very ill should be struggling about and going to the lavatory on their own If (as happened in my friend's case) the outside and the inside wound reopens, they just have to be in for another week—too bad To boast about young people being out of bed twenty four hours after an appendicitis operation seems to me like boasting about car speed records—and on the same level

Judging by what I have seen, and heard from patients who have had major operations, no forty five minutes pass between 6 30 A M and 10 P M but a nurse appears with a needle for an injection of penicillin (every four hours), or of some vitamin, or of something to prevent the blood from

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[1] Jolly H *Lancet*, 1955, ii 1136

[2] See Hesling G *Ibid* p 1246

[3] di Sant Agnese P A Darling, R C Perara G A Shea, E *Amer J Med* 1953, 15, 777

[4] Forssell, P *Acta pædiat*, *Stockh* 1938, 23, suppl 1

[5] Hubble, D *Lancet*, 1955, ii, 1246

[6] Biskind, M S, Biskind G R *Endocrinology*, 1942, 31, 109

4, to December, 1955) About 50 were, in fact, sent during the whole two years In January, 1955, re were 58 chronic schizophrenics, 9 deteriorated leptics, 1 G P I, and 1 case of organic dementia The erage stay in hospital was over eleven years

The Ward was on the ground floor, shaped liked a V, th entrances on the main corridor at each end It ntained a dining room and day-room, separated by a ass partition, with a single large dormitory leading off e day-room The floors were of parquet The ward d not been painted since 1925, and the prevailing colour heme was olive green and black The day room urniture consisted of bench-type seats and single chairs n a bad state of repair and many damaged by patients), There was full size billiards table, and a television set closed garden leading out of the ward

THE PROBLEM

his ward, with its drab and depressing appearance, d complement of deteriorated patients, was looked on the nursing staff as a hopeless task Their attitude wards it was one of resignation and acceptance of the recarious equilibrium The main object was to prevent ny aggressive behaviour by patients, who were put to ed if they were at all disturbed About two thirds of them spent most of the day sitting in the day-room or (in fine weather) in the ward garden The remaining third were actively employed on ward work, or in other simple occupations The junior nurses regarded their duties on this ward as a necessary part of their syllabus, but beyond this they showed no interest, counting it only as so much time to be passed Routine within the ward was sadly lacking, and the behaviour of patients left much to be desired

The general feeling in the hospital was that something must be done, but it was difficult to see where to begin

THE METHOD

In April, 1955, two new charge nurses were appointed, one on each shift, and the problem was presented to them as a challenge There were never more than three nurses on each shift, including the charge nurse, and the working parties which were formed comprised about 17 patients

An important first step was to ensure that all the nurses understood clearly the aims in view and were aware of the support they would receive This was done by meetings between the administrative and ward staff and by frequent ward meetings, two or three times a week at first Within a general framework the charge nurses were given considerable freedom of action and were largely responsible for the details of the reorganisation

This reorganisation was based on three principles useful employment of all patients physically fit, a routine pattern of life within the ward community, and increased attention to social needs

Employment —Owing to their deterioration it was impossible to make any great increase in the proportion of patients employed in hospital departments, though an additional 8 were considered suitable for work in the closed occupational therapy centre All those who had been euphemistically designated as ward workers were reviewed 6 were chosen for ward duties under the charge nurse and the remaining 35 were divided into two working parties Each party was always supervised by the same junior nurse and it was not difficult to find routine work in which even the most withdrawn patient could be encouraged to share For example, these parties have been lifting potatoes, clearing brushwood, and moving and cleaning bricks for use in building a new occupational therapy centre It is important for the nurse as well as for the patients that the work should be useful and not just a way of passing the time

Routine —A set pattern was laid down from the start, and all nurses concentrated on teaching patients this new social pattern at all times in the ward At first it was uphill work Changing of outdoor boots, washing, toilet routine, behaviour at meal times, attention to person and dress, and so on, were continually emphasised, and the routine was underlined wherever possible by association and by adhering to a fixed time table (table I)

During the period of this study 10 patients from this ward participated in a habit training experiment in which efforts at improvement were more intensive This will be described elsewhere

Social Activity —As habits and behaviour improved, more and more patients joined in mixed social activities in the main hall Weekly social evenings were also started on an exchange basis with a similar ward of women patients, when games and dancing were organised on the wards These social evenings evoked more spontaneous reactions from patients, who entered into dancing and team games with less and less encouragement The two working parties were also sent to "Movement with music" classes once a week, where they mixed with similar women patients under the charge of a visiting instructor In addition, they had P T classes every morning with emphasis on team games

In September, 1955, the ward was entirely redecorated in modern pastel shades The staff were pleased, and, though the patients expressed no very positive opinions, there was no defacing of walls and in their cleaning duties patients have preserved the new appearance. Furniture was repaired and re upholstered in the hospital departments and the black iron bedsteads were stripped and repainted in bright colours by patients in the occupational-therapy centre

TABLE I—AVERAGE DAY ON LONG STAY WARD FOR DETERIORATED MALE PATIENTS

35 patients in two groups (I and II)
4 patients unfit
25 reasonably well preserved and working in various hospital departments
6 patients as regular ward workers

7 15 A M	Rise Nurses in charge of groups I and II issue clothing to them from their individual lockers and supervise their toilet and bedmaking Charge nurse supervises remainder who being better preserved mostly look after themselves
8 00 A M	Breakfast
8 30 A M	Group I taken for physical training by instructor Group II ward work Remaining patients out to work in various departments
9 15 A M	Tea break and change into outdoor boots
9 30 A M	The two groups in the charge of their respective nurses do work specified by occupational therapy supervisor (e g, cleaning bricks or digging) or 'basic movement,' Mondays and Thursdays (I or II)
11 30 A M	All patients back in ward Change boots supervision of toilet
12 NOON	Lunch
12 45–1 15 P M	Double shift on—therefore Shaving bathing hair cutting
2 00 P M	All patients including groups out to work or visitors on visiting day or organised games Tuesday and Thursday on recreation field
3 45 P M	All patients back in ward Change boots, supervision of toilet
4 30 P M	Tea
5 00 P M	Social events Cinema, plays dancing, inter ward games inter ward parties television
8 15–8 45 P M	Preparation for bed

THE RESULTS

The Fergus Falls Behaviour Rating Scale[1] was used to assess the behaviour of the 54 patients who were in the ward throughout 1954 and 1955 The 10 in the habit training group showed an average gain of 5 4 points in the six months between April and October, 1955, while the remaining 44 gained 4 2 points

The ward records reflect changes in behaviour and socialisation (table II) The comparison is made between conditions in 1954 and 1955, since the type of patient in the ward remained stable during that period There was aided, if necessary, by an Oxford inflating bellows, using a face mask In cases with moderately severe respiratory paralysis, a portable cuirass respirator, such as the Monaghan, was tried but was ineffective Some patients with very extensive respiratory paralysis, already in a tank respirator, were transferred to the unit A large coach type ambulance with seats removed was supplied, and the patients were transported in an iron lung, the pump unit being operated manually Before the journey a Ryle's tube was passed and *the stomach emptied in case acute dilatation occurred in* the ambulance

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[1] Lucero, R J, Meyer, B T J clin Psychol 1951, 7, 250

1377

Combined Bulbar and Respiratory Paralysis

These cases can be divided into two categories (*a*) established respiratory paralysis with definite bulbar signs, and (*b*) established bulbar paralysis with slight respiratory involvement

Patients in the first of these two groups were, usually not difficult to manage during transport as they had already had a tracheotomy done They were placed on *their back on the ambulance stretcher*, and pulmonary ventilation was maintained by manual operation of an intermittent positive pressure apparatus (e g, Oxford inflating bellows), with or without added oxygen run through the inflation circuit These cases appeared to be the safest to transport, since there was an established airway well below the pooled secretions in the pharynx and larynx Since the endotracheal tube was cuffed, these secretions could not leak into the trachea and main bronchi Tracheal phlegm was easily aspirated by suction through the endotracheal tube Pharyngeal pooling was prevented by frequent suction through the patient's mouth

The patients that caused most anxiety during the *ambulance journey were those with fully established* bulbar paralysis with slight respiratory involvement (e g, with paresis of the lower intercostal muscles) The problem was *to* assess how well *this type of patient could* tolerate a journey of up to thirty miles If a tracheotomy is not considered necessary the patient must be transported in a prone and tilted position, because of the bulbar paralysis But there are certain disadvantages in this position, especially in a moving vehicle The diaphragm has extra work to do, because of the weak lower intercostal muscles, the added weight of the abdominal viscera, and compression of the chest against the stretcher and the paralysis may not yet be at its maximum Some of these patients who had not had a tracheotomy (respiratory aid not seeming necessary) caused considerable anxiety during the journey Their general condition deteriorated, with vomiting, copious secretion of saliva and mucus, and laboured breathing, this happened despite continuous suction from the mouth and pharynx to maintain a clear airway—a life saving but, for the patient, extremely exhausting measure On arrival at the unit some of these patients were very exhausted, with an apparent increase of the respiratory paralysis, in 1 patient an immediate tracheotomy was necessary on arrival In view of our experiences, we feel that a tracheotomy should always be seriously considered in this type of case before the journey, especially if it is a long one It is always safer to transport such a patient with a cuffed tracheotomy tube in position It may then not even be necessary to aid the patient's breathing by intermittent-positive pressure apparatus, and the patient can lie in comfort on his back during the journey Pharyngeal secretions are prevented from entering the trachea by the cuffed tube, and by adequate suction

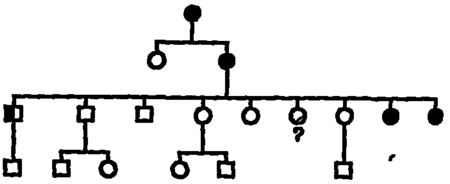
We should like to emphasise the importance of seeking early assistance for patients with the types of poliomyelitis described here Where this was done we found that, as a rule, the transport of the patient caused less anxiety and the prognosis was correspondingly better

We should like to thank Dr E James, under whose care these patients were admitted, for his helpful criticism and advice, and for the opportunity of supervising their transfer

ANTHONY F C SCOTT
BEULAH R KNOX

HAMMER-TOES IN THREE GENERATIONS

SIR,—The accompanying pedigree shows hammer toe in three generations of a family, involving the second toe of both feet in the four females affected and of the left foot alone in the one male affected A fifth female in the second filial generation is said to have shown this condition as a baby but was cured by the application of little splints to stretch the toe, little malformation can be observed now



The flexor digitorum brevis muscle arises from the calcaneum, passes forwards across the arch of the foot, and divides into four tendons, one of which is inserted into the middle phalanx of each of the four minor toes Their action is to flex the middle phalanges on the proximal ones In the present cases the tendon supplying the second toe only is congenitally short, resulting in a hammer toe The parents and two siblings of the progenitor of this condition, together with their fairly closely inbred descendants, show no sign of it

It has been suggested that this is an example of sex limitation

London, E 2 PATRICK JAMES

TREATMENT OF BEDSORES

Dr L GUTTMANN, director of the National Spinal Injuries Centre, Stoke Mandeville Hospital, Aylesbury, Bucks, writes It has been brought to my notice that in 1954 you reported me as recommending, in the course of a lecture, the application to bedsores of a pack moistened with 'Dettol' solution[1] In fact I did not mention dettol, and I consider that the use of this substance is absolutely contra indicated in the treatment of such lesions My views on their treatment have been set out elsewhere[2]

AMATEUR BOXING

Dr J L BRONSTEIN, hon medical officer of the London Amateur Boxing Association, writes Under its medical welfare scheme the association has made it compulsory for all boxers to have an initial medical examination Will those doctors who are interested in amateur boxing and are not already on the panel of boxing medical officers please communicate with me at the London A B A, 69, Victoria Street, London, S W 1, *if they would like to participate in this scheme?*

Appointments

CHURCH R F M D Camb, M R C P part time consultant dermatologist duties at Grimsby, Scunthorpe Louth, and Lincoln

HIND A W, M B Lond F F A R C S, D A consultant anaesthetist Royal Masonic Hospital London

SIMPSON J H M D Camb M R C P asst physician in geriatrics Norfolk and Norwich area

SMITH P A J M B Lond M R C P consultant dermatologist Queen Mary's Hospital, Roehampton, London

STILLER, L V, M D Lond M R C P asst physician (geriatrics) Buckinghamshire area

THORNTON D J M R C S registrar in ophthalmology, Norfolk and Norwich Hospital

TROWBRIDGE G E M B Birm, M R C P asst chest physician, Hawkmoor Chest Hospital, Bovey Tracey Devon

WETHERELL G A, M B, M CH ORTH Lpool F R C S whole time asst orthopaedic surgeon Clatterbridge Hospital

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1 *Lancet* 1954, ii 98
2 e g, *Brit J plast Surg* 1955, 7 106

enzyme was also responsible for inactivation of sero- n He considered the storage of serotonin in cyto- mic granules in relation to the ability of reserpine elease serotonin

)r H McIlwain described biochemical work by A Wollenberger on protoveratrine, one of the vera- m alkaloids It greatly increased the respiration and colysis of cerebral tissue, decreased its anaerobic colysis and increased its response to electrical pulses ese actions appeared to be due to delaying the ccumulation of potassium ions

Pharmacology of Hypotensive Drugs

Dr J Tripod (Basle) discussed some pharmacological fferences between hypotensive drugs, with special ference to hydrallazine and reserpine Such drugs nded to fall into different groups according to their teraction with a series of pharmacological antagonists, pending on the concentration of oxygen or electro- tes in the medium He had found that the fall in blood- essure produced by hydrallazine could be entirely oolished by previous incubation with certain sera It ad not been possible to identify the constituent of serum ith which hydrallazine reacted Other hypotensive gents, including reserpine did not show this feature

The site and mode of action of reserpine were discussed y Dr Marthe Vogt (Edinburgh) Its hypotensive ction was central in origin and this and its sedative ction might be mediated through the hypothalamus These central actions might be due to the release of large uantities of serotonin (5-hydroxytryptamine) from the owel, brain, and platelets All rauwolfia alkaloids which had a tranquillising action also released serotonin The central actions of reserpine and serotonin were antagonised in the same way by substances such as lysergic acid diethylamide, morphine and methadone On the other hand, central nervous effects resembling those of reserpine had not been reported in patients with argentaffin tumours and a high level of circulating serotonin

Dr W S Peart discussed the β haloalkylamines, which are potent antagonists to adrenaline and noradrenaline One of the most active of these compounds was dibenyline (n-phenoxyisopropyl-n-benzyl chlor ethylamine) In man these compounds produced postural ypotension, miosis and vasodilatation in the skin Their action seemed to be entirely peripheral, locally in the arteriolar wall Dr J G Widdicombe, who dealt with the veratrum alkaloids, said that although they were first investigated over eighty years ago, we still do not know for certain their mode of action in man In animals they produced hypotension and bradycardia by eliciting the Bezold reflex, the sensory end-organs for which lay in the ventricular muscle of the heart In addition it was known that veratrum could cause hypotension by a direct action on the central nervous system The fact that they seemed to exert no effect on the motor side of ardiovascular reflexes, so that postural reflexes were tained had been cited in favour of their therapeutic e in hypertension

The pharmacology of ganglion-blocking agents was discussed by Dr E Zaimis They interrupted transmission in autonomic ganglia by competition with acetylcholine—a mechanism which left preganglionic nerve endings and the ganglion cells unaffected Referring to the tolerance to the hypotensive action of these drugs observed clinically during the initial weeks of their administration Dr Zaimis thought that it was unlikely that this was due to a decreasing sensitivity of the ganglia to the blocking action of the drugs Clinical observations suggested that no tolerance developed in parasympathetic ganglia Further, animal experiments showed that sympathetic ganglia acquired increasing rather than decreasing sensitivity to subsequent doses It appeared possible that the reduced effect on blood-pressure resulting from repeated administration was due to sensitisation of the periphery to adrenaline and noradrenaline

In the discussion Prof F H Smirk (Dunedin New Zealand) described pharmacological experiments in his department suggesting that reserpine had a peripheral action Dr P B Bradley (Birmingham) said that in the cat the effect of reserpine on the electro-encephalogram was similar to that produced by the intraventricular injection of serotonin Dr M Harington described experiments demonstrating the summation of the actions of single intravenous doses of reserpine and hexamethonium in hypertensive patients There was some evidence to suggest that the hypotensive action of hexamethonium might be potentiated after reserpine

Clinical Applications of Hypotensive Drugs

Prof J McMichael described the results of treating patients with malignant hypertension with methonium compounds for five years Hexamethonium or pentolinium was given by parenteral injection, oral administration being avoided because of irregularity of absorption Recently, small doses of reserpine had been added Of 73 patients with malignant hypertension 11 were unsuitable for treatment, being admitted moribund from cerebral hæmorrhage or advanced uræmia The results were most favourable in 52 patients whose blood-urea level was initially under 60 mg per 100 ml; with methonium treatment, in this group the five year life expectancy was 50% The disappearance of retinitis was the most dramatic event following reduction in blood-pressure, fresh hæmorrhages and exudates vanishing in a few weeks, but papillœdema took from two to ten months to disappear The intense morning headache was immediately and completely relieved Gross and severe heart-failure could vanish dramatically The heart size often diminished notably, but the electrocardiographic changes decreased more slowly In 5 patients a peculiar type of organising œdema of the lungs had developed There was no evidence that treatment with methonium drugs led to deterioration of kidney function Pathological study showed that fibrinoid necrosis in arterioles and glomeruli could undergo collagenisation and healing, but the risks of cerebral thrombosis and hæmorrhage and of coronary thrombosis were still present in proportion to the severity of already established arterial disease

The principles of treatment at the hypertension clinic in the University of Otago were described by Professor Smirk He said that the improvement in clinical manifestations and in prognosis were closely related to the degree of control over the blood-pressure The systolic blood-pressure was kept if possible, between 110 and 140 mm Hg, measured in the standing posture although the range was often 85–160 Over a period of six years, there were 25 survivors out of 44 with malignant hypertension or nearly 57%, the survival-rate in the Keith-Wagener series of untreated patients was 2% in the same period In the past six years 320 patients in grades II, III, and IV had been treated and there had been 80 deaths—a survival-rate in all groups of 75% In the past eighteen months treatment had been with pentolinium usually administered orally, together with one of the rauwolfia alkaloids Patients first spent five whole days a week at the clinic and the blood-pressure was recorded every half-hour by a technician As improvement took place, the patients attended for two whole days a week, then one day, and finally they attended only occasionally Advantage was taken of the standing or sitting posture to enhance the decrease in blood-pressure Patients sat propped up at night, or else the head of the bed was raised on blocks Professor Smirk said that he had tried 'Ecolid' and mecamylamine, but they both produced malaise, and parasympathetic side-effects were prominent

Royal Australasian College of Physicians

At the annual meeting of the college held in Wellington, New Zealand, in March, the following took office for 1956–58

President, Dr E G Sayers, vice presidents, Dr Bruce Hunt, Dr C H Fitts, Dr C R Burns censor in chief Dr T M Greenaway, honorary treasurer, Dr W P MacCallum, honorary secretary Dr H M Rennie, past president, Dr C G McDonald

The following were elected to the fellowship

Dr A J Barnett Dr J J Billings, Dr H W Garlick Dr D R Gauld, Dr E A North, and Dr R F A Strang (Victoria), Dr S P Bellmaine, Dr A E McGuinness and Dr R B Perkins (New South Wales), Dr O Hirschfeld (Queensland), Dr E G Saint (Western Australia), Dr E G Sims and Dr R T Binns (South Australia)

The following, having satisfied the board of censors in New Zealand, were admitted to membership

Dr J Apthorp, Dr D W Beaven, Dr M I Bostock Dr D S P Dickson Dr G L Glasgow Dr J D Sinclair, Dr P Fleischl Dr J V Hodge, Dr M J A McDonald, Dr A R Stone, Dr V I E Whitehead, Dr A C H Wilkinson

Dr R H Black and Dr H M Whyte of New South Wales were admitted to membership under the special provisions of article 37

Institute of Diseases of the Chest, London

Clinical demonstrations are being given by Dr F P Lee Lander at the institute (in the grounds of the Brompton Hospital, Fulham Road, S W 3) on Fridays and will continue till July 6 All the meetings are open to doctors without fee and will be held at 5 P M

Vital Statistics in Psychiatry

The Society for Visiting Scientists is holding a discussion on this subject on Wednesday, April 25, at 7 30 P M, at 5, Old Burlington Street, London, W 1 Prof Aubrey Lewis will preside, and the speakers will be Dr Vera Norris, Prof L S Penrose, F R S, and Dr Peter Sainsbury

Service Appointments

Dr F C Golding has been appointed honorary civil consultant in diagnostic radiology to the Royal Air Force

Sir John Parkinson, on resigning his appointment as civil consultant in cardiology, has been appointed honorary consultant in cardiology to the R A F

Miss B Nockolds, R R C, has been appointed matron in chief of the Queen Alexandra's Royal Naval Nursing Service

Cancer Consultation Clinics

For twelve years the Royal Marsden Hospital has been running joint cancer consultation clinics between physicians surgeons, and radiotherapists in association with a group of London hospitals including the Brompton Hospital for Diseases of the Chest, the Chelsea Hospital for Women, the Royal National Throat, Nose, and Ear Hospital, Moorfields, Westminster, and Central Eye Hospitals, the National Hospital, Queen Square, and St Peter's, St Paul's, and St Philip's Hospital Over 1000 new patients are now seen each year On Friday, May 11, an all day meeting (10 A M – 5 P M) is to be held at the Royal College of Surgeons, Lincoln's Inn Fields, W C 2, to report on the work of the group, and on the following morning there will be a demonstration at the Royal Marsden Hospital Programmes of the meeting may be had from the House Governor, Royal Marsden Hospital, London, S W 3

Presentation to Sir Thomas Fairbank

Sir Thomas Fairbank's former house surgeons at King's College Hospital, and other colleagues who worked with him there and at the Hospital for Sick Children, Great *Ormond Street*, have presented him with his portrait by Mr Maurice Codner, R P Proposing his health at an informal dinner held in London on April 14, Mr Harold Edwards said that the reason for the presentation was not his world renown as an orthopædic surgeon (though they were intensely proud of him on this account) but their respect and affection for him as a leader and a friend To those who had had the good fortune to work for him during their formative years he had set a standard, both professional and ethical, which had been of incalculable benefit The portrait was formally presented by Dr Alfred Mitchell the oldest house surgeon present, and Mr H L C Wood the present senior orthopædist to the King's College Hospital Dr W H Scriven then presented Lady Fairbank with a framed photograph of the portrait, in recognition of her many kindnesses to the former house surgeons, both before and since Sir Thomas's retirement

Chelsea Clinical Society

The annual dinner of this society will be held at the Rembrandt Hotel, Thurloe Place, S W 7, on Tuesday, May 1 at 7 30 P M The Marquess of Salisbury will attend

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At the invitation of the Royal Colleges of Surgeons of England and Edinburgh and the British Council, Prof Peter Andreevich Kupriyanov, principal of surgery in the Kirov Military Medical Academy at Leningrad, Prof Andrew Gregorievich Savinikh, principal of surgery at Tomsk Medical Institute, and Dr D D Benediktov, director of the surgical clinic of the Second Moscow Medical Institute are visiting this country from April 15 to May 5

CORRIGENDUM *Pulmonary Embolism and 5 hydroxytryptamine*—In the second paragraph of Dr Kenneth Carter's letter last week (p 446) the third sentence should begin "Replacing one benzyl group by a phenoxyisopropyl group results in *n* phenoxyisopropyl *n* benzyl β chlorethylamine hydrochloride "

Diary of the Week

APRIL 22 TO 28

Monday, 23rd

MANCHESTER MEDICAL SOCIETY
9 P M (University of Manchester) *General Practice* Dr H P Fay Responsibilities in General Practice (Presidential address)

Tuesday, 24th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln s Inn Fields W C 2
3 45 P M Prof R J Last Pectoral Girdle (Arnott demonstration.)

ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street W 1
8 P M *Medicine* Dr J G Scadding, Dr Peter Kerley, Dr A H T Robb Smith, Mr A G Cross Sarcoidosis

INSTITUTE OF NEUROLOGY, The National Hospital, Queen Square W C 1
5 P.M Dr J Richardson (Toronto) Cerebral Anoxia and Hypoglycæmia

Wednesday, 25th

ROYAL SOCIETY OF MEDICINE
5 P M *Endocrinology* Dr M D Milne, Dr Oliver Garrod Dr S A Simpson Dr J F Tait Aldosterone

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S W 3
5 P M Dr F J Prime Emphysema

WEST LONDON MEDICO CHIRURGICAL SOCIETY
8 30 P M (Royal Society of Arts John Adam Street, W C 2) Sir Henry Cohen Old English Silver and its Medical Uses (Cavendish lecture)

RENAL ASSOCIATION
4 30 P M (Ciba Foundation, 41 Portland Place W 1) Dr R Muehrcke Renal Biopsies in the Nephrotic Syndrome Dr T Freeman and Dr A M Joekes Nephrotic Proteinuria Dr Patricia Lindop Renal Response to Hypotensive Anæsthesia in the Aged

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W 12
2 P M Dr A L Woolf Hydrocephalus

BIRMINGHAM MEDICAL INSTITUTE, 154, Great Charles Street Birmingham 3
8 P M *Psychiatry* Dr J L Clegg, Dr J J O Reilly The Amsterdam Experiment

Thursday, 26th

ROYAL SOCIETY OF MEDICINE
8 P M *Urology* Mr J Mason Brown, Dr Ian Gordon Mr Ashton Miller Mr Innes Williams, Dr D Edwards Urology in Children

POSTGRADUATE MEDICAL SCHOOL
2 P M Prof Dos Santos (Lisbon) Treatment of the Small Tuberculous Bladder

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM
9 45 A M (1 Wimpole Street W 1) Sir Stewart Duke Elder Mr P L Blaxter Mr S J H Miller Prof G P Sourdille Early Diagnosis of Glaucoma (Opening of three day annual congress)

NUFFIELD ORTHOPÆDIC CENTRE Oxford
8 30 P M Prof J Trueta Vasculature of the Growing Head of Femur

BIRMINGHAM UNIVERSITY
4 P M (Medical School) Dr H L Kottmeier (Stockholm) Radiation Treatment of Carcinoma of the Cervix (First of two Ingleby lectures)

Friday, 27th

POSTGRADUATE MEDICAL SCHOOL
10 A M Sir Heneage Ogilvie Elementary Errors in Surgical Diagnosis

ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington, W 2
5 P M Mr S G Clayton Placenta Prævia

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330 Gray's Inn Road W C 1
3 30 P M Miss Edith Whetnall Management of Deafness in Children

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES
7 30 P M (11 Chandos Street W 1) Mr A J King Intradermal Tests in the Diagnosis of Lymphogranuloma Venereum (Presidential address)

BIRMINGHAM UNIVERSITY
4 P M Dr Kottmeier The Radiumhemmet Experience in Carcinoma of the Corpus (Second of two Ingleby lectures)

Saturday, 28th

INSTITUTE OF ORTHOPÆDICS 234 Great Portland Street W 1
10 A M Mr V Logue Spinal Tumours of Orthopædic Interest

In England Now

Running Commentary by Peripatetic Correspondents

IVING in Canada is a long-term proposition I bled oldest donor yesterday—a little old man, spry as come, a bit deaf, and with bright blue eyes which sed nothing peering out through slits in parchment

Want you to take some blood," he said "S'alright, tor sent me Been having headaches all winter an' got a in me shoulder" His hands quietly rolled invisible pills monstrated "Go on," he said, "nothing like it to set ye Do it for meself if I didn't shake too much"

e jumped up on our high donor couch like a 10 year old illed up the sleeves of his sweater and of a long woollen Across each elbow, over the cephalic veins, were old, te, transverse scars "Used to do it in the bush," he said, st thing when you're out of sorts Laid up all one winter a pains in me ear Doctor filled me up with pills, tons of , got fed up with it So I bled meself—into a soup plate I sweated Must 'a been a quart of it Next day, back to k, good as ever"

is pulse never wavered as I bled him, and he reminisced unting All me life Love it Got me a buck last month 't carry 'em home now, though Can't walk like I used to ried 200 lb *once*" *He accepted hot milk, refusing tea,* showed me his blood letting implement It was a small ss sheathed gadget like a penknife, a triangular steel de protruding from the end You pressed it back against a ng, held it against the vein, and released a catch The de sprang down, incising the vein with a clean, 0 5 cm, cut on t think he ever sterilised it

e is 89 And in November we're going up North moose

* * *

or many years twelve learned men met once a month study the appearance and behaviour of strange mals They examined their form, their appetites, ir desires, and above all they were well up in the rature of their subject They then classified each mal and gave it a number with up to three decimal nts

ut all was not well For some time they had used a egory for the unicorn, and after ten years they found t they had classified no less than eleven animals in s way, giving them the code number 1 322 Soon the ling began to spread that there might be no such mal, and they called a special meeting to consider the nt The literature on the subject was definite The icorn was an animal like a horse which had a single nder horn projecting from the centre of its forehead e Chairman maintained that most of the animals so ssified either lacked the horn, in which case they were rses, or else they really had the horn, in which case y were rhinoceroses

But this was not all The Secretary was loth to andon his belief in the reality of the unicorn He inted out that according to the oldest authorities the icorn was sterile The Chairman agreed, but added that number of the animals they had to consider were rile, also "Are we therefore," he said, "to regard em all as unicorns?"

The specialists in animal behaviour said that apart m their appearance, which might be deceptive, a icorn was always wild in its ways and could only be ned by a virgin dressed in white The unicorn, they d, would lay its head down in her lap and become fectly tame Against this point of view the specialists taxonomy objected that although they had often served this phenomenon, yet every time they had tained a good view of the animal it always turned out be something else, such as a dog or a gazelle and ce even a giraffe

This last observation gave rise to trouble When ch of the eleven cases was reviewed in detail, two or ee of them were clearly giraffes But the Secretary sented, he preferred to call them camelopards hen pressed to conform to the majority opinion he named firm "We are agreeing," he said, "not to call this animal a unicorn, but I see no reason why these debatable cases should be classified as giraffes I call them camelopards because they are tall like a camel and spotted like a leopard"

"Surely," said the Chairman, "that is rather an old-fashioned view? When I was a student we called all these sorts of animals camelopards, but we now know them to be giraffes The name camelopard is merely descriptive, while the name giraffe is specific one of the greatest of recent advances is the ability to give these animals specific names"

So one by one these eleven animals under review were removed from the category of unicorn Some were called horses, others giraffes (always with one dissentient voice, the Secretary's), and one was clearly a rhinoceros It was late when the twelve learned men went home to their beds, but they each had the satisfaction of knowing that never again would any of their number call a strange animal a unicorn

* * *

When I visited the Hubbards' I could never understand why their dog was hustled into the back-kitchen I never heard it bark nor look in the least aggressive It was a Borzoi, finely groomed, very long in the nose, and it always looked unspeakably bored Usually when I knocked I heard a scuffle while Mike was being dragged with skidding paws along the narrow hall to the back of the house But last Monday when I knocked I heard Mike sniffing diagnostically on the other side I inferred that the family was out and that Mr Hubbard was either too deaf to hear my knock or too immobilised by his lumbago to come to the door Accordingly I walked straight in As I anticipated, the dog came up to me and was perfectly friendly I pride myself that I understand dogs and that this sympathy is reciprocated Dogs only bite if they know you are afraid

I walked along the dark hall to the kitchen where Mr Hubbard was bending over the table holding his back with both hands At that moment I felt a sudden tug on my coat Mike had taken a grip on it "I say, call your dog off Mr Hubbard, it s got hold of my coat!"

"I can almost touch my toes," said Mr Hubbard bending with a conspicuous lack of confidence towards the floor Mike released his grip on my coat, opened his jaws and sank his teeth into my hamstrings This was very painful "Hubbard!" I screamed, "Call this cursed blood-hound away, it's got hold of my leg!" Mr Hubbard was, unhappily, fixed in flexion In this position he advanced towards us clicking his tongue in mild abuse ' Tch tch, come away, come away, now, boy, it's only the doctor"

* * *

PRESCRIBERS' NOTES III

"An advertisement is a rich man asking you to give him more money" (G K C)

or

Circles, vicious, one

The postman homeward plods his weary way,
  His shoulders lightened of his heavy load,
Thinking he ought to get a rise in pay
  With seven doctors on his daily road

Pamphlets and pictures to ensnare the eye,
  Samples their young will eat and sicken, he hoped
Blotters enow to suck the salt sea dry,
  Into the dustbin straight they go, unoped

The P.M G has heard his heartfelt cries,
  His wages raised, up must the postage go
The cost is added to the products' price
  The hopeful man thinks that will stem the flow

But when the State will pay, let money burn!
  We need not dam the ever widening stream
Yet animated bust and *stoned* urn
  Whisper, the State is you and me—and him

Epitaph

Full many a Flower is born to blush unseen
  And waste its sweetness in a bonfire's air
Full many a View of Zermatt or the spleen
  The dark unfathom'd caves of ocean bear

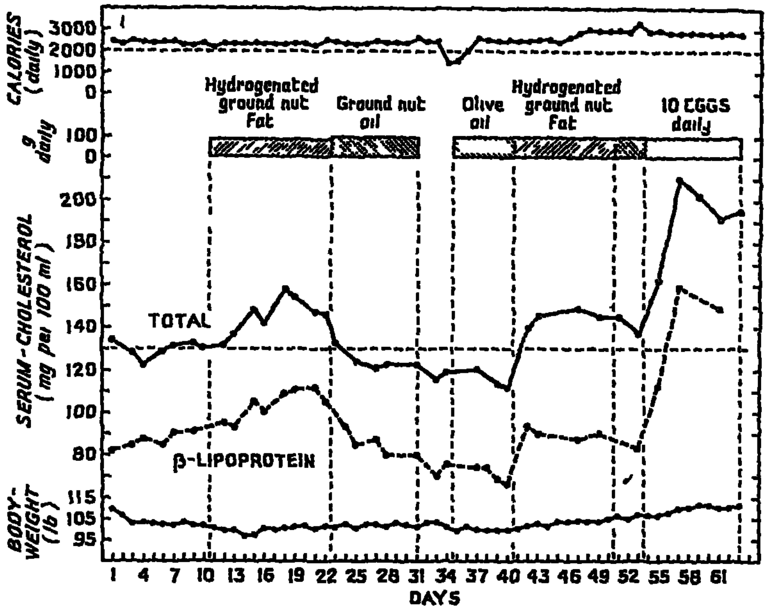

Fig 2—*A slight rise in the serum-cholesterol level of a male Bantu, aged 65, coincided with the feeding of hydrogenated ground-nut fat On switching to the natural oil the changes were reversed On re-feeding with hydrogenated fat the serum-cholesterol level rose again The amount of the rise was slight compared with that from an equivalent amount of fat as eggs The mean serum cholesterol level before the fat feeding was 129 6 ± 3 5 mg per 100 ml*

at low temperatures (Markley 1947) The saturated fraction, a palmitate stearate mixture, was removed at –20°C, and the temperature was lowered successively to –50°C and –70°C to separate off the oleic and linoleic fractions respectively Subsequently the saturated fraction and the most highly unsaturated fraction so obtained were esterified with ethyl alcohol, followed by fractional distillation in a high vacuum

The unsaturated fraction contained no sterol, determined by the Liebermann Burchard reaction by the method of Abell et al (1952) The iodine values (140–150) indicated that in using this method of fractionation we could not obtain a linoleate fraction completely free from other less unsaturated fatty acids The vitamin-E content, measured by the method of Quackenbush et al (1941), never exceeded that present in the sunflower seed oil and in most instances was far less (18–70 mg per 100 g)

Results

The effects of the short-term feeding experiments on the serum-cholesterol levels are shown in figs 1–7, which show that differences in the serum-cholesterol levels are usually paralleled by differences in the cholesterol contained in the β lipoprotein fraction

Investigation of the effects of different fat fractions on the excretion of sterols in the stools are in progress Some results are shown in figs 6 and 7 In 1 case (not illustrated) fæcal sterol during the period of administration of hydrogenated fat alone was 0 39 g daily, with the addition of the unsaturated fatty acid fraction 0 83 g daily, and after withdrawal of both supplements 0 53 g daily These values are insufficient for drawing firm conclusions

ANIMAL FATS AND VEGETABLE OILS

Changes in the serum cholesterol levels coincided with changes in the intake of fat In the first 2 cases it appeared that the findings of the inter racial survey had been confirmed, in that olive oil, representing a vegetable oil, had no effect, whereas butter and beef dripping (tallow) in equivalent amounts and beef muscle promptly raised the serum cholesterol level (fig 1) Olive oil substituted for the butter or tallow could not maintain the raised level, which remained low even when the olive oil supplement was doubled so that more than 60% of the total calories was provided by this oil

A hardened or hydrogenated ground nut fat was tried (iodine value 55) In the first case studied there was a slight but prompt rise of the serum cholesterol level When the non-hydrogenated natural oil (iodine value 89) was substituted, the serum cholesterol level fell (fig 2) The same effects were seen later in the same person and in 2 others This effect of hydrogenation influenced the design of subsequent experiments

Sunflower seed oil was fed in the presence of high serum cholesterol levels In the post hemiplegic patient the serum cholesterol level rose on the administration of 100 g of beef dripping When the intake of fat was raised to 200 g with 100 g of sunflower seed oil (iodine value 135), the serum cholesterol levels fell, only to rise again when the sunflower seed oil was withheld (fig 3) In the same volunteer the effect of ten boiled eggs was reversed when the eggs were scrambled or fried in 100 g of sunflower seed oil After a control period on 50 g of animal fat the intake of fat in the 2 European volunteers with coronary heart disease was increased to 150 g by the addition of 100 g of sunflower seed oil Immediately the serum-cholesterol levels fell (fig 4) When the sunflower seed oil was withheld and the total intake of fat thereby decreased, the serum cholesterol level returned to its original value The experiment was repeated in 1 of these 2 volunteers with 100 g of ground nut oil, which produced a similar but smaller effect

Marine Oils

Neither pilchards fried in pilchard oil (iodine value 180) nor seal oil (iodine value 166) raised the serum cholesterol levels in 3 volunteers On the contrary, the level attained during the feeding of these oils was lower than that on the fat free basic diet (fig 5) The effect of the highly unsaturated fraction segregated from pilchard

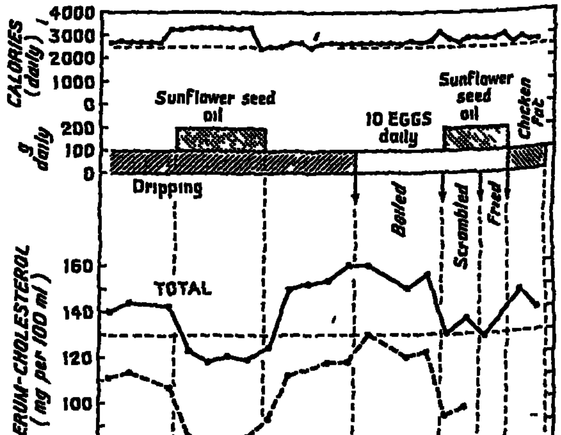

Fig 3—*The effect is shown in a male Bantu aged 37, of feeding 100 g of animal fat daily followed by an increase of the total intake of fat to 200 g by feeding equal quantities of an animal fat and a vegetable oil The egg ration was given first as ten boiled eggs daily followed by ten eggs scrambled or fried in sunflower seed oil*

Dr Peter Davey leans towards an M R C P (PATH) and then smisses it as a vain hope Since Sir Ernest Finch wrote[1] it as been generally agreed that diplomas are not badges of ntability for training as consultants Despite public suggestions[2] and informal conversations, the Royal College of hysicians so far appears to have done nothing, but perhaps r Peter Davey's hope of an M.R C P (PATH) is not, in the ng run, as vain as it appears now it is less unlikely than the lternatives

The adulation of Dr Peter Davey's last three paragraphs istresses me Of course, if he is one of the ruling class in the orld of pathology, it is understandable there never was an ligarchy yet which did not believe its rule to be for the best in he best of all possible worlds Dr Peter Davey calls it aristarchy The *Oxford English Dictionary* defines an aristarchy s a body of severe critics I am not sure that it is an appro riate title for my pathological professional acquaintances If aristarchy were intended to mean government by the élite —largely self appointed and self named—I can only cry '*A bas les aristos*' *A la lanterne*!"

It would be needless to bedevil these exchanges with personalities Perhaps some may seek to knock me off my self allotted perch and I will crave your permission to sign myself

HUMPTY-DUMPTY

LOCALISATION OF ACUTE INFLAMMATORY SWELLING

SIR,—Acute inflammatory swelling in its early stages is manifestly due to local excess of a fluid exudate rather than to cellular aggregation It is not obvious, however, why this fluid should not disperse into the surrounding tissue rather than localise as it usually does The following observation suggests that one reason for this localisation may lie in the peculiar properties and arrangement of connective tissue

Experiments with mice showed that unrestricted subcutaneous injection of water at pressures in the region of 10 cm water always resulted in a localised bleb at the injection site But when small quantities (2 c mm or so) were injected, using a fine glass needle loosely packed with minute glass spheres (ballotini), the water diffused away evenly and rapidly for a distance of 1–2 cm without any tendency to bleb formation But even in these circumstances continued infusion did not increase the area of spread Thus while small quantities of water disperse to some extent, larger quantities merely accumulate at the point of injection. It appears as though wetting of the tissue provides a barrier against the further passage of water

Previous work affords some explanation of this phenomenon Connective tissue has been considered to have an essentially lamellar constitution[3–5] The lamellæ offer considerable resistance to the passage of water across them,[6] so that water may be expected to find its way between rather than through the layers Further it has been shown that at hydrogen ion and salt levels such as exist in living tissues, the substance of the lamellæ is intensely hydrophilic[7] Free water must therefore pass through interstices which are bounded by hydrophilic material It is easy to see that such an arrangement might allow the rapid passage of small amounts of free water while blocking the passage of larger quantities completely

In-vitro studies[7] have drawn attention to a dynamic equilibrium between chemical forces which promote the taking up of free water by connective tissue and mechanical forces which lead to its extrusion It may be conjectured that ordinarily the equilibrium may allow the presence of a little free water, but injection experiments show that the addition of only a few cubic millimetres at pressures such as obtain in blood capillaries is enough to bring the localising mechanism postulated into play Since there is nothing in the composition of inflammatory exudates in general which is likely to lessen the affinity of connective tissue for water it is probable that the same mechanism operates in the early stages of all acute inflammatory processes in which interstitial connective tissue is involved

T D DAY

Department of Experimental Pathology
and Cancer Research University of Leeds

SCLERODERMA TREATED BY VERATRUM ALKALOIDS

SIR,—Assuming that in scleroderma the vascular changes are an important factor in the progress of the disability, and that the gradual diminution of blood-supply to the peripheral tissues is the cause of the muscular weakness particularly in the hands, I have treated three cases of generalised scleroderma with veratrum alkaloids in the form of 'Veriloid'

CASE 1 —A married woman, aged 54, gave a history of Raynaud's disease since 1933 This had been getting worse and she had trophic ulceration on the fingers of both hands in the winter months In 1949 she had undergone bilateral cervical and lumbar sympathectomy, which improved the peripheral circulation especially in the legs Despite the circulatory improvement she still had trophic ulcers on the fingers in cold weather and had become progressively less able to use her fingers for fine work such as sewing It was realised that she had generalised scleroderma involving the face, bib area, and both arms and hands

In December, 1951, she was started on tab veriloid 1 mg t d s, which was increased gradually to 3 mg t d s She has continued this dose steadily ever since Improvement started quite soon, her fingers became more supple, and by 1953 she could sew and knit again She has had no trophic ulcers during the past two years despite the hard winters She can now grip quite strongly The only other medicinal treatment which she has had is tab phenobarb gr ½ at night, prescribed because she complained that her nerves were bad, she was not sleeping, and she felt sick in the mornings

CASE 2 —A married woman, aged 52 was seen in February 1952, with generalised scleroderma involving the face, bib area both arms and hands, and the legs She had noticed stiffness and gradual loss of power in the hands for about two years and increasing stiffness and tightness of the skin of the face for about a year She was unable to dress herself, carry on her housework and cook or look after her family

She was started on veriloid 1 mg t d s which was gradually increased to 3 mg t d s Within two months there was definite improvement of the condition of the skin and increasing power of movement in the hands and fingers For some time now she has been able to do everything for herself, has done her cooking and housework and has walked and got about normally Since the early part of this year the dose of veriloid has been increased to 4 mg t d s, and this has hastened the improvement particularly in the hands

CASE 3 —A married woman, aged 45, who was seen on Dec 8 1955, three years ago had been operated on for repair of the pelvic floor Since then her hands and feet had been intermittently purple and stiff She had never had trouble with her circulation when she was younger During the past six months she had had dysphagia, her hands and arms had become puffy and swollen, and she had difficulty in holding things as she was unable to close her hands properly and grip On examination the patient had typical generalised scleroderma involving the face, neck, bib area, arms and hands combined with a Raynaud's condition involving the arms and legs

Treatment was started with 1 mg of veriloid three times a day On Dec 22 the dose was increased to 2 mg three times a day By Jan 26 there was much improvement in swallowing, and dysphagia was noticed only in the evenings There was also noticeable improvement in the appearance of the skin of the forearms and hands By Feb 23 the œdema of the hands had considerably diminished and the patient could grip normally despite the very cold weather Her arms were quite warm down to the wrists, although the hands were still bluish they were not unduly cold The dose of veriloid was increased to 3 mg three times a day

Of these three cases two have been treated with veriloid for four years In both cases improvement has

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1 *Lancet* 1952 i 1
2 Jordan A *Ibid* p 156
3 Laguesse E *Arch Biol Paris* 1921 31 173
4 Day T D *Lancet* 1947 ii 945
5 Day T D Eaves G *Biochim biophys Acta*, 1953, 10, 203
6 Day T D *J Physiol* 1952 117, 1
7 Day, T D *Ibid* 1949 109 380

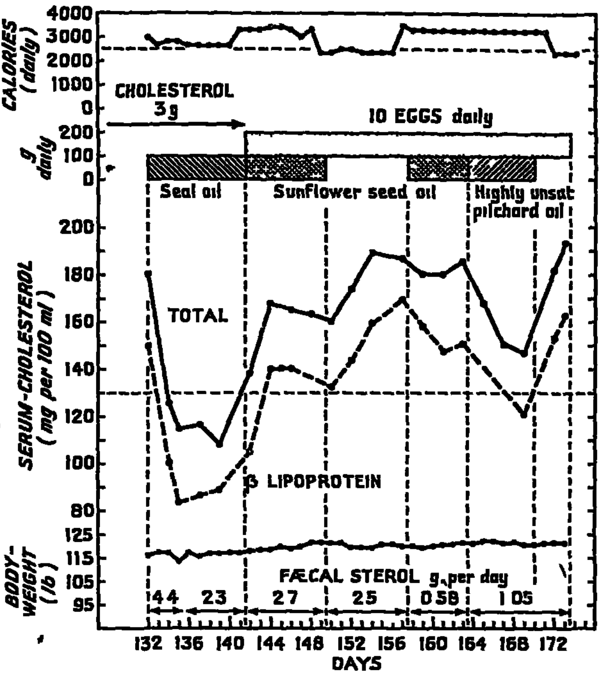

Fig 6—In same Bantu as in fig 2 a change from the saturated fraction of sunflower seed oil to seal oil was followed by a sharp drop in the serum-cholesterol level, although the intake of cholesterol was maintained Withdrawal of seal oil and addition of ten eggs daily caused a rise, which was apparently checked by giving sunflower-seed oil Highly unsaturated pilchard oil caused a sharp drop, and its withdrawal was followed by a sharp rise

We are currently investigating whether the saturated fatty-acid fraction alone, on the basic cholesterol-free diet, can raise the serum cholesterol level

OTHER DIETARY FACTORS

Vitamins

The 2 patients with scurvy had the lowest serum-cholesterol levels on admission One of them was treated with vitamin C during the first olive oil supplement, and no sudden change in the serum cholesterol level followed Later it was noticed that the cholesterol contained in the α-lipoprotein fraction may have increased, because the serum cholesterol level did not return to its value before vitamin-C therapy In the other patient with scurvy the lipoproteins were not fractionated on admission when he received vitamin C therapy, but his serum cholesterol level rose slowly and steadily during this period

In the 2 cases with vitamin B deficiency (one with beriberi and the other with pellagra) the serum cholesterol levels fluctuated under treatment with vitamin-B complex on admission Vitamin B complex administered later and to the other volunteers did not affect the serum-cholesterol levels before period of fat feeding

Protein Intake

The changes that coincided with alterations in the intake of fat took place on protein-poor and on protein rich diets Increasing or decreasing the intake of protein by adjusting the intake of casein during the control period did not affect the serum-cholesterol levels In some cases changes of this nature made a difference of more than 100 g of protein Furthermore by adjusting the intake of casein the diets in most instances could be kept isonitrogenous during feeding with supplements of different fats

Calories and Changes in Body-weight

From the figures it will be seen that only minor changes in body-weight took place in most cases A rapid gain in weight in 1 volunteer during the control period was not associated with changes in the serum cholesterol level

When the calorie intake was suddenly increased with an extra olive oil supplement in 2 non-Europeans (fig 1), and with sunflower-seed oil and marine fish and mammal oils in 2 other persons (figs 3 and 6), the serum cholesterol levels did not rise

Discussion

In these short term experiments changes in the serum cholesterol levels coincided with changes in the intake of fat The consistency of the results to date has not been affected by alterations in the protein, calorie, or vitamin intake Brief reference to some of these findings has already been made (Bronte Stewart et al 1955b, 1956) The changes appeared to be more closely related to the quality rather than the quantity of the change in intake of fat

In quantitatively equivalent amounts animal fats in the form of butter, beef dripping, beef muscle, and eggs caused a rise in serum-cholesterol levels Marine animal oils had the reverse effect on the serum cholesterol levels either when fed alone after a fat free diet or with eggs

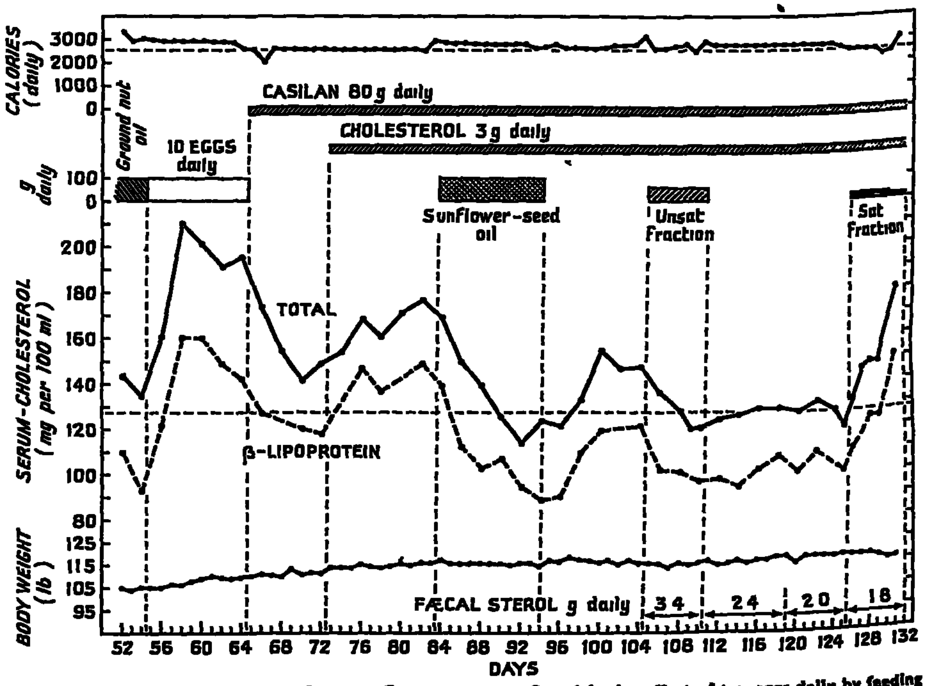

Fig 7—Attempts to reproduce, in the same Bantu as in figs 2 and 6, the effect of ten eggs daily by feeding in turn quantitatively equivalent amounts of protein, cholesterol, and fat in a qualitatively dissimilar form When an equivalent amount of cholesterol (3 g) was added to the protein, the serum-cholesterol level rose Supplementation firstly with sunflower-seed oil (100 g) and secondly with the unsaturated fraction from the same oil (60 g of ethyl linoleate) produced a sharp fall in the serum cholesterol level, which rose only when 15 g of the saturated fraction was added (at this stage the total intake of fat constituted only 8% of the total calories)

nplete, disappeared on the 13th day The temperature, ich fluctuated around 100°F, went above 101°F twice in 1st week and was normal on the 9th day Spasms were oderate until the 4th day and mild until the 12th day raldehyde needs were small The patient was discharged the 32nd day

It is hazardous to draw definite conclusions from this all series of five cases But we suggest that injected drocortisone suppresses spasms, unlike injected cortine which aggravates them although checking pyrexia tter It is our impression that, compared with oral rtisone, parenteral hydrocortisone is somewhat less fective in controlling pyrexia and somewhat more fective in controlling spasms It was not possible to mpare their effectiveness quantitatively We cannot redict which of the two will be found to give greater provement in survival rate In severe tetanus, when ormone therapy is being considered as an adjunct to utine measures, if there is dysphagia or total trismus, arenteral hydrocortisone is the best choice We have uggested[2] that cortisone given orally is converted to hydrocortisone to a greater extent than the same ormone given parenterally, which might account for he difference in their actions Now we have one more vidence for this hypothesis, in the present series njected hydrocortisone acted rather like oral cortisone nd definitely unlike injected cortisone A somewhat milar situation is well known in the treatment of rthritis, where temporary relief following intra articular ydrocortisone or oral cortisone is greater than that ollowing intra articular cortisone as free alcohol or acetate

We wish to thank Merck & Co, Inc, Rahway, New Jersey, who kindly supplied infusion concentrate and saline suspension of hydrocortisone used in the treatment of these cases

R A LEWIS
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HUMAN SURVIVAL PRIZE FOR AN ESSAY

SIR,—The Medical Association for the Prevention of War (London) offers a prize of £75 for the best essay under the title "A World Approach to Human Survival and Health" It is offered as a memorial to the late John Ryle, professor of social medicine at Oxford

Earlier letters by members of the M A P W, published in your columns, have stressed the immediate urgency of action designed to reduce the risk of the outbreak of a third world war We are now concerned to emphasise the need for the steady development of a more responsible attitude of medical men and women towards the broad problem of human survival and health, and it has seemed to the committee that our best approach might be by way of a memorial to John Ryle, whose life and work were devoted so consistently to these constructive ends

Ryle's professorial interests widened from the health and disease of the individual to that of the community—not only in his own country but the world over He had always been devoted to the cause of international understanding, and between the wars he was the first president of the Medical eace Campaign He felt strongly that the doctor's humane alling gave him a special responsibility to work for the cause f peace He had friends of many races and nationalities, and he helped many individuals—members of his own profession and others—who came to this country as refugees

For Ryle the Hippocratic injunctions were binding on doctors of all countries He gave much thought to the problems facing the doctor in the modern world, and the final essay in *Changing Disciplines* is entitled "Medical Ethics and the New Humanism" While he praised the work of doctors in war—"They alone among professions have turned inhuman war to humane account and have seized opportunities to develop and improve their life saving techniques"—he warned against the dangers of being drawn into ad hoc military research, as in biological warfare He thought that doctors should insist on the right to publish their discoveries, and that the war time secrecy in the preparation of penicillin and D D T was unethical The following aptly summarises his views "The physician is, of necessity, both scientist and humanist Science and ethics, both of man's contriving, are complementary, they find their common ground in human need"

Further information may be obtained from the hon secretary of the M A P W, Dr D L Kerr, 291, Burnt Wood Lane, London, S W 17

J NORMAN GLAISTER

London, W 1

PERFORATED ACUTE AND CHRONIC PEPTIC ULCER

SIR,—I have read with much satisfaction last week's excellent paper by Mr Hermon Taylor and Mr Warren on the conservative treatment of perforation, and I should like to congratulate them on a most valuable contribution

I am particularly gratified because their approach to the peptic-ulcer problem is based on the fundamental distinction between the acute and the chronic lesion The follow-up of their cases clearly demonstrates that the acute ulcer, which invariably heals rapidly and should therefore be left alone, never becomes chronic—a view which I have repeated for the past twenty five years

I trust that the logical approach by Mr Taylor and Mr Warren to the complications of peptic ulcer will be generally accepted and extended to hæmorrhage, which is essentially a parallel manifestation caused by the same morbid process It will save the doctor many a headache and the patient many a bellyache

J JACQUES SPIRA

London W 1

SILICONE-RUBBER TUBING FOR TRANSFUSIONS

SIR,—The rubber of the standard intravenous infusion set is probably often responsible for the local thrombosis or thrombophlebitis which may follow transfusions,[1] and consequently alternative materials are being sought and tested

I have recently been using infusion sets made with silicone rubber, and it seems that this material is worthy of more extensive trial

Silicone rubber is an almost white translucent substance with a consistency similar to that of natural rubber It is unreactive with body fluids, and it is believed not to contain substances which leach out when it is in contact with water It does not melt but rapidly loses elasticity at about 500°C, and it will withstand repeated heating to 200°C without any deterioration It is an excellent insulator and will readily acquire and hold a static charge of 2000 volts, and therefore its use constitutes a potential fire risk The price is about seven times that of normal rubber

Silicone rubber is made into tubing by extrusion and a new vulcanising process which avoids contamination with any particulate matter such as talc

The tubing used was 9 mm external diameter, with a 5 mm bore, and was assembled into infusion sets of the standard blood transfusion service pattern Some of the bungs used were of normal red rubber

21 transfusions have been given with these sets ranging in duration from two to twenty hours, 8 of them lasting eight hours or more Most of the transfusions were of blood, but all the usual fluids have been given and several different needles and cannulæ used The site of the infusion was in the arm in 19 cases, and the leg in 2 cases The patients were aged 3–65 years In no case was there any local or general adverse reaction to the infusion

From such a small series no firm conclusions can be drawn, but the complete absence of reactions is encouraging The sets are pleasant to use, and it is convenient

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[1] Hadfield Jones, R P C , Lewis, H B M *Lancet*, 1952, i, 585

Epidemiology

Inter-racial studies (Keys and Anderson 1954) and the drop in mortality during the German occupation of Norway (Malmros 1950, Strom and Jensen 1951) have been largely responsible for the general acceptance of the dietary-fat theory of coronary heart-disease This is always countered by reference to the fat eating Eskimo (Page 1954, Schmidt 1955) Sinclair (1953) has shown that the diet of the Eskimo consists predominantly of seal, fish, and other marine animals—an intake of fat characterised by a high content of unsaturated fatty acids—but the Eskimo diet apparently varies from area to area (Scott 1956) Fish is a major factor in the diet of the Japanese, who have one of the lowest death-rates from coronary heart disease in the world (Keys and Anderson 1954) Coronary heart disease is not prevalent in the olive oil eating Latin peoples or in primitive communities such as Africa and China, where maize, soybean, and sunflower seed allow the amount of unsaturated fatty acid to exceed that of saturated fatty acid in the diet (Tuttle 1952)

In more civilised and prosperous areas developments in animal husbandry are aimed at the greater priming of beef, improvements in egg production by battery farming, &c, and greater yields of dairy produce Moreover butter from stall-fed cows contains less iodine and linoleate than does that from cows feeding in summer pastures (Bailey 1945) More and more people are allowed the opportunity for over-indulgence in saturated fatty acids The consumption of saturated fatty acids is increasing (Fullerton 1955), often at the expense of the unsaturated fatty acids owing to the processing of natural foodstuffs Hydrogenation of vegetable oils is a recent luxury for the housewife and processed breakfast cereals are superseding porridges, with consequent loss of the natural oil contained in the germ

The decrease in mortality during the German occupation of Norway was associated not only with decreased consumption of animal fat but also with bomb damage to hydrogenation plants

The yearly increasing incidence of coronary heart-disease is seen in females as well as in males, and the death-rate in European females exceeds by far that in Bantu males (Phillips 1956) There must therefore be a factor additional to the circulating œstrogens of the female

It is as well to re emphasise that the present work has done no more than illustrate that the serum cholesterol level may be influenced by the nature of the fatty acids in the diet The results of these short-term feeding experiments agree with the findings of the inter-racial survey reported earlier (Bronte-Stewart et al 1955a), which imply that the customary dietary habits of communities may be reflected in their mean serum-cholesterol levels The evidence that the dietary fat influences the development of coronary heart disease in man, although strong, is purely circumstantial and has been derived mainly from epidemiological studies The nature of the fatty acids constituting the dietary fat may provide the basis for a better hypothesis We agree that to attribute this disease to a single cause would be a cardinal error at this stage (*Lancet* 1955) If, however, the nature of the modern diet is a major factor in the development of coronary heart-disease, there is hope that this disease may eventually be controlled and prevented

Summary

To confirm the findings of an inter racial survey in this area (Bronte Stewart et al 1955a), we fed several different fats and oils to volunteers under controlled conditions and studied the effect on the serum cholesterol levels

Animal fats and hydrogenated vegetable fat behaved differently from vegetable and marine fish and mammal oils The most likely common difference between these fats and oils is the proportion of unsaturated and saturated fatty acids in the fats and oils concerned

Sunflower seed oil and a segregated highly unsaturated fatty-acid fraction from pilchard oil have, in the persons studied, consistently depressed the serum cholesterol levels when fed alone, with a supplement of cholesterol, or with one of animal fat

The possible application of these findings is discussed, and it is suggested that certain discrepancies in the dietary-fat theory of the ætiology of coronary heart disease may be explained by variations in the nature of the fatty-acid composition of the fats concerned

This study was undertaken as part of the programme of the Research Unit in Clinical Nutrition supported in the University of Cape Town by the South African Council for Scientific and Industrial Research We wish to thank Dr Ancel Keys of the University of Minnesota, for his suggestions at the outset of these studies, and Dr W Odendaal, of the National Nutritional Research Institute, Pretoria, for the advice given later Technical and other assistance was given by Mrs C Damstra, B SC, Miss J Ethelston, B SC, Miss C Solms, Miss E Volks B SC, Mrs A Betts, Mrs E Pallett, Dr M Fewster, Mr T J Turner, Mr R Thompson, Mr D Brock, Mr G F J Schoonraad, and the staff of the Metabolism Unit We wish to thank also the directors and chief chemists of Messrs Lever Bros (S A) (Pty) Ltd, Marine Oil Refiners of Africa Ltd and the Government Guano Island authorities for the supply of fats and oils and other valuable assistance given. Finally we should like to record our gratitude to our volunteers, who consumed on many occasions malodourous oils without demur

ADDENDUM

Since submitting this paper we have seen Sinclair's (1956) stimulating analysis of the possible role of deficiency of essential fatty acids in the ætiology of atheroma, &c We cannot comment critically on his analysis here, but we are intrigued by some of the possibilities which it raises in interpretation of our own experiments with fats of differing degrees of saturation

We have also seen the detailed report of the Minnesota Arteriosclerosis Symposium The pronounced fall in serum cholesterol levels reported by Malmros and Wigand (1955) in eight cases of familial hypercholesterolæmia accompanied the institution of a diet rich in corn oil They felt these effects might possibly be due to the high essential fatty acid content of corn oil (57% linoleic acid)

These views are in line with our short-term investigations of the effects of hydrogenated and natural fats and oils which we suggest are related to their unsaturated/saturated fatty-acid content

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vide some evidence against it in that affected males have ısmitted the disease to male and female offspring in roximately equal numbers

There seems to be a close connection between hemiplegic graine, when it occurs and ordinary migraine One ividual may have both types, and the ordinary type may ur in families with hemiplegic migraine Unfortunately records fail to show how often this happens The ssibility that hemiplegic migraine is the homozygous dominant of which the heterozygous expression is ordinary migraine ms to be ruled out by the great rarity of the hemiplegic m and its transmission through three and four generations

Thus recorded genetic data on hemiplegic migraine e consistent with an autosomal dominant transmission ordinary migraine is conveyed by a dominant gene, miplegic migraine does not appear to be its homozygous pression

ROBERT PLATT

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RELEASE OF 5-HYDROXYTRYPTAMINE BY RESERPINE

SIR,—It has recently been shown that reserpine causes ı mammals and birds a conspicuous release of 5 hydroxyyptamine (5 H T) from the blood-platelets, spleen, and astro intestinal tract[1–3] A similar, although less intense, ffect has been observed on the 5-H T contained in the entral nervous system[2–4] In view of the growing nterest in reserpine in the treatment of hypertension nd mental diseases—disorders which require long-ontinued administration of the drug (0 5–5 0 mg a day) —the effect of repeated administration of small doses on ndogenous 5 H T was investigated in the rat

Four groups of 6–8 animals each were treated for thirty days ith daily intraperitoneal doses of 0 01, 0 02, 0 05, and 0 1 mg f reserpine per kg of body weight The 5 H T content of erum, spleen, and gastro intestinal tract, determined on the atropinised oestrous uterus of the rat, is shown in the accompanying table For comparison the normal 5 H T values and the values observed after a single injection of 0 1 mg of reserpine per kg of body weight are included

5 H T LEVELS IN THE RAT

Reserpine administered	5 H T content (free base)		
	Serum (μg per ml)	Spleen (μg per g)	Gastro intest tract (μg per g)
Nil	0 62	1 66	2 12
0 1 mg (single dose)	0 38	1 03	1 45
0 1 mg (30 doses)	0 04	0 11	2 15
0 05 mg (, ")	0 12	0 31	1 42
0 02 mg (,)	0 16	0 40	1 55
0 01 mg ( )	0 21	0 52	1 81

Two facts emerge clearly (1) subsequent doses of reserpine cumulate in regard to their 5 H T -releasing effect, (2) reserpine in a dosage as low as 10 μg per kg, administered over a thirty day period, produces a 60–70% reduction in the 5-H T content of blood-serum and spleen The action of reserpine on the 5-H T in the gastro-intestinal tract was less consistent

The possibility of provoking experimentally a long-continued low blood-level of 5 H T is of obvious interest, especially in respect to the problem of the biological significance of 5 H T Further investigations are needed to decide whether the results obtained in the rat apply to man If this were so, the question would arise whether the low blood-level of 5 H T produced and maintained by reserpine is advantageous in treatment or, on the contrary, an undesired, and perhaps dangerous, side effect

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1 Pletscher A, Shore, P A, Brodie B B Science 1955 122 374
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OBSERVER ERROR

SIR,—In 1949 during the spring semester at the University of California, 1800 new students were enrolled Radiographs of their chests on 70 mm films were interpreted by a panel of observers so that each film was read ten times 254 films thus brought to light were suspect —that is, contained abnormal shadows All of the 254 were repeated on 14 × 17 in films and 30 were unanimously regarded as requiring further clinical study These 30 were called positive No reader selected all of the 30 The most successful selected 22 and the least successful only 17 On an average, readers missed 32 2% of positives These results published by Yerushalmy et al,[1] have received widespread notice

In January, 1954, you, Sir discussed[2] the lack of conformity in opinions on X ray films, and you stated that the significance of this lack of conformity in general medicine was probably very small but that there were times when it was very important You added "In mass radiography surveys the films are read only once, and even though the greatest possible care be taken, it is inevitable that some patients will be given a clean bill of health to which they are not entitled Their number (which may amount to 30% of all positive cases) can be significantly reduced if the films are read again by a second independent observer" Much of the evidence for this statement was based on Yerushalmy's paper and the results of this state of affairs amongst Californian students were assumed to apply to all mass X ray surveys in Britain

TABLE I—FOLLOW UP OF 30 POSITIVE FILMS (YERUSHALMY ET AL)

Activity status	No of patients	Total readings	Positive readings	Negative readings	% overlooked
Active total	7	70	44	26	37 1
(a) Bacteriologically positive	4	40	23	17	42 5
(b) Clinically active	3	30	21	9	30
Inactive	23	230	161	69	30
Total positive	30	300	205	95	31 7

Yerushalmy et al go on to give a highly interesting follow up of the 30 positive cases which is summarised in table I, taken from their paper

The day your leader appeared, the *Manchester Guardian*[3] reported 'Mass Radiography Fallible Double Check Urged One third of all people examined by mass miniature radiography with lung disease are liable to be mistakenly given a clean bill of health" Thus, a survey in an American university which revealed only 4 bacteriologically positive cases and 3 clinical ones became the basis of a half column report in a national newspaper about British miniature radiography

More recently[4] you said "It is quite clear that a single observer attempting to pick out cases of pulmonary tuberculosis from a largely normal population is likely to overlook about a quarter of the abnormal films" You do not say whether these abnormal films are significant of active disease, but that is probably what is meant, for later you point out that "this proportion has been remarkably constant in repeated trials in several countries", and you go on to quote Groth Petersen and Moller, who have shown that of the cases missed at a single reading, 86% were sputum positive 35% were of bilateral disease, and in 15% there were cavities

These results are so conspicuously different that it seems highly unwise to apply surveys in other countries to Britain

During 1954 we decided to double check the readings of 10,000 miniature films The method was as follows

The miniature films were first read by the director of the unit concerned and a list of persons requiring recall for large

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1 Yerushalmy J Garland L H Harkness J T Hinshaw H C, Miller E R Shipman S J Zwerling H B *Amer Rev Tuberc* 1951 64, 225
2 *Lancet* 1954 i 87
3 *Manchester Guardian* Jan 8, 1954
4 *Lancet*, 1955 i 1257

severe hæmorrhagic diathesis developed followed by septicæmia due to *Escherichia coli* and *Pseudomonas pyocyanea*. Electrocardiography showed pronounced myocarditis. Bone-marrow biopsy revealed severe damage to the blood-forming cells "presumably due to some drug or other." A few days after the anæsthesia had been discontinued signs of remission developed in the bone-marrow, yet on the twenty-ninth day the boy died from cardiac insufficiency and septicæmia.

When we reviewed the case-histories of the first 2 patients, who had recovered, it became clear that they also had shown signs of hæmatological complications. The 1st, a boy aged 10 years, had thrombocytopenia, hæmaturia, and retinal hæmorrhage on the fourteenth day of treatment. In the 2nd case, that of a boy aged 11 years, between the sixth and tenth days in hospital the leucocyte count fell from 12,500 to 2200 per c.mm. Treatment was discontinued on the twelfth day, and the blood was not examined again.

The 4th patient had moderately severe tetanus and hæmatological complications did not appear.

In March, 1955, a 5th patient, a woman aged 53, was admitted with severe tetanus.

Very early after admission tracheotomy had to be done. After the operation she was treated according to the principles previously outlined, including anæsthesia with nitrous oxide and oxygen.

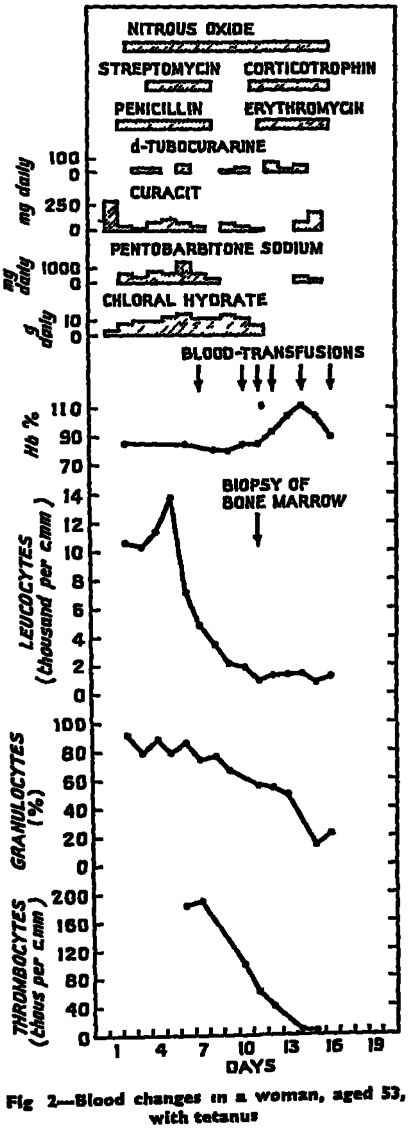

Fig 2—Blood changes in a woman, aged 53, with tetanus

CHANGES IN PERIPHERAL BLOOD IN RELATION TO DRUGS USED IN PATIENTS WITH SEVERE TETANUS

Treatment	Granulocytopenia and/or thrombocytopenia	No hæmatological complications
Chloral hydrate	3	7
Pentobarbitone sodium	5	5
Phenemal sodium	0	1
Pethidine	0	1
d-Tubocurarine	3	0
Bromethol	0	1
'Curacit'	1	0
'Largactil'	1	0
Continuous nitrous oxide	6	0

Fig. 2 shows how the tetanus gradually subsided and the dosage of sedatives was reduced considerably. Blood counts were made daily and already on the fifth day a pronounced granulopenia was observed, and this was soon followed by thrombocytopenia.

Pentobarbitone was suspected of having depressed the bone marrow. On the eleventh day, therefore, it was withheld. This did not have any effect. On the same day a bone marrow biopsy showed "Hypoplastic bone marrow with reduced erythropoiesis of megaloblastic type, granulopoiesis with a pronounced shift to the left, and numerous myeloid cells of undetermined character." The pathologist concluded that all the observed changes might be due to severe drug allergy.

Treatment with large doses of vitamin B_{12} was instituted on the thirteenth day, but no increase of reticulocytes or other sign of remission was observed. In all other respects the treatment remained unchanged. Septicæmia caused by *Esch. coli* now developed, and the patient died on the sixteenth day with signs of severe hæmorrhagic diathesis. Post-mortem specimens of bone marrow revealed "pronounced atrophy with greatly reduced or probably totally abolished myelopoiesis."

Gormsen (1955) published a case of severe tetanus showing agranulocytosis and thrombocytopenia in a boy treated by prolonged anæsthesia with nitrous oxide and oxygen, chlorpromazine, and curare. In this case also a reduced number of leucocytes in the peripheral blood was observed on the fifth day of treatment, followed by a decrease in the number of thrombocytes. Gormsen presumed that the hæmatological changes were due to the large doses of curare.

It thus became clear that the complex treatment to which our patients with tetanus had been submitted produced with great regularity signs of acute depression of the bone-marrow at the end of the first week of treatment. What could the cause be? Did extremely severe tetanus cause bone marrow damage which had hitherto been unobserved because formerly these patients died? Or was it due to the heavy dosage of pentobarbitone? Or chloral hydrate used for several weeks? Could nitrous oxide anæsthesia continued for many days be responsible despite the accepted innocuousness of this widely used anæsthetic agent? Or could the hæmatological complications be traced back to the large doses of curare used over several weeks?

In an attempt to detect the cause we have studied 13 cases of tetanus, most of them of short incubation and rapid evolution.

In the accompanying table the cases have been divided into two groups with and without granulocytopenia and thrombocytopenia. In the first group all the patients underwent tracheotomy, but in the second group only 6 of 8. This fact shows that the cases in group 1 were more severe than those in group 2. The difference, however, is not pronounced; hence the conclusion that the hæmatological complications could be due to the severity of the tetanus seems unlikely. Nor were signs of a hyperimmunising effect observed with abnormal hæmolysis, and electrophoresis did not reveal an increase of the gamma globulin fraction of the serum proteins.

The possibility remained that one or other of the drugs used was responsible.

The table shows that only nitrous oxide was a common factor in the treatment of all the patients who presented blood changes. The use of the other drugs—e.g., pentobarbitone—was equally distributed in both groups, or else they were used only sporadically. Suspicion was thus directed towards the anæsthesia, and the fact that the hæmatological complications regularly appeared from five to seven days after its introduction further incriminated the nitrous oxide.

The extensive literature on nitrous oxide contains no information about toxic effects on the bone marrow. This anæsthetic, in fact, is considered completely using two ordinary plaster bandages The ordinary bandage was not strong enough Satisfactory body-casts have been made and tube plasters for patients with knee-joint lesions, the casts in each case being lighter yet as strong as or stronger than conventional plasters

Similar results have been reported by Maudsley,[3] Arden and Ward,[4] and Sayle-Creer [5]

I am indebted to Messrs Smith & Nephew Ltd for their assistance in these experiments

Abergele Chest Hospital,
North Wales **JOHN B MORRISON**

GIANT HYPERTROPHIC GASTRITIS

SIR,—Dr Einan Williams describes (April 7) a case of what is undoubtedly Menetrier's *polyadenome en nappe*, but Dr Williams describes the lesion under the title "giant hypertrophic gastritis" and makes it quite clear that he considers it to have an inflammatory origin It is our view [5] that the condition described by Ménétrier was not primarily an inflammatory one but one for which the name "giant rugal hypertrophy" is more apt The term "chronic hypertrophic gastritis" has a different connotation, as pointed out by Dr Williams This is very much more common than "giant rugal hypertrophy," is mainly a gastroscopist's diagnosis, and is believed by many to be physiological

H DAINTREE JOHNSON
London **ALFRED STANSFELD**

SCOTLAND'S LEAD

SIR,—In your issue of March 24 you discuss the policy on joint training in hospital and general practice agreed between the Joint Consultants' Committee (Scotland), the General Medical Services Subcommittee (Scotland), and the Department of Health for Scotland

The initiative in such joint training was taken by the Northern Regional Hospital Board (Scotland) with the cooperation of the local executive council early in 1952,[6] and the scheme has been operated since then This scheme, which has provided experience in the various specialties in turn (in the grade of senior house officer) with parallel training in general practice, has proved most successful The proposed "new" scheme is, in essentials, the same

JAMES SOUTH
Inverness Formerly chairman Northern Regional Hospital Board

DEATH UNDER CHARLES II

SIR,—In his interesting note (March 31) Dr Hall confesses to being puzzled by the term "flox" He writes "Three people died of 'flox,' which apart from the obvious mis spelling has me puzzled"

"Flox" is defined in Charles Creighton's *History of Epidemics in Britain* (Cambridge, 1894, vol 2, p 436, note 2), which states

"The original heading in the Bills of Mortality was 'flox and smallpox' 'Flox' meant flux or confluent smallpox which was so distinguished, as if in kind, from the ordinary discrete form seldom fatal Huxham, in 1725, *Phil Trans* xxxiii, 379, still used these terms 'When the pustules broke out in less than twenty four hours from the seizure, they were always of the flux kind, as is commonly observed Pocks which at first were distinct would flux together during suppuration' Dover, *Physician's Legacy*, 1732, p 101, has 'the flux smallpox, or variolae confluentes,' as one of the varieties and again, pustules 'fluxing in some parts, in others distinct'"

Wellcome Historical Medical Library
183 Euston Road London N W 1 **F N L POYNTER**

STREPTOKINASE AND STREPTODORNASE IN INFLAMMATORY ŒDEMA

SIR,—Good results have been reported [1] with intramuscular injections of streptokinase and streptodornase in the treatment of inflammatory œdema This action was attributed to the dispersal of fibrinous clots in the intra-tissue spaces around the site of infection To avoid the very unpleasant local application of the drug, and to study the general action of streptokinase and streptodornase, I gave intramuscular gluteal injections to 45 patients with acute inflammatory and traumatic œdema and 18 patients with chronic infiltrations

The patients' ages ranged from 18 to 54 years They were chosen because they had widespread acute œdema or extensive hard infiltration without fluctuation and reddening of the skin

After trying small and large doses I concluded that the best results were obtained by giving 2000 units of streptokinase and 500 units of streptodornase per dose The injections were usually repeated every second day, and 2 to 4 injections were generally sufficient In most acute cases penicillin was given as well, patients with tuberculous cervical lymphadenitis had streptomycin and isoniazid

The results in patients with acute œdema are shown in the accompanying table Very recent infiltrations sometimes receded after a single injection, usually without penicillin Infiltrations present for several days required 2 or 3 injections The softening infiltrations opened spontaneously within twenty four hours, and œdema subsided rapidly

With fresh hæmatomas the results were distinctly worse, and in patients with subacute infiltrations there were visible results in a few cases only In chronic œdema there was no definite improvement

Occasionally the injection of the enzymes provoked a strong reaction, especially in acute inflammatory conditions The reaction appeared three to six hours after the injection The features were fever, joint pains, headaches, epigastric pain and nausea, tachycardia, and increase in blood pressure The symptoms usually disappeared in six to twelve hours These reactions also occurred in healthy controls, so they may be an allergic response to protein in the enzymes The symptoms pointed to a transient, intense stimulation of the sympathetic system, and the administration of a sympathetic blocking drug (e g, dihydroergotamine) relieved the symptoms in some cases

Because of the possibility of a reaction, this treatment should not be used in persons with cardiovascular disease, in old persons, and in those with a history of tuberculosis

TREATMENT OF ACUTE INFLAMMATION WITH INTRAMUSCULAR STREPTOKINASE AND STREPTODORNASE

Condition	No of patients	Disappearance of œdema and infiltration or rapid softening and rupture				Doubtful result (14–28 days)	No improvement
		In 24 hours (1 injection)	In 24–72 hours (1–3 injections)	In 3–7 days (2–4 injections)	In 7–14 days (4–5 injections)		
Mastitis	7	2	3	1		1	
Acute non specific epididymitis	6		1	2	2	1	
Periproctitis fistula in ano	4	1	3				
Phlegmonous infiltration of the gluteal region	4		3	1			
Acute periostitis of mandible and maxilla	3			1	1	1	
Carbuncles of the face lips and neck	6		2	2	2		
Acute lymphadenitis	5	1	2	1			1
Osteomyelitis	2		1			1	
Hæmatoma	7		1	1	1	2	2
Total	44	4	16	9	6	6	3

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3 Maudsley, R H *Lancet* 1953 i, 847
4 Arden G P, Ward F G *J Bone Jt Surg* 1955 37B 639
5 *Brit J Surg* (in the press)
6 See *Lancet* 1951 ii 1221

1 Miller, J M *Sci News Lett*, *Wash* November 1954.

severe hæmorrhagic diathesis developed followed by septicæmia due to *Escherichia coli* and *Pseudomonas pyocyanea*. Electrocardiography showed pronounced myocarditis. Bone-marrow biopsy revealed severe damage to the blood-forming cells "presumably due to some drug or other". A few days after the anæsthesia had been discontinued signs of remission developed in the bone-marrow, yet on the twenty-ninth day the boy died from cardiac insufficiency and septicæmia.

When we reviewed the case-histories of the first 2 patients, who had recovered, it became clear that they also had shown signs of hæmatological complications. The 1st, a boy aged 10 years, had thrombocytopenia, hæmaturia, and retinal hæmorrhage on the fourteenth day of treatment. In the 2nd case, that of a boy aged 11 years, between the sixth and tenth days in hospital the leucocyte count fell from 12,500 to 2200 per c.mm. Treatment was discontinued on the twelfth day, and the blood was not examined again.

The 4th patient had moderately severe tetanus, and hæmatological complications did not appear.

In March, 1955, a 5th patient, a woman aged 53, was admitted with severe tetanus.

Very early after admission tracheotomy had to be done. After the operation she was treated according to the principles previously outlined, including anæsthesia with nitrous oxide and oxygen.

CHANGES IN PERIPHERAL BLOOD IN REL
IN PATIENTS WITH SEVERE

Treatment	Granuloc penia o thromb pen
Chloral hydrate	
Pentobarbitone sodium	
'Phenemal' sodium	
Pethidine	
d-Tubocurarine	
Bromethol	
'Curacit'	
'Largactil'	
Continuous nitrous oxide	

treatment remained unchanged
coli now developed, and the p
day with signs of severe hæmor
specimens of bone-marrow re
with greatly reduced or prol
poiesis."

Gormsen (1955) publis
showing agranulocytosis
boy treated by prolonged
and oxygen, chlorproma
also a reduced number
blood was observed o
followed by a decrease

coagulating, or to relieve the pain When the needle is not at work, there is a trolley with more doses to be taken by mouth

One of the results of this continual attention is immense tiredness The very sight of a nurse with a glass or syringe is exhausting It is bad enough having to be in a ward with perhaps 30–50 other patients (although this has its advantages in taking one's mind off oneself), but any brief nap is interrupted ruthlessly, so that the patient gradually becomes aware that this is not a hospital at all, but a factory in which certain procedures are performed every few minutes, regardless of circumstance

Though I have heard it said, proudly, that "the days when one walked on tiptoe if someone was ill" are gone forever, it is not the nurses who are at fault They do not invent these new methods They obey orders and many of them do so with all the gentleness and grace they can summon to aid them in their lives of devotion and service But I do suggest that a new callousness is creeping into our hospitals, and I think that certain practices should be frequently reviewed in the hope of eliminating the distress and discomfort they cause In particular, since it is mainly the old who have to submit to them, I would like very senior doctors to be consulted And most of all, I would like the human being, rather than the human being's ailment to have top priority—however unscientific that may sound

A PATIENT'S FRIEND

MALARIA AND THE THAMES

SIR,—Almost the whole of the initial historical section of this paper (*Lancet*, April 14) has been borrowed from a paper of mine,[1] sometimes word-for-word, sometimes with so little care that mistakes have been introduced that cannot be passed uncorrected In his *Ecclesiastical History* the Venerable Bede never mentions the *lencten adl* ("spring ill," i e, malaria), nor does he "draw attention" to any "prevalent" fever He refers only to a single case of fever where the sufferer went and sat by St Oswald's tomb, so that the attack did not return either on the second or third day, or subsequently All that interested Bede was the miracle The point of my story was, that the translator of Bede's Latin, presumably King Alfred, in turning this passage into Anglo-Saxon did not render Bede's vague "*febris*" by an A-S equivalent, but replaced it by the specific "*lencten adl*", thus naming the disease malaria, which probably it was Shakespeare did not use "ague" in *Macbeth* "mistakenly", this old name for typhus still lingered on in his day, and survived still longer in Ireland Samuel Butler, Charles II's favourite poet, is called "the essayist"—here perhaps he is confused with Samuel (*Erewhon*) Butler Horace Walpole was not the first person to employ the word malaria, he was merely the first, so far as is known, to introduce this existing Italian term into English He was not writing to Thomas Gray, and Gray was not in London—he was with Walpole in Italy The letter in question was not dated "1840" but July 5, 1740, and was addressed to the Hon H S Conway In it Walpole explains that he has left Rome because of the horrid thing called the mal'aria, and adds, "I do not care for being killed so far from Christian burial!" And, finally, the author of the *Elegy* did not spell his surname "Grey"

The British Council
London W 1

W P MACARTHUR

*** This letter has been shown to Dr W D L Smith who writes "At one point in my article I gave a reference to Sir William MacArthur's article, but I quoted from this work several times and should have acknowledged the source on each occasion For these omissions I apologise to Sir William I am indebted to him for pointing out my misinterpretation of certain historical facts"—ED L

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[1] *Brit med Bull* 1951, 8 76

CERVICAL VERTIGO

SIR,—I have read with great interest the article by Dr Ryan and Dr Cope (Dec 31) I fully agree that vertigo is often unconnected with disorder of the inner ear.

In 1940 I described[1] a disorder of the neck muscles—especially trapezii—which is often associated with giddiness, notably on movement of the head, and sometimes with occipital headache I have since again drawn attention to the frequency of this form of giddiness[2] which can be rapidly cured by treatment of the muscular lesion This remarkable fact is explained by the experimental finding[3] that the neck muscles, largely concerned with equilibrium and maintaining the posture of the head have a nervous connection with the labyrinth It is obvious that the position of the head, relative to that of the body determined by the tonus of the neck muscles serves as do the eyes the function of equilibrium

London, N W 11

M G GOOD

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[1] Good M. G *Lancet*, 1940 ii 326
[2] *Proc R Soc Med* 1950 43 290
[3] Mies, H *Klin Wschr* 1937 16 593

TRANSPORTING PATIENTS WITH POLIOMYELITIS AND BULBAR OR RESPIRATORY PARALYSIS

SIR,—Last summer we supervised the transport of 12 patients with severe acute poliomyelitis to the regional poliomyelitis unit at Rush Green Hospital, Romford, Essex These patients had either bulbar paralysis or paralysis of diaphragm and/or intercostal muscles, or combined bulbar and respiratory paralysis

The ambulances used were of the usual type in service in Essex, except when transporting a patient in a complete "iron lung" The equipment carried included all the instruments, drugs, and endotracheal tubes necessary for tracheotomy under general or local anæsthesia, positive-pressure apparatus, consisting of an Oxford inflating bellows and a Beaver Mark I or II machine, portable suction apparatus, oxygen cylinders, bronchoscope laryngoscope, torches, and spatulæ This equipment is fairly compact and takes up little space in an ambulance or police car The distances covered varied from 12 to 30 miles

Bulbar Paralysis

These cases were either "dry" or "wet"—that is, with partial or complete pharyngeal paralysis, this factor determining the degree of "pooling" of saliva and mucus in the pharynx and larynx

"Dry" bulbar cases were not difficult or worrying to transport The patients were conveyed prone with the head turned to one side, a few pillows placed under the abdomen facilitating postural drainage on the ambulance stretcher bed, secretions ran out of the mouth easily since the head was inclined downwards This is the position adopted for patients immediately after tonsillectomy, except that in poliomyelitis cases the tilt often needs to be steeper The patients were given swabs and encouraged to spit out their saliva, and suction was usually not necessary to maintain a clear airway

"Wet" bulbar cases with complete pharyngeal paralysis were often very irritable and, because of severe headache, were reluctant to remain in the safe prone position with head inclined downwards Vomiting was common, partly because the frequent suction necessary irritated the pharyngeal wall Torch spatula, and suction apparatus were the essential instruments during the journey with these cases A stethoscope was invaluable for listening over the trachea to check that the airway was clear

Respiratory Involvement

When the respiratory paralysis was slight (e g, some intercostal weakness) there was no difficulty in transporting the patient in an ordinary ambulance Respiration was

The unchanged state of cases 3–6 may not be an entirely negative result Certainly in cases 3 and 4 a further deterioration as a result of renal disease was to be expected, even within the limited follow up

Control of Diabetes

It is difficult to calculate, except in general terms, any change in the ease with which the diabetes was controlled These patients after operation were attending frequently and were under close observation, hence adjustments of insulin dosage or of diet were readily made There did not appear to be any significant difference in average blood sugar level, total glycosuria daily, or incidence of hypoglycæmia after the operation, except in case 5, who achieved an average blood sugar level of 150 mg per 100 ml and a daily output of less than 5 g of glucose on the same dosage of insulin—16 units daily Possibly the improvement was entirely due to improved care with diet The patient has had one attack of insulin coma, due to delay of a meal, since operation This is the only major episode of hypoglycæmia in the whole series

Insulin Dosage

In Wortham and Headstream's (1953, 1954) series the insulin dosage after adrenalectomy was two thirds of that before operation After hypophysectomy in Olivecrona's series (Luft et al 1955) the average was from a quarter to a third of the preoperative dosage In the present series there was no significant reduction in insulin dosage This may be due to the use of a comparatively large maintenance dosage of cortisone (50 mg) The possibility of supplementing a lower dosage with deoxycortone acetate was considered but rejected Luft et al (1955) no longer use deoxycortone acetate, because of its unfavourable effect on damaged blood-vessels

Retinopathy

In case 2 vitreous hæmorrhages, which were taking place at least once a fortnight, have ceased, there being no recurrence since the operation The appearance of retinitis proliferans persists, but the visual acuity in each eye is 6/6 In cases 3 and 4 there has been no detectable change in the retinopathy, but, since massive vitreous hæmorrhage had already obscured the fundus, it is impossible to be certain

In case 5 fresh vitreous hæmorrhage recurred two months after the operation and was followed by glaucoma with total loss of vision in the left eye Fortunately the right eye, amblyopic because of a squint, was only slightly affected by retinopathy, and the visual acuity is slowly improving Case 6 has been followed for only four months, and the absence of change is not significant

Albuminuria

Apart from case 1, already in advanced renal failure, cases 3 and 4 have shown no sustained improvement in daily albuminuria Six months after the operation both showed a significant decrease—from 5 to 2 g and from 2 to 0 g —but three months later there had been a return to the preoperative levels

Blood pressure

In cases 3 and 4 there was no reason to doubt that the hypertension was renal in origin, the reduction in blood pressure cannot be considered significant after so short a follow up In case 5 a rising blood pressure had been noted for seven years, and a diagnosis of essential hypertension was accepted

Discussion

If these results are considered in conjun [illegible] those of Wortham and Headstream (1953, 195 [illegible] conclusions may be advanced in spite of the smal [illegible] of patients, they are those which common sense s [illegible]

(1) The operative mortality of total adrenalectomy in patients with diabetic vascular disease not having renal failure is negligible

(2) Maintenance with cortisone after total adrenalectomy is simple

(3) The general health is not made worse by total adrenalectomy

(4) Control of the diabetes is unaffected by total adrenalectomy

(5) Retinopathy and renal damage may be halted at an early stage, this cannot be established until after a longer follow up Advanced retinopathy is not altered, and renal failure, if established, is accelerated

Selection of Material

It is now generally agreed that the most urgent clinical problem in diabetes is the vascular disease which seems to develop inevitably if the patient lives sufficiently long Those whose diabetes starts after the age of 50 may live to old age without apparent acceleration of arteria degeneration, but the young are condemned to certain death from a characteristic disorder of small vessels, i other hazards of diabetes are avoided (Mirsky 1946) Now that these hazards are becoming relatively unimportant, the patient with advancing vascular disease is becoming rapidly more common That vascular disease both atherosclerosis and capillary damage, is more common in diabetics than in non diabetics is the finding of all substantial inquiries both in living and in dead subjects (Liebow et al 1955, Bell 1950) Capillary lesions are seen with increasing frequency the longer diabetes persists, but atherosclerosis, though abnormally common, seems not to be related to the duration of diabetes (Mirsky 1946)

Atherosclerosis and diabetic "angiopathy," as Lundbæk (1954) has named the capillary disease of diabetes, may be considered separately, it is not to be assumed too readily that they are unrelated, for we have to remember that the angiopathy can be detected in the retina at a very early stage and in the kidney by inference from examination of the urine, whereas atherosclerosis can only be diagnosed in life by rather gross clinical signs At present there is no conclusive evidence that the arterial lesions differ from those of patients without diabetes On the other hand, the picture of diabetic angiopathy is gaining definition The histological changes in the retina described by Ballantyne and Loewenstein (1943) remain specific for diabetes Ashton (1951) found similar, though not identical, changes in non diabetic eyes, but the over-all picture is entirely individual The same is true of the renal disorder In view of the tendency of pathologists to disagree, the relation of the nodular lesions in the glomeruli to diabetes has been accepted to a remarkable extent (Bell 1950) Apart from other resemblances, the staining reactions of the hyaline material with the periodic acid stain suggest that the lesions in the kidney and the retina are manifestations of a single disorder, and studies of necropsy material (McManus 1950) confirm that they coexist in all fatal cases It is this angiopathy, believed to be a specific complication of diabetes, which is under consideration for possible relief by adrenalectomy Perhaps the lesions occur elsewhere than in the retina and kidney, but it is in these sites that arise the symptoms which justify a desperate remedy To make a firm criterion for such an interference it is necessary first to consider the clinical course of retinopathy and nephropathy in the absence of specific [illegible]ent

Course o [illegible] athy

The op [illegible] opic picture of diabetic retinopathy, first descr [illegible] any accuracy by Hirschberg (1890), was classif [illegible] n [illegible] 46) on the basis of many histological [illegible] lution from the earliest hanges (mi [illegible] nal destruction of the

Parliament

The Budget

SYMPTOMS of severe inflation were described by Mr Harold Macmillan, Chancellor of the Exchequer, in his Budget speech last Tuesday The few new measures by which he proposes to counter this are directed mainly towards encouraging saving and curbing industrial investment There are to be a new issue of National Savings Certificates, yielding over 4% tax-free in a seven-year period an increase in the interest on Defence Bonds from 4% to 4½%, and for the first time premium bonds involving tax-free prizes The bread subsidy is to be terminated in September. The Chancellor announced an immediate increase in tax of 2*d* for 20 cigarettes, with corresponding increases for other tobacco preparations His one or two concessions include an increase of 2*s* in the family allowance for a third and subsequent children and a proposal to give effect to a recommendation of the Millard-Tucker Committee, so that the self-employed, including professional men in practice, shall gain relief from income-tax and surtax on premiums to buy a deferred annuity on retirement Income-tax is to be unchanged

Shortage of Nurses in Hospitals

On April 11 in a debate on the adjournment Dr A D D Broughton raised the question of the shortage of nurses in hospitals Though there were now more nurses than at the start of the National Health Service there were still not enough and their distribution was uneven Why were not more women entering the profession, why were so many leaving before completing their training, why were so many leaving hospital after completing their training? In recruitment the nursing profession faced the competing claims of other professions, of business, and of industry Even in hospitals themselves, other departments drew girls away from nursing and provided interesting work with regular hours and good pay

Turning to wastage during training, he asked for a review of the curriculum In 1947 the Working Party had suggested two years' basic training, but this had still not been implemented Many trained nurses, he continued, were drawn from the hospitals by local authorities and industrial firms From a national point of view first-class women were being wasted on work which could sometimes be done by capable women trained in first-aid and home-nursing When things were going well it was sensible to leave matters in the hands of the Whitley Council and the General Nursing Council, but when more than 16,000 beds were closed through lack of nursing staff it was time (Dr Broughton thought) for the Minister himself to examine the whole problem

Miss Patricia Hornsby-Smith, parliamentary secretary to the Ministry of Health, agreed that there was no reason for complacency, but she was concerned that in a year when the Government were doing their utmost to stimulate recruiting, particularly for mental nurses, the picture should not be painted in the wrong colours There had been substantial and steady progress since the National Health Service came into being The total nursing staff in hospitals in 1948 numbered 117,000 full-time, in 1955 it was 143,000 There were 20 000 part-time nurses in 1948 now there were 32,000 There were 44 000 full-time trained nurses in 1948, now there were 55,000 In 1948 there were 6000 part-trained nurses against 12,000 at present In 1948 the number of enrolled student nurses was 42 000 and in 1955 it was 48 000 Pupil assistant nurses had increased from 2600 in 1948 to 4000 in 1955 On the general nursing side, with a few local bad patches, the number of students was fully adequate for a continuing and steady increase in the number of nurses The rate of entry in general nursing was over the whole country satisfactory, but it was still inadequate on the mental side She was sure that the new scheme of training allowances (see p 518) would stimulate recruiting

Clean Air Council

The Clean Air Bill was considered on report in the House of Commons on April 10 On the motion of Mr Duncan Sandys, Minister of Housing and Local Government a new clause was agreed to providing for the appointment of a consultative council, to be called the Clean Air Council of which the Minister will be chairman, to keep under review the progress made in abating the pollution of the air and to obtain the advice of people with special knowledge experience or responsibility in regard to the prevention of air-pollution The clause provides for the appointment of a similar council for Scotland

QUESTION TIME

Smoking and Lung Cancer

Lieut -Colonel Marcus Lipton asked the Minister what information he would now publish on the connection between smoking and lung cancer —Mr Turton replied I am not yet ready to add to the answer I gave on March 26 Lieut - Colonel Lipton Why is the Minister so hesitant about following the advice of his own medical advisory committee and the Central Health Services Council over a month ago that the public should be informed of the known facts will he give an assurance that this inexplicable delay on the part of the Government is not prompted by financial considerations ?—Mr Turton It is for me to see what are the known facts compared with what they were when my predecessor made his statement in February, 1954,

Whitley Council Machinery

Replying to a question Mr R H Turton, Minister of Health, said that he and the Secretary of State for Scotland had accepted the Guillebaud Committee s recommendations on Whitley Council machinery The management and staff sides of the councils were being invited to explore the methods used in other large scale undertakings to introduce flexibility into national agreements The management sides were being asked to propose alterations in the constitutions of the councils that would add 3 hospital representatives to each To facilitate this he and the Secretary of State for Scotland were willing for the representation of their departments to be reduced by the same number on all the councils except the optical and pharmaceutical where there were special departmental interests The views of the management sides were being sought on the question of consultation with hospital authorities, but it would be made clear that in the opinion of the Government any arrangements that might cause further delay in the reaching of settlements should not be contemplated The attention of both management and staff sides was being drawn to what the Guillebaud Committee had said about delays Negotiations on pay and conditions of service necessarily took time but the Government were confident that all concerned would do their utmost to ensure that there were no avoidable delays

Tooth-paste Advertisements

Replying to a question Mr Derek Walker Smith, parliamentary secretary to the Board of Trade, said that after taking expert advice the Minister had come to the conclusion that the available evidence dealing with false claims by tooth paste manufacturers would not support a prosecution under the Merchandise Marks Acts The British Dental Association deprecated the form of the advertisement which it thought might be the result of inadequate evidence, but it was not prepared to say that the claim was false

N.H S Estimates

Replying to a question Miss Hornsby Smith said that £2½ million was included in the estimate for N.H.S expenditure in 1956–57 to cover increases in salaries and wages already agreed or still under negotiation The new award for nursing staff would require a supplementary estimate

Unemployed Doctors

Dr D Johnson asked the Minister whether he was aware that there were 35 doctors in receipt of unemployment benefit on March 19, 1956 what steps he was taking to find opportunities for employment for them in the National Health Service whether he was aware of the existence of a permanent reservoir of unemployed or underemployed doctors unable to find work under the National Health Service ?—Miss Hornsby-Smith replied It is estimated that there are 53,000 doctors in active employment in Great Britain, the proportion receiving unemployment benefit is therefore extremely small. Every effort is made to bring vacant posts to notice A committee had been appointed to inquire into future requirements for doctors and students

The unchanged state of cases 3–6 may not be an entirely negative result Certainly in cases 3 and 4 a further deterioration as a result of renal disease was to be expected, even within the limited follow-up

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Course of Retinopathy

The ophthalmoscopic picture of diabetic retinopathy, first described with any accuracy by Hirschberg (1890), was classified by Ballantyne (1946) on the basis of many histological examinations The evolution from the earliest changes (micro aneurysms) to the final destruction of the

FFECTS OF FEEDING DIFFERENT FATS ON SERUM-CHOLESTEROL LEVEL

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A SURVEY of the multiracial community residing in he Cape Peninsula revealed that the widely differing nter racial incidence of coronary heart disease was associated with a parallel difference in the mean serum-cholesterol levels (Bronte Stewart et al. 1955a). Within each racial group the serum cholesterol level was highest in those on the highest economic plane and bore a parallel relationship to the intake of foods rich in fat of animal origin. There was no correlation with the intake of vegetable fat. Diets which through economic privilege have increasing quantities of foods containing animal fat also have increasing quantities of animal proteins, with resulting changes in the intake of vitamins, and decreasing quantities of starch and cellulose. It became necessary, therefore, to study the effect of various foodstuffs on the serum cholesterol level under controlled conditions.

Material

This study was conducted on two groups of people: volunteers with initial low serum-cholesterol levels and ccustomed to a low-fat diet (about 17% of calories rom fat), and 2 patients with initial high serum-cholesterol levels and accustomed to a diet rich in animal fat. The 2 patients, who agreed to cooperate in the investigation, were European males, aged 38 and 42, with angina pectoris and electrocardiographic evidence of coronary heart disease. The 6 volunteers were 5 Bantu males and 1 Cape Coloured male from the poorer economic strata. With 1 exception, no abnormal physical signs were observed in the volunteers during the study. 4 had been admitted with vitamin deficiency syndromes and had received vitamin therapy before the start of this study, and these vitamin supplements were continued throughout. The 1 exception was studied during physiotherapeutic rehabilitation after hemi plegia, probably syphilitic. Physical activity was minimal throughout the study.

Diets Used

Throughout the study the 2 Europeans with coronary heart disease were kept on a constant diet containing a moderate amount of fat (50 g. daily) almost exclusively of animal origin in the form of butter, milk, and meat. The basic diet of the 6 non-European volunteers consisted of maize-meal products and white bread supplemented by sugar and casein to maintain by suitable adjustment an isocaloric and isonitrogenous state. This diet is free from cholesterol, and the small amount of fat present is that contained in the maize and bread, estimated to be not more than 3% of the total calories (Fox and Golberg 1944). The first 2 non-Europeans were studied without casein supplements and were maintained on a protein-poor diet (28 g. daily) throughout by the use of finely sifted maize meal (baker's cones). In another volunteer the intake of protein was deliberately altered by changing from baker's cones to standard maize meal (an increase of about 7 g. of protein daily) and later supplementation of this daily intake of protein with 100 g. of casein.

To these diets various fats and oils were added one at a time, usually in amounts of 100 g., to increase the proportion of calories derived from fat from the basic 3% to 36% and 45% and, on occasion, to 60–70% (200 g.). With this sudden increase in intake of fat transient diarrhœa developed on two occasions but ceased spontaneously without reduction of the intake of fat. The oils were administered either as a draught or incorporated in the food, according to individual preference. When the oils were given in cooked food, this was fried at moderate or low temperatures. In view of Page's (1954) warning that there may be an individual variation in the response to fat feeding, our policy was to try several different fats on the same person.

Methods

Blood was drawn every other day with the subject fasting, and the cholesterol was estimated in duplicate, firstly in the fresh sera, and secondly on filter-paper containing the electrophoretically separated lipoproteins by the method of Abell et al. (1952) modified by Anderson and Keys (1955) as in the previous survey (Bronte-Stewart et al. 1955a). Cholesterol in stools was estimated by the same method.

With this method, storage of the frozen sera did not affect the cholesterol values. Use was made of this to cross check the trends that evolved by re estimating a specimen of serum from the previous week. By these methods the same fat given three months later to the same volunteer produced almost identical serum-cholesterol levels (figs. 2 and 6).

Isolation of Fatty acid Fractions

Two fatty acid fractions were separated from sunflower seed oil by fractional crystallisation from acetone

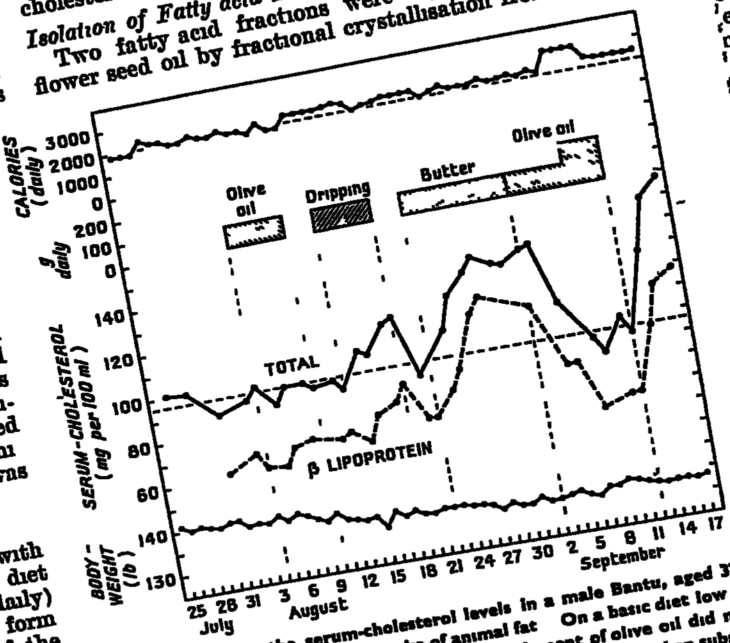

Fig. 1—Changes in the serum-cholesterol levels in a male Bantu, aged 37, coincided with changes in the intake of animal fat. On a basic diet low in protein and fat and free from cholesterol a supplement of olive oil did not raise the serum cholesterol level or maintain the raised level when substituted for butter. Even when the olive-oil supplement was doubled so that it provided over 60% of the total calories, the serum-cholesterol level did not rise again until a "full diet" consisting of beef and vegetables (fat-content about 140 g.) was given. The mean serum cholesterol level before fat feeding was 95.6 ± 5.5 mg. per 100 ml.

The unchanged state of cases 3–6 may not be an entirely negative result Certainly in cases 3 and 4 a further deterioration as a result of renal disease was to be expected, even within the limited follow-up

Control of Diabetes

It is difficult to calculate, except in general terms, any change in the ease with which the diabetes was controlled These patients after operation were attending frequently and were under close observation, hence adjustments of insulin dosage or of diet were readily made There did not appear to be any significant difference in average blood-sugar level, total glycosuria daily, or incidence of hypoglycæmia after the operation, except in case 5, who achieved an average blood-sugar level of 150 mg per 100 ml and a daily output of less than 5 g of glucose on the same dosage of insulin—16 units daily Possibly the improvement was entirely due to improved care with diet The patient has had one attack of insulin coma, due to delay of a meal, since operation This is the only major episode of hypoglycæmia in the whole series

Insulin Dosage

In Wortham and Headstream's (1953, 1954) series the insulin dosage after adrenalectomy was two thirds of that before operation After hypophysectomy in Olivecrona's series (Luft et al 1955) the average was from a quarter to a third of the preoperative dosage In the present series there was no significant reduction in insulin dosage This may be due to the use of a comparatively large maintenance dosage of cortisone (50 mg) The possibility of supplementing a lower dosage with deoxycortone acetate was considered but rejected Luft et al (1955) no longer use deoxycortone acetate, because of its unfavourable effect on damaged blood-vessels

Retinopathy

In case 2 vitreous hæmorrhages, which were taking place at least once a fortnight, have ceased, there being no recurrence since the operation The appearance of retinitis proliferans persists, but the visual acuity in each eye is 6/6 In cases 3 and 4 there has been no detectable change in the retinopathy, but, since massive vitreous hæmorrhage had already obscured the fundus, it is impossible to be certain

In case 5 fresh vitreous hæmorrhage recurred two months after the operation and was followed by glaucoma with total loss of vision in the left eye Fortunately the right eye, amblyopic because of a squint, was only slightly affected by retinopathy, and the visual acuity is slowly improving Case 6 has been followed for only four months, and the absence of change is not significant

Albuminuria

Apart from case 1, already in advanced renal failure, cases 3 and 4 have shown no sustained improvement in daily albuminuria Six months after the operation both showed a significant decrease—from 5 to 2 g and from 2 to 0 g —but three months later there had been a return to the preoperative levels

Blood pressure

In cases 3 and 4 there was no reason to doubt that the hypertension was renal in origin, the reduction in blood-pressure cannot be considered significant after so short a follow up In case 5 a rising blood-pressure had been noted for seven years, and a diagnosis of essential hypertension was accepted

Discussion

If these results are considered in conjunction with those of Wortham and Headstream (1953, 1954), certain conclusions may be advanced in spite of the small number of patients, they are those which common sense suggests

(1) The operative mortality of total adrenalectomy in patients with diabetic vascular disease not having renal failure is negligible

(2) Maintenance with cortisone after total adrenalectomy is simple

(3) The general health is not made worse by total adrenalectomy

(4) Control of the diabetes is unaffected by total adrenalectomy

(5) Retinopathy and renal damage may be halted at an early stage, this cannot be established until after a longer follow up Advanced retinopathy is not altered, and renal failure, if established, is accelerated

Selection of Material

It is now generally agreed that the most urgent clinical problem in diabetes is the vascular disease which seems to develop inevitably if the patient lives sufficiently long Those whose diabetes starts after the age of 50 may live to old age without apparent acceleration of arterial degeneration, but the young are condemned to certain death from a characteristic disorder of small vessels, if other hazards of diabetes are avoided (Mirsky 1946) Now that these hazards are becoming relatively unimportant, the patient with advancing vascular disease is becoming rapidly more common That vascular disease, both atherosclerosis and capillary damage, is more common in diabetics than in non-diabetics is the finding of all substantial inquiries both in living and in dead subjects (Liebow et al 1955, Bell 1950) Capillary lesions are seen with increasing frequency the longer diabetes persists, but atherosclerosis, though abnormally common, seems not to be related to the duration of diabetes (Mirsky 1946)

Atherosclerosis and diabetic "angiopathy," as Lundbæk (1954) has named the capillary disease of diabetes, may be considered separately, it is not to be assumed too readily that they are unrelated, for we have to remember that the angiopathy can be detected in the retina at a very early stage and in the kidney by inference from examination of the urine, whereas atherosclerosis can only be diagnosed in life by rather gross clinical signs At present there is no conclusive evidence that the arterial lesions differ from those of patients without diabetes On the other hand, the picture of diabetic angiopathy is gaining definition The histological changes in the retina described by Ballantyne and Loewenstein (1943) remain specific for diabetes Ashton (1951) found similar, though not identical, changes in non diabetic eyes, but the over-all picture is entirely individual The same is true of the renal disorder In view of the tendency of pathologists to disagree, the relation of the nodular lesions in the glomeruli to diabetes has been accepted to a remarkable extent (Bell 1950) Apart from other resemblances, the staining reactions of the hyaline material with the periodic acid stain suggest that the lesions in the kidney and the retina are manifestations of a single disorder, and studies of necropsy material (McManus 1950) confirm that they coexist in *all fatal* cases It is this angiopathy, believed to be a specific complication of diabetes, which is under consideration for possible relief by adrenalectomy *Perhaps the lesions* occur elsewhere than in the retina and kidney, but it is in these sites that arise the symptoms which justify a desperate remedy To make a firm criterion for such an interference it is necessary first to consider the clinical course of retinopathy and nephropathy in the absence of specific treatment

Course of Retinopathy

The ophthalmoscopic picture of diabetic retinopathy, first described with any accuracy by Hirschberg (1890), was classified by Ballantyne (1946) on the basis of many *histological examinations* The evolution from the earliest changes (micro aneurysms) to the final destruction of the

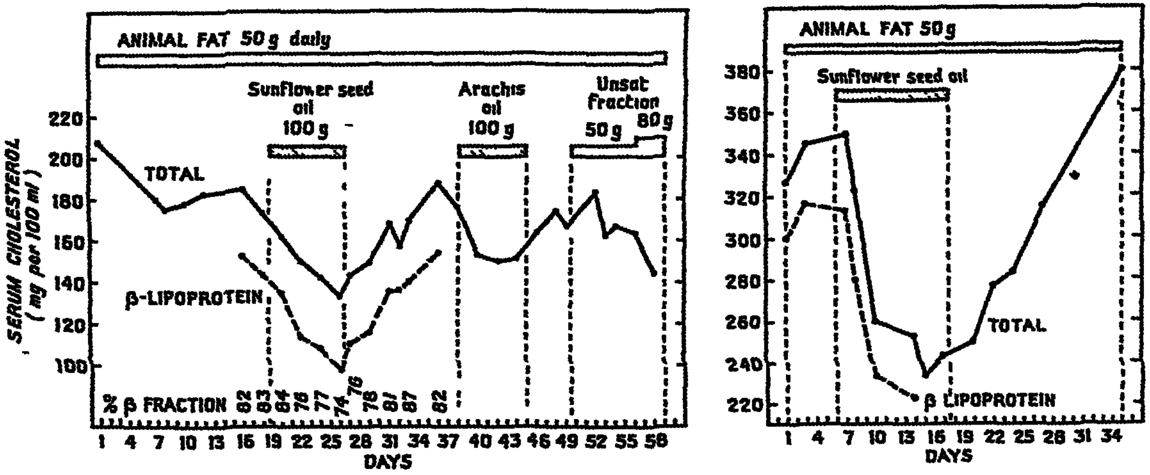

Fig 4—The effect is shown, in 2 Europeans, aged 38 and 42, with coronary heart-disease of increasing the intake of fat from 50 to 150 g daily by the addition of 100 g of sunflower-seed oil In the lower register withdrawal of sunflower-seed oil was followed by a large rise in serum-cholesterol level In the upper register both arachis oil and the unsaturated fraction prepared from sunflower-seed oil produced a similar response to that of sunflower-seed oil

oil (iodine value 230), used industrially in the hardening of hardboard, appeared to be more effective than sunflower-seed oil in countering the effect of ten eggs daily (fig 6)

USE OF SATURATED AND UNSATURATED FATTY-ACID FRACTIONS

In Supplementation of Hydrogenated Fat

These attempts might have been more convincing had we known earlier that the unsaturated fatty-acid fraction used in this experiment contained only 60–65% of linoleate When this became known, the 100 g of hydrogenated fat had to be supplemented with as much as 84 g of this unsaturated fraction to achieve the desired 27% of linoleate, the estimated proportion in the non-hydrogenated oil At this dosage there was insufficient for more than three days' feeding, but despite this great increase in the intake of fat, the serum cholesterol level fell On withdrawal of this unsaturated fraction the serum-cholesterol level rose again

In Substitution for Sunflower-seed Oil

Apart from the experiment outlined above, the unsaturated fatty-acid fraction was fed to 1 European volunteer with coronary heart disease in an attempt to reproduce the effects of the 100 g of sunflower seed oil and ground-nut oil supplements (fig 4) In this volunteer the serum-cholesterol level promptly fell when these oil supplements were given, despite the continued consumption of the basic diet containing 50 g of animal fat When 50 g of the unsaturated fatty acid fraction (estimated linoleate content 37 g) was added to this basic diet, no immediate effect was noted until a freshly prepared fraction was used This delay, which may be attributable to isomerisation, is discussed below

Rôle of Intake of Cholesterol with Highly Unsaturated and Saturated Fatty Acids

The effect of 100 g of fat consumed as ten eggs far exceeds that of equivalent amounts of hydrogenated ground nut fat (fig 2) Eggs contain protein cholesterol, and fat In 1 volunteer (fig 7) keeping the diet isonitrogenous by feeding casein after the withdrawal of the ten eggs did not maintain the rise in the serum cholesterol level The addition of 3 g of cholesterol (equivalent to that in ten eggs) raised the serum-cholesterol level but not so high as it had been When the quantitatively equivalent fat-content of ten eggs was supplied in a qualitatively dissimilar form (as sunflower seed oil) the serum cholesterol level fell despite the continued consumption of cholesterol and casein On withdrawal of the sunflower seed oil the serum-cholesterol level rose again At this point 60 g of the ethyl-linoleate fraction (the amount estimated to be present in 100 g of sunflower-seed oil) given daily for six days reproduced these effects When 15 g of the saturated fatty-acid fraction from sunflower-seed oil was fed, the serum-cholesterol level rose sharply At this stage the total intake of fat represented only 8% of the total calories

The use of 30 g of the saturated fraction in another subject was not associated with the same sharp rise Over 18 days there was a gradual rise in the serum-cholesterol level from 100 to 145 mg per 100 ml From the eighth day of this period a more freshly prepared saturated fraction was given together with 0 6 g of cholesterol, and the effect appeared to be more pronounced The subsequent administration of massive doses (1000 mg daily) of commercially prepared vitamin E ('Natopherol,' Abbott) in addition on the twenty-third day was not associated with an immediate fall in the serum-cholesterol level such as was seen with the pilchard oil, but six days later a slight fall occurred (Not only was this dose far in excess of that present in natural oils but also the vehicle is an oil which may have a high unsaturated fatty-acid content)

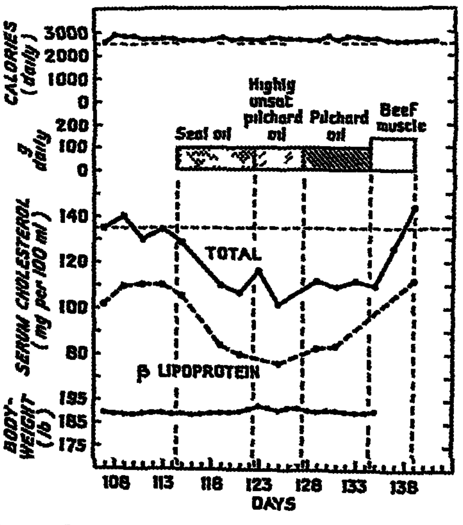

Fig 5—In same Bantu as in fig 3 during feeding of supplement of 100 g of various marine oils the serum-cholesterol levels remained considerably lower than during the low-fat cholesterol free control period Substitution of beef muscle for marine oils was followed by a prompt rise in serum-cholesterol level

the diagnosis, but glomerulosclerosis may accompany this disorder (Rifkin et al 1952) The term " nephropathy " is preferred by Wilson et al (1951) because of the difficulty in making this distinction The finding of doubly refractile lipoid casts in the urine is the most characteristic sign of glomerulosclerosis, but serial examinations are required, and their presence is not pathognomonic Recent experience indicates that the overwhelming majority of diabetic patients under the age of 50 with chronic renal disease have glomerulosclerosis In all my 17 cases the diagnosis was confirmed at necropsy, after having been made clinically from the finding of persistent symptomless albuminuria This is the first clinical manifestation and continues for a variable period before there are added hypertension, impaired renal function, and perhaps œdema Death takes place from renal failure or less often from congestive cardiac failure in fact, these conditions usually coincide in the terminal phase

Glomerulosclerosis is a progressive condition with a grave prognosis, death taking place in from two to five years Mann et al (1949) give an average survival of 6 4 years after the onset of nephrosis in 16 fatal cases of renal disease complicating diabetes, but in 8 of these there was no necropsy Rifkin et al (1952) did not feel justified in stating the duration of life, because they could not date the onset exactly In my series the onset of albuminuria could be dated to within six months because the urine was examined for albumin at each routine attendance If the first finding of albuminuria, rather than the onset of nephrosis, is taken as the point of onset of glomerulosclerosis, the average survival in the 17 cases was 5 2 years

Indications for Adrenalectomy

If we accept the view that the vascular disease of diabetes is progressive and will ultimately lead to disablement and death, and that adrenalectomy is worth considering as a possible means of arresting this process, we are confronted with a most awkward problem when we come to select the suitable case The earliest detectable lesions (in the retina) may remain stationary for years, and only an extreme enthusiast would consider so drastic an operation as adrenalectomy at this stage On the other hand, the later stage of retinitis proliferans or of renal insufficiency is almost certainly beyond the possibility of reversal by any form of treatment We have to hit on a period when we can say with reasonable certainty that the vascular disease has reached a point from which it will, if untreated, inevitably progress to blindness or renal failure within five years, yet the damage must *not* have reached an irreversible stage Such a period may be brief and implies frequent examination of those in whom vascular disease has been detected

The positive indications seem to be (1) retinitis proliferans as soon as diagnosed, and (2) glomerulosclerosis of a degree indicated by the following positive features albuminuria constantly present for six months, a diastolic blood-pressure above 90 mm Hg after a week of rest in bed, and diabetic retinopathy Doubly refractile lipoid casts in the urine strongly support the diagnosis but are not pathognomonic The same applies to œdema of insidious onset Negative features are the absence of blood casts from the urine and the absence of urinary infection, but it has to be remembered that such do not absolutely exclude glomerulosclerosis Either of these indications found alone would justify adrenalectomy

Contra-indications against Adrenalectomy

(1) *Advanced renal disease* —If the blood-urea level, in the absence of fluid and electrolyte disturbance from vomiting or from uncontrolled diabetes, is persistently above 70 mg per 100 ml, renal failure is likely to be aggravated by adrenalectomy

(2) *Retinopathy at Ballantyne's stage 4* —There are unusual cases in which episodes of repeated vitreous hæmorrhage are succeeded by years of adequate vision, and others, more rare, in which renal damage seems to remain stationary for several years, but the overwhelming majority of diabetics with capillary lesions tend to deteriorate progressively If good functional results are to be achieved, the risk of treating an occasional patient unnecessarily may have to be taken and the decision to intervene reserved for relatively early lesions It would be easier to convince our patients and ourselves that this decision is right, if evidence of arrest of vascular damage over a substantial time by adrenalectomy could be brought forward At present the apparent successes are not outside the range of spontaneous remission It can at least be said that total adrenalectomy is safe, and that the postoperative maintenance of the patient need not be a burden A life as tolerable as that before operation is possible, and control of the diabetes will be no less easy

Summary

Total adrenalectomy was undertaken for vascular disease in 6 diabetic patients Retinopathy was the indication in all the cases The follow up period was from five to sixteen months

1 patient, already uræmic, died of renal failure two weeks after the operation In the remainder the operation was uneventful Retinopathy was improved in 1, unchanged in 3, and worse in 1 Albuminuria was unchanged in the 2 patients in whom it was found before the operation

Control of the diabetes was unchanged

The general health was better in 1 patient and unchanged in 4

The main indications, if any, for adrenalectomy are retinitis proliferans as soon as it is diagnosed and persistent albuminuria in the absence of urinary infection

I should like to thank Dr F E Higgins, who was largely responsible for the care of these patients at the time of operation, and Mr J A C Edwards for carrying out the operations faultlessly

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ive oil and ground-nut oil did not raise the serum- holesterol levels Ground-nut oil fed as the hardened r hydrogenated form behaved differently from the atural oil This was regarded as a significant finding because one of the changes consequent on hydrogenation of oils is the destruction of the highly unsaturated fatty acids in their conversion to more saturated fatty acids which raises the melting-point (Deuel et al 1951) The highly unsaturated fatty acid affected predominantly in ground-nut oil is linoleic acid, which has been regarded by Burr (1942) as an essential fatty acid having metabolic functions other than the supply of calories Oleic acid and the saturated fatty acids did not appear to have these functions

Other essential fatty acids listed by Burr (1942) are linolenic, hexahydroxystearic, arachidonic, and docosahexaenoic acids , the last named two being present in high concentration in marine oils (Bailey 1945, W S Rapson personal communication) In a given dosage the biological activity of these latter essential fatty acids exceeds that of linoleic acid (Deuel 1955) Marine oils approach vegetable oils in their consistency at room-temperature and fatty-acid composition They do not ontain sitosterol and have a very low content of vita in E, but the cholesterol content does not greatly differ rom that of beef (Lange 1950)

Rôle of Dietary Intake of Cholesterol

We concur with the views of Messinger et al (1950), Keys (1952), and Mayer et al (1954) that the changes in the serum cholesterol level are due to some factor additional to the cholesterol content of the dietary fat Messinger et al (1950) noted greater effects when the cholesterol supplement was given with cream , we believe that this supports our view that an additional factor is the type of fatty acid in the fat concerned Our view is based on the fact that a possible common difference between animal fats and hydrogenated vegetable fat, on the one hand, and natural vegetable oils and marine oils, on the other, is not the cholesterol, sitosterol, vitamin, or protein content but is in some way connected with the proportion of highly unsaturated and saturated fatty acids in the fat concerned

In feeding experiments on rats Swell and others (1955) found greater rises of the serum cholesterol level when cholesterol was given with saturated fatty acids compared with unsaturated fatty acids They emphasise the importance of the nature of accompanying fatty-acid intake in the esterification and absorption of cholesterol

Our results with sunflower seed oil (iodine value 130–138) containing about 60% of linoleic acid (Bailey 1945) are not unlike those described by Kinsell and Michaels (1955) In their diabetic patient the extent of the fall in the serum-cholesterol level could be related to the unsaturated fatty-acid content of the vegetable oil used The most active was soy oil (iodine value 134) containing about 55% of linoleic acid and 6% of linolenic acid (Bailey 1945) Ahrens et al (1955) too found that corn oil, an oil rich in linoleic acid, was effective in this regard

Effect of Fatty acid Fractions

It appears to us that the data obtained in these experiments may reasonably be explained by the concept that the fatty-acid composition of the fat consumed determines the effect on the serum cholesterol levels Whether the effects produced depend on the fatty acids or on some accompanying factor is not yet explained Experiments with the pure fatty-acid fractions are being made, and a highly unsaturated fraction, when used soon after preparation, produced effects similar to those of sunflower seed oil , this fraction was free from sitosterol but contained a little vitamin E Although vitamin E in 1 volunteer appeared to produce a moderate fall of the serum cholesterol level, the dosage used was far in excess of that present in vegetable oils , moreover this preparation (derived from vegetable oils) may be rich in unsaturated fatty acids Vitamin E is not present in high concentration in marine oils, which nevertheless consistently depressed the serum cholesterol level

The unsaturated fraction that did not affect the serum-cholesterol levels had been redistilled in vacuo (±1 mm Hg) three times and, on subsequent testing, was found to contain about 20% of conjugated linoleic acids formed by isomerisation either during distillation or in the initial saponification of the sunflower seed oil Burr (1942) has shown that the isomer of linoleic acid, 9–11 linoleic acid, has no biological activity

The estimated vitamin-E content of this fraction was about four times that of the fresh unsaturated fatty-acid fraction that was effective later

Possible Applications to Coronary Heart-disease

The magnitude of the problem of coronary heart-disease has prompted us to publish these preliminary results Owing to difficulties in obtaining a sufficiency of the pure fatty acid fractions, or the pure fatty acids contained therein, our results are incomplete, but they show a very consistent trend

This consistency has applied particularly to the depressant effect on the serum cholesterol level of oils with high unsaturated fatty acid content On feeding supplements of animal fat the serum cholesterol levels were consistently raised, but not so high in the post-hemiplegic patient as in the others This raises the possibility that individuals may vary in their response to the dietary intake of fat

The serum cholesterol levels usually changed within forty eight hours of the dietary change, which is the time taken for the specific activity to reach its peak in isotope studies (Hellman et al 1955) Although the length of the feeding periods varied, it is quite possible that different effects might have been observed if these experiments had been continued longer

The application of these findings to certain problems in the ætiology of coronary heart disease depends on the acceptance of the views that coronary heart disease is in part a disorder of cholesterol and related lipoid metabolism, that there is a relationship between natural atherosclerosis in man and experimental atherosclerosis in laboratory animals, and that epidemiologically there is a relationship to the dietary intake of fat

Metabolism

The interrelationship of the essential fatty acids and cholesterol metabolism is becoming well documented (Kelsey and Longenecker 1941, Alfin Slater et al 1954, Deuel 1955, Peifer and Holman 1955, Shapiro and Freedman 1955, Swell et al 1955) Apart from the different sex requirements in the younger age groups (Cheng et al 1952) there are reported differences in capillary permeability and fragility which can be reversed by changing the intake of fat from animal to vegetable in man and by feeding ethyl linoleate in the rat (Kramar and Levine 1953)

Kritchevsky et al (1954) noted lower serum cholesterol levels and less atherosclerosis in rabbits fed cholesterol with 9% corn oil (iodine value 130) compared with rabbits on comparable cholesterol diets with 9% hydrogenated fat (iodine value 92) The possibility exists that atherosclerosis is intensified by a dietary deficiency of essential fatty acids In support of this theory is the finding of Alfin Slater et al (1954) of an increase in cholesterol ester in the livers of rats on low-fat diets On the other hand, Hartroft (1955) has reported increased deposition of fat in the liver when the intake of saturated fatty acids is high It is therefore of interest that, in man, Hammond and Lundberg (1955) have demonstrated differences between the fatty-acid content of the blood of atherosclerotic patients and blood donors, the former having a lower proportion of linoleate and arachidonate

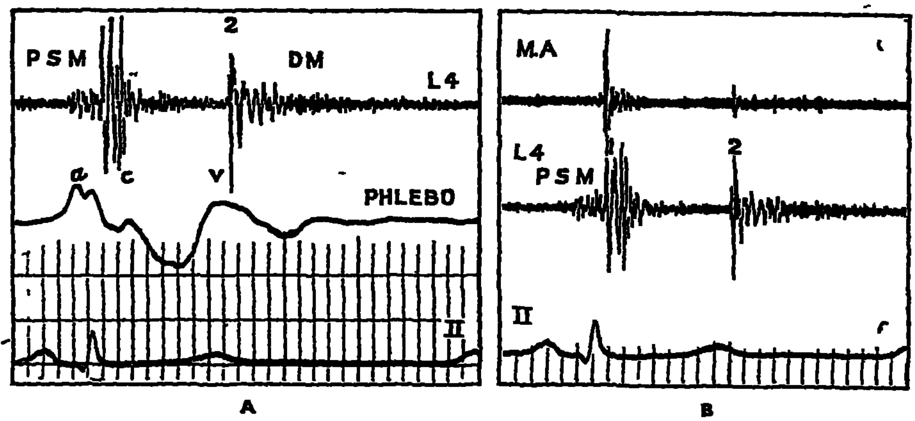

Fig 4—A, phlebogram showing dominant *a* wave in jugular venous pulse, B, phonocardiograms from mitral area and left 4th space, showing absence of mitral murmurs after mitral valvotomy

Postoperative Course—This was uneventful apart from a short attack of precordial pain, probably due to pericarditis, on the tenth day

Follow-up—Six months after valvotomy the patient was slightly improved but still had severe effort intolerance, being able to walk only 200 yards She was now, very interestingly, limited mainly by angina, the dyspnœa (due to pulmonary venous congestion) having been diminished by the mitral valvotomy Auscultation showed that the apical presystolic murmur and opening snap were now absent and the first sound was softer (fig 4) A fairly loud opening snap, presumably from the tricuspid valve, was recorded graphically from the left 4th space during inspiration (fig 5) but was not detected clinically During the next six months the angina became more severe, bringing the patient to a halt after walking only 50 yards on the flat, and sometimes being present at rest Electrocardiography after effort showed ischæmic changes (ST depression)

Tricuspid valvotomy was done a year after the mitral valvotomy The cavity of the right atrium was very large The tricuspid orifice was small, being just under 1 cm long, palpation gave the impression of a round opening in a fairly thin resilient membrane moving very little with systole A small regurgitant jet was felt near the posterior wall A finger was thrust through the opening without any difficulty, and the valve was felt to split, apparently posterolaterally Some ballooning of the anterior part of the valve could be felt which was comparable to that in the aortic cusp of a stenosed mitral valve, though not nearly so pronounced After the split the orifice measured 3 × 1 5 cm and was 7 cm in circumference, and a definite increase in the regurgitant stream was felt A systolic thrill was now palpable over the right atrium The atrium was less distended, its surface appearing wrinkled instead of smooth, and atrial contraction was stronger and more effective On direct auscultation before valvotomy a fairly long and rather low pitched diastolic murmur was heard over the right ventricle, but an opening snap was not detected

Postoperative Course—After the operation the patient got up on the third day and was discharged on the eighteenth day, there were no complications After tricuspid valvotomy there was a dramatic symptomatic improvement the anginal pain completely disappeared even on exertion, whereas before operation it occurred daily while the patient was at rest in bed in hospital The patient was, however, still limited by breathlessness and could only walk slowly about half a mile on the flat, stairs were managed if taken slowly On examination there was still a prominent though diminished 4 cm *a* wave in the neck The tricuspid diastolic murmurs were still present, and the tricuspid opening snap was still recorded on the phonocardiogram In addition a soft tricuspid systolic murmur had appeared since the valvotomy The aortic diastolic murmur was unchanged

Cardiac catheterisation three months after tricuspid valvotomy showed that the tricuspid gradient had been diminished in atrial systole from 10 to 6 mm Hg and in diastole from 4 to 2 mm Hg Since the cardiac output had risen by 25% between the two observations, the reduction of the gradient by about 50% is undoubtedly significant The P C V pressure of 9 mm Hg was slightly less than the figure of 11 mm Hg obtained before mitral valvotomy, as was the degree of obstruction at the mitral valve measured by the Ry/V of 1 38 compared with 0 9 Some degree of mitral stenosis is present, accounting for the breathlessness still experienced

Discussion

Cossio and Perianes (1949) described the production of incompetence of the normal tricuspid valve by passing an instrument through the jugular vein for the relief of chronic pulmonary congestion Surgical relief of rheumatic tricuspid stenosis was first reported by Brofman (1953), and since then, including the present case, 19 cases have been published, with no operative deaths (Bailey 1955, Chesterman and Whitaker 1954, Doghotti 1954, Krook et al 1955, O'Neill et al 1954, Rubio and Lason 1954, Swan et al 1955, Trace et al 1954)

The sex ratio was 7 women to 2 men in the 9 cases in which the sex was stated, with an age range of 21-43 (mean 29) The mean age at mitral valvotomy is 36 8 years (Wood 1954) This accords with the finding of Thompson and Levine (1937) that the average age at onset of symptoms in rheumatic heart disease is earlier when tricuspid stenosis is present Of the 19 cases, the diameter of the tricuspid valve orifice was 5-13 mm in 5, and was described as tight in 3 others and moderate in 1, no details being given of the remainder The shape was triangular, circular, or slit-like In some cases, as in the present one and that of Chesterman and Whitaker (1954), the valve orifice appeared as a circular opening in a smooth diaphragm, and it was impossible to feel the individual commissures In others it is stated or implied that one or more of the commissures could be detected Calcification in the valve has not been reported

A direct approach to the valve was used by all except Rubio (Rubio and Lason 1954), who uses a cutting wire in the end of a ureteric catheter Most workers have found that instrumental division of the valve was often required, although none states that valvotomy was especially difficult

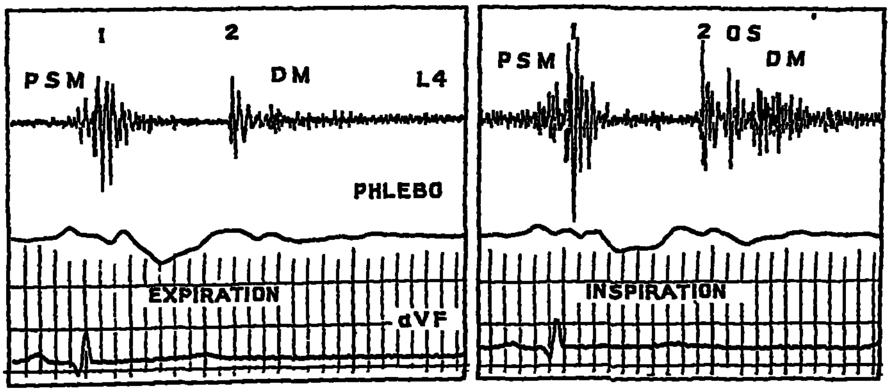

Fig 5—Phonocardiograms from left 4th space, showing increase in intensity of diastolic murmurs on inspiration, and emergence of opening snap (O.S)

TREATMENT OF TETANUS

SEVERE BONE-MARROW DEPRESSION AFTER PROLONGED NITROUS-OXIDE ANÆSTHESIA

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Since the 1952 epidemic of poliomyelitis in Copenhagen the therapeutic measures introduced in the management of the life-threatening forms of infantile paralysis have been adapted to several other diseases presenting similar problems—e.g., tetanus.

Bjorneboe et al. (1953) were the first to describe a severe case of tetanus cured by treatment along these lines, and Lassen et al. (1954) gave a detailed account of 4 such cases. Since then cases have been published by Shackleton (1954), Forrester (1954), Haglund (1955), and Mollaret et al. (1955).

When the conventional treatment of tetanus with barbiturates, chloral hydrate, or bromethol does not totally suppress the spasms, or if adequate ventilation is threatened by accumulation of secretion in the upper respiratory passages, eventually followed by atelectasis, a high tracheotomy under general anæsthesia preceded by oral intubation should be done and an inflatable rubber cuff-tube inserted into the trachea.

This procedure secures against suffocation due to laryngeal spasms or tetanic standstill of the respiratory muscles. At the same time aspiration through the tube makes it possible to keep the airway free from secretions.

Convulsions and rigidity can be kept in check with *d*-tubocurarine chloride given either continuously through an intravenous drip or by repeated intravenous injections. When, however, convulsions are severe, the requisite dosage of tubocurarine invariably produces inadequate ventilation because of failure of the respiratory muscles, and artificial respiration (some kind of positive pressure ventilation) becomes necessary.

Tetanus does not affect the patient's mental state, nor does curare. In severe curarised cases therefore the patient is totally paralysed but fully conscious, aware of everything that is going on around him, and no doubt subjected to great emotional strain. He appears stuporous, cannot talk, and, since even the slightest movement of the muscles is suppressed, cannot communicate with anybody by either gestures or facial expression. The treatment of tetanus often has to be continued for many weeks, and we tried to find ways to avoid the long-continued psychological strain. For this purpose nitrous-oxide anæsthesia seemed ideal. It produces a mild narcosis, which reduces the need for curare and sedatives. No harmful side-effects are known, and the anæsthetic is easy to administer continuously to patients on spontaneous respiration as well as to patients on artificial respiration. In most cases we used a mixture of 50% oxygen and 50% nitrous oxide.

Hæmatological Complications

The first 2 patients treated on these lines were cured and left the hospital without sequels. Severe tetanus is thus a self-limited disease and all its symptoms and all complications are reversible.

At that time we felt rather optimistic, but further experience proved us to be too optimistic. The 3rd patient treated in this way was a boy aged 15 with fulminant tetanus. After seventeen to eighteen days' treatment the tetanus subsided, continuous anæsthesia with nitrous oxide and oxygen was discontinued, medication with curare was stopped, and he only needed moderate doses of chloral hydrate to keep him relaxed. But at this time signs of aplastic anæmia developed.

Fig. 1 shows that, despite repeated blood-transfusions, pronounced granulocytopenia and thrombocytopenia with

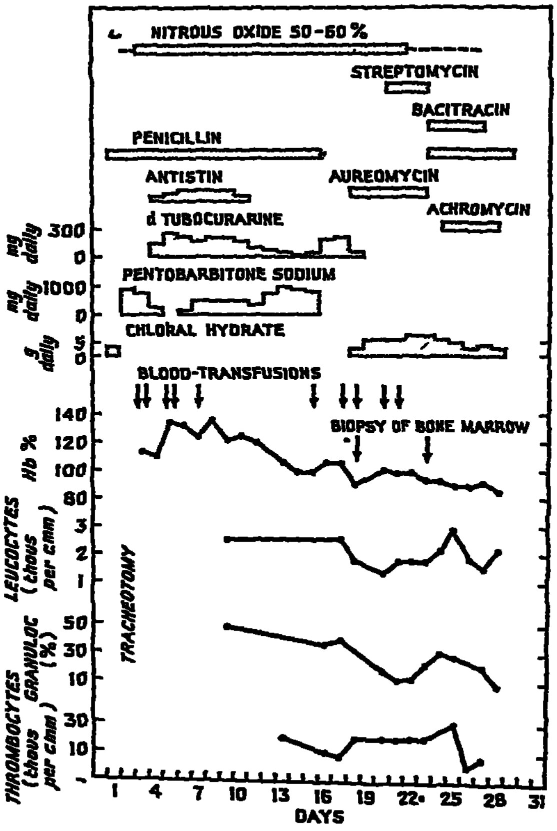

Fig. 1—Changes in peripheral blood in relation to medication in a boy, aged 15, with severe tetanus.

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TABLE I—INITIAL RESPONSE

Case no	Date of starting treatment with hydrocortisone	Complete freedom from symptoms		No of days before response
		Nose	Eyes	
Patients taking anti histamine substances				
1	May 11	+	+	2
2	May 24	+	+	1
3	June 2	+	+	2
4	June 10	+	+	2
5	June 16	+	+	2
6	June 16	+	−	2
7	June 21	+	+	2
8	June 22	+	−	7
9	June 23	+	+	1
10	June 23	+	+	2
11	June 24	+	+	2
12	June 29	+	+	2
13	July 5	+	+	9
Patients not taking anti histamine substances				
14	May 14	+	+	2
15	May 24	+	+	2
16	May 27	+	+	1
17	May 31	+	+	2
18	June 2	+	+	2
19	June 2	+	+	3
20	June 10	−	−	
21	June 16	+	−	3
22	June 16	+	+	1
23	June 30	+	+	1
24	July 1	+	+	7
Total responding		23	20	

Hydrocortisone powder was used rather than the suspension, because in this way the substance reaching the mucosal surface is undiluted, non-irritant, and retained in the nose more easily The powder, which was ground very finely * was supplied in 100 mg capsules containing 15 mg of hydrocortisone acetate and 85 mg of lactose The capsules were pierced at the upper end and placed in a nasal insufflator from which a fine spray was produced This spray was applied to both nostrils three times a day, the whole 15 mg being used in twenty-four hours

In many cases the initial blockage of the nose by the hay fever made it necessary to create an airway to allow the powder to reach the nasal mucosa These patients were therefore asked to instil into both nostrils one or two drops of 0 02% naphazoline ('Privine'), to unblock the nose When the naphazoline had freed the airway, the hydrocortisone powder was inhaled, and this pre treatment with naphazoline was discontinued when the airway remained clear (in most cases after two days).

The hydrocortisone inhalations were kept up for five days and then omitted to see if relapse occurred, but further hydrocortisone was given if and when symptoms recurred Those patients in whom a partial control of symptoms had previously been obtained by anti-histamine substances continued with the same drug and dosage throughout in addition to the hydrocortisone

Results

No side effects of any kind were observed during the treatment The powder was applied without difficulty once the patients had mastered the fact that it was useless to apply it to a blocked or watering nose With perseverance every patient except 1 (case 20) was able to free the nose temporarily with the naphazoline before applying the powder In no case was local irritation of the nose produced by the powder

The initial response to hydrocortisone was excellent (table I) All the patients but 1 obtained relief from nasal symptoms within ten days, and most of them responded dramatically within forty eight hours The slower responses were in those patients who had profuse rhinorrhœa preventing the powder from being retained in more than small quantities

The later results were also very encouraging (table II) 19 patients were followed up for the whole season, and only 2 of these relapsed while taking hydrocortisone 9 of the successful patients had to take the powder until the end of the pollen season but had perfect control of their symptoms all the time they were taking it After the first five days' treatment most of these patients did not relapse immediately when the drug was withdrawn but remained free from symptoms for up to sixteen days When hydrocortisone was resumed, they responded and remained symptom-free for as long as they were taking it In the remaining 8 successful cases the patients discontinued hydrocortisone permanently after five to twenty days and remained satisfactorily controlled thereafter These patients tended to have a return of minimal symptoms but to a degree so slight as not to justify taking further hydrocortisone 6 of these 8 patients were on anti histamine substances and continued with them after stopping hydrocortisone

An unexpected and remarkable result was seen in the effect of hydrocortisone on the eye symptoms associated with rhinitis initially in all cases Itching and watering of the eyes and accompanying conjunctival injection disappeared in 20 of the 24 patients during their initial response A further point of interest was the behaviour of the 10 patients who previously had had pollen asthma every year in addition to hay-fever In 4 of them no chest symptoms developed, all being patients taking hydrocortisone to the end of the season It is likely that in these cases the part of the hydrocortisone which penetrated into the bronchi had a curative effect, as has been observed by Foulds et al (1955) The remaining 6 patients had their asthma as usual

There was no significant difference in the results between the group taking anti histamine substances and the others

Discussion

The initial response to this form of local hydrocortisone treatment was dramatic As could be expected, relapse occurred in some cases as soon as the treatment

TABLE II—LATE RESULTS

Case no	Date of starting treatment with hydrocortisone	No of days' treatment	Whole season control		Degree of freedom from symptoms
			Nose	Eyes	
Patients taking anti histamine substances					
1	May 11	Whole season	+	+	Complete
2	May 24	Whole season	+	+	Complete
3	June 2	15	+	+	Complete
4	June 10	5	+	+	Complete
5	June 16	Whole season	+	+	Complete
6	June 16	10	+	−	Almost complete
7	June 21	5	Not followed up		
8	June 22	20	+	−	Almost complete
9	June 23	Whole season	+	+	Complete
10	June 23	10	+	+	Only fair
11	June 24	5	Not followed up *		
12	June 29	5	+	+	Almost complete
13	July 5	Whole season	+	+	Complete
Patients not taking anti histamine substances					
14	May 14	5	Not followed up *		
15	May 24	15	+	+	Complete
16	May 27	10	+	+	Complete
17	May 31	Whole season	+	+	Complete
18	June 2	15	−	−	Relapsed
19	June 2	10	−	−	Relapsed
20	June 10	10	Not followed up		No response
21	June 16	5	Not followed up		
22	June 16	Whole season	+	+	Complete
23	June 30	Whole season	+	+	Complete
24	July 1	Whole season	+	+	Almost complete
Total (19 cases followed up)			17	15	12 complete 4 almost complete 3 failures

* Corticotrophin administered because of asthma

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* The particle size was not determined accurately An approximate survey indicated a mean diameter of 5 µ

innocuous After considerable discussion in the correspondence columns of this journal Sykes (1955) declared: "I am aware of no work which suggests that nitrous oxide per se is dangerous." This statement, of course, applies only to the usual surgical use of nitrous oxide and not to its use over many days.

In view of the fact that our first 2 patients who recovered had shown signs of bone-marrow depression, and thus had proved that the hæmatological changes were not invariably fatal, it was felt permissible to try the effect of prolonged anæsthesia with nitrous oxide and oxygen under strict hæmatological control.

Clinical Trial of Nitrous-oxide Anæsthesia

On Sept. 1, 1955, a boy, aged 10 years, was admitted with severe tetanus.

Twelve days previously he had been run over by a tractor and had sustained a compound fracture of his right leg. Trismus and severe backache appeared ten days later, but despite this rather long incubation time severe tetanus developed with alarming rapidity.

On the day after admission respiration became inadequate through accumulation of secretion in the airway and incipient atelectasis, and tracheotomy had to be done. During the next two weeks the tetanus was kept in check with pentobarbitone given through an indwelling stomach tube. Because of the severity of the tetanus the dosage of the pentobarbitone had to be so large that spontaneous respiration failed and it became necessary to institute manual artificial respiration or to use a positive pressure machine.

Fig. 3 shows that during the first two weeks' treatment the leucocyte and thrombocyte counts and granulocyte percentage remained normal. General anæsthesia was then started with 50% nitrous oxide and 50% oxygen and immediately proved beneficial. The tetanus promptly became more easy to handle, and the dosage of sedatives was reduced.

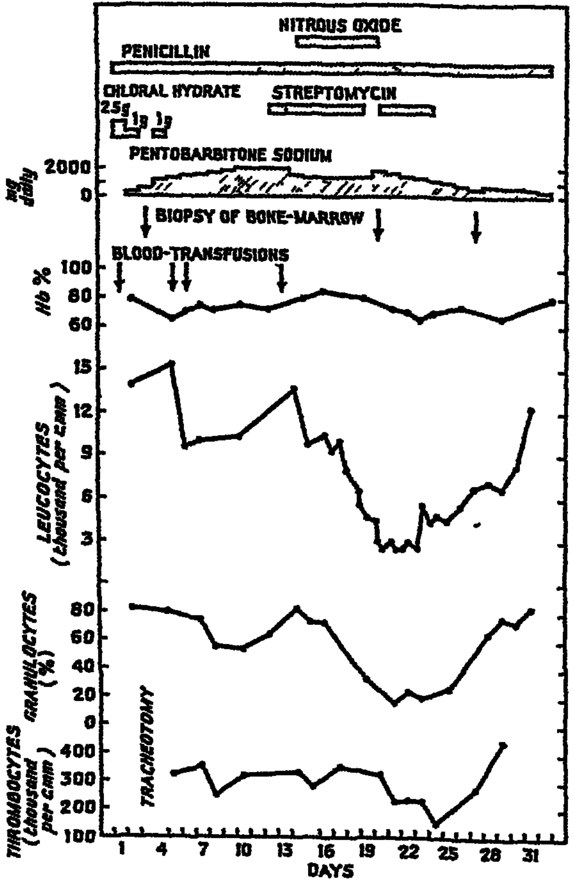

Fig. 3—Blood changes in a boy, aged 10 years, with tetanus.

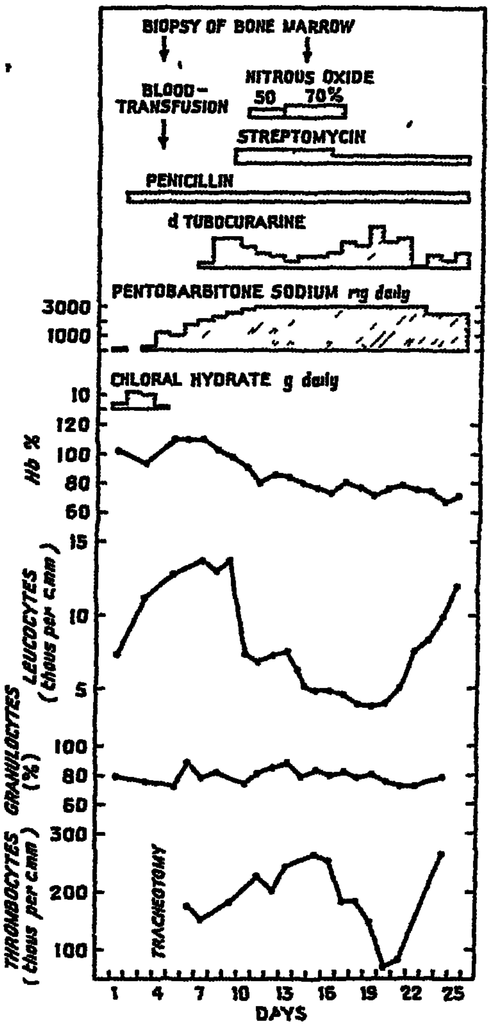

Fig. 4—Blood changes in a girl, aged 13, with tetanus.

On the fourth day of nitrous oxide anæsthesia the percentage of granulocytes decreased so sharply that next day the administration of nitrous oxide was discontinued. In the next few days a rather considerable decrease in the number of thrombocytes was also observed.

Bone marrow biopsy on the fifth day of anæsthesia revealed that erythropoiesis was strikingly megaloblastic and the changes in granulocytopoiesis were so pronounced and typical that, unless one knew the clinical history, one would not hesitate to diagnose pernicious anæmia.

After the anæsthetic had been discontinued we followed the course of the tetanus with apprehension although the boy's general condition was satisfactory. On the next three days the leucocyte counts remained low. The tetanus became active and the doses of sedatives had to be increased. On the fourth day, however, the number of leucocytes began to increase although transfusion and anti-pernicious anæmia drugs had not been given and the general regime remained unchanged. A few days later the white cell count was normal and bone marrow biopsy showed changes consistent with toxic infectious damage, and no signs of lack of anti-pernicious anæmia factor. The further course of the tetanus was uneventful, and the boy was transferred to the local hospital a few weeks later.

At this juncture Mollaret et al. (1955) published a severe case of tetanus in which agranulocytosis developed after the patient had been treated by tracheotomy and artificial respiration and with chlorpromazine, *d*-tubocurarine, and various sedatives, but no nitrous oxide anæsthesia. Only the white cells (especially the granulocytes) were involved; apart from this the bone marrow was normal (R. Bastin, personal communication).

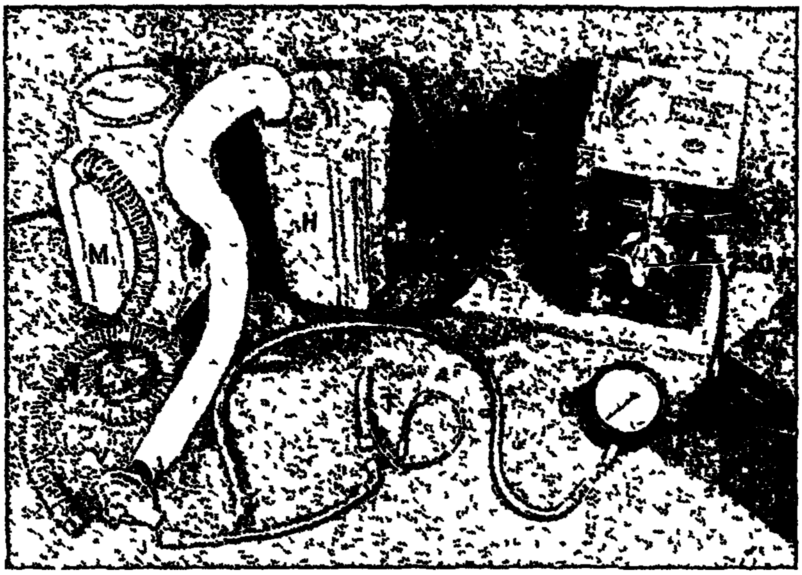

Fig 1—Radcliffe respiration pump in its most used form The items shown are the bellows (P), humidifier (H), Stott valve (V), tracheotomy tube (T), gas meter (M), pressure gauge (G), and 12-volt D C and 230 volt A C motors

Simple and Easy Hand Operation—A handle is inserted and turned at the appropriate speed No clutch is required to disconnect the motor, because there is a free wheel in the gear box, and the weight controlled wave form and pressure of delivery remain entirely uninfluenced by the operator's actions

Respiratory rate Control—For use with adults respiratory rates of 12, 16, 20, and 25 are available For young children an alternative sprocket is used in the drive to provide respiratory rates of 20, 23, 30, and 37

Oxygen Intake—Though oxygen is rarely used for these cases, a simple system is available whereby the continuous flow of oxygen from a cylinder meets the intermittent requirements of the positive pressure bellows, any required mixture of air and oxygen being easily provided This consists of a length of corrugated breathing tube, of which one end is open to the air and the other is attached to the pump intake Oxygen is led in at the pump end of this tube so that it accumulates in the tube to form a reservoir for each intake This device is seen below the bellows (P) in fig 2

Positive pressure control providing pressure from +10 to +30 cm water

Humidifier gauge showing the amount of water in the humidifier

Pressure Gauges—There are two pressure gauges, one reading from the inspiratory valve, the other from close to the patient Water traps are included to insure that water cannot reach and block the gauges

Removable trap in which secretions contained in the expired air are collected

A *gas meter* is incorporated and is switched in or out of the expiratory side of the circuit at will

Negative pressure control providing pressure from 0 to −10 cm water

Safety devices include a rod attached to each bellows (R in fig 2) and providing a visible indication of the bellows' action An audible and visible warning device will also be incorporated because the snore of the Stott valve has in practice proved a most effective safety device which is lost with cam operation of the valves The readings on the pressure gauges and gas meter provide additional safeguards, and if the patient can cooperate he can be provided with foot operated or chin operated switch for an electric bell

The complete apparatus is mounted on a trolley measuring 2 ft 6 in × 1 ft 8 in × 2 ft-6 in The trolley includes a folding shelf and an arm to support the tubes going to and from the patient Extra apparatus—e g, throat

Figs 2-4—Radcliffe positive negative respiration pump (side plates removed) showing main components positive-pressure bellows (P), negative pressure bellows (N), humidifier (H), cam-operated valves (V), gas-meter (M), and 12 volt D C and 230 volt A C motors

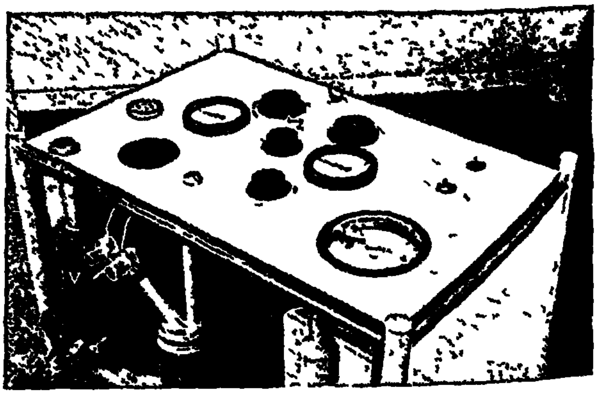

Fig 4

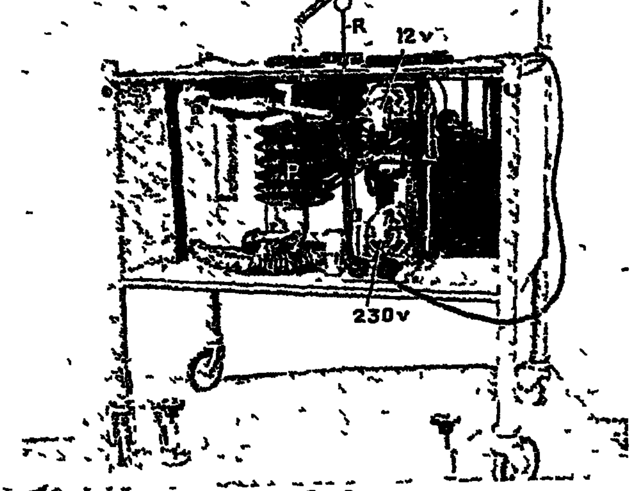

Fig 2

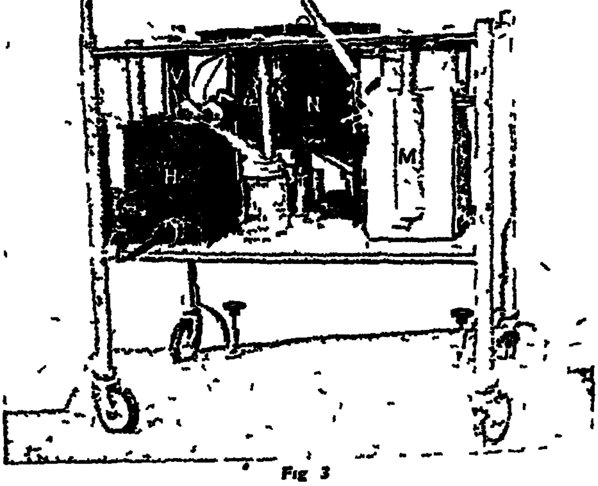

Fig 3

TABLE I—CLINICAL DATA

Case no	Sex	Age (yr)	Estimated duration of diabetes (yr)	Duration of vascular disease (retinopathy) (yr)	Albuminuria (g per litre)	"Severity" of diabetes (units of insulin)	Control (5 yr)
1	M	31	20	5	5	24	Brittle
2	M	49	20	13		40	Good
3	M	53	23	6?	4	30	Good
4	M	60	?	?	1	36	Good (1 year only)
5	F	57	20	2		16	Fair
6	F	53	?	?		52	Good (2 years only)

programme is simpler; (3) the preoperative and post-operative management of adrenalectomy was already well understood at the hospital to which the diabetic clinic was attached; and (4) intractable hypoglycæmia after hypophysectomy had been reported (E. B. C. Hughes, W. G. Oakley, personal communications).

Material

6 patients were subjected to total adrenalectomy for diabetic vascular disease at the General Hospital, Birmingham. The main facts are set out in tables I and II.

In case 1 there had for years been fluctuation between abnormally high and low blood-sugar levels, though ketosis requiring admission to hospital had only occurred once. Cases 2 and 3 had no glycosuria in fasting specimens, and the blood-sugar level at 2 P.M. was below 180 mg. per 100 ml. at each attendance. The duration of the retinopathy in case 3 was unknown because he only began to attend hospital six years before admission, when he already had retinopathy. Case 4 was only found to have diabetes two years before admission, when the retinal changes impaired his vision. Case 5 had been well controlled by dietetic restriction for the first fourteen years of her diabetes, but for the last six years only symptomatic control had been maintained. There was glycosuria in all specimens of her urine, and her average blood sugar level at 2 P.M. was 250 mg. per 100 ml. Case 6 had been treated for two years following the discovery of advanced retinopathy, though glycosuria had been first found twenty-eight years earlier.

TABLE II—FINDINGS BEFORE OPERATION

Case no	Stage of retinopathy (Ballantyne)	Albuminuria (g. per litre)	Blood-urea (mg. per 100 ml.)	Blood pressure (mm. Hg)	Indication for operation
1	3	8	220	180/110	Retinopathy failing vision
2	3	0	39	150/80	Retinopathy vitreous hæmorrhages
3	4	5	50	200/100	Retinopathy vitreous hæmorrhages albuminuria
4	4	2	41	200/100	Retinopathy failing vision albuminuria
5	3	0	38	210/130	Retinopathy vitreous hæmorrhages
6	3	0	28	140/80	Retinopathy failing vision

Retinopathy is graded by Ballantyne's classification: (1) micro aneurysms singly or in small numbers near the macula; (2) blot hæmorrhages and confluent waxy exudates; (3) addition of venous changes—tortuosity, loops, coils, and plexuses on the anterior surface of the retina or in the vitreous; and (4) intraocular hæmorrhage preventing ophthalmoscopy, blindness, and perhaps glaucoma. In cases 1, 3, and 4 there was no reason to doubt that the hypertension was renal in origin. In case 5 a gradual rise of blood-pressure had been noted throughout ten years; there was a family history of high blood-pressure, and the hypertension was regarded as "essential."

Operations

All the operations were done by Mr. J. A. C. Edwards in two stages by the lumbar approach, and in every case the adrenal glands were believed to have been removed entire. The preoperative and postoperative routines were the same in every case and were applied to both the first and the second stages.

(1) Soluble insulin in divided doses was used for three days before the operation to avoid any depot effect of long acting preparations. On the morning of the operation soluble insulin in a dose of a third of the normal daily total was given with glucose 30 g. three hours before the operation. On the day following the operation a dose of a quarter of the normal daily total was given, and on the second postoperative day treatment with delay insulin was resumed.

TABLE III—RESULTS OF OPERATION

Case no	Follow up	General state	Diabetic control	Retinopathy	Albuminuria	Insulin (units) Before	Insulin (units) After
1	2 weeks (died)					24	
2	16 months	Better	Unchanged	Better	Unchanged	40	44
3	9 months	Unchanged	Unchanged	Unchanged	Unchanged	36	20
4	11 months	Unchanged	Unchanged	Unchanged		36	44
5	9 months	Unchanged	Better	Worse		16	16
6	5 months	Unchanged	Unchanged	Unchanged		52	48

(2) Twelve hours before the operation intramuscular cortisone 200 mg. was given and 50 mg. by the same route six hourly for the following forty eight hours. Cortisone 25 mg. was given orally three hours before the operation, then no more until the second postoperative day, when four doses of 25 mg. were given, the dosage thereafter being gradually decreased to 50 mg. daily.

(3) During the operation and the following twenty four hours an intravenous infusion of 4 pints of physiological saline solution was given. Glucose was not used, because it makes estimations of the blood sugar useless. By the second day a full diet was resumed, and thereafter no special modification of the diet was used.

Results

The major effects of the operations are set out in tables III and IV. "General state" refers to the sense of well being, maintenance of body weight, and capacity to work. The improvement in case 2 partakes of all these features, with a return to normal visual acuity

TABLE IV—FINDINGS AFTER OPERATION

Case no	Stage of retinopathy Before	Stage of retinopathy After	Albuminuria (g. per litre) Before	Albuminuria (g. per litre) After	Blood urea (mg. per 100 ml.) Before	Blood urea (mg. per 100 ml.) After	Blood pressure (mm. Hg) Before	Blood pressure (mm. Hg) After
1	3		8		220		180/110	
2	3	3	0	0·0	39	35	150/80	120/80
3	4	3	5	5·0	50	40	200/100	150/80
4	4	4	2	1·8	41	45	200/100	180/80
5	3	4	0	0·0	38	28	210/130	150/80
6	3	3	0	0·0	28	30	140/80	130/80

know which specimen belonged to a given patient, whether it was fresh or 24 hours old, and whether or not it had been already estimated the previous day The results could only be interpreted when the key to the many names used was consulted In this way it was possible to check the accuracy of the estimations and to find out what effect 24 hours' delay had on the results

No statistical study was made, but table I shows that there is a close relationship between the two sets of readings There are minor variations, partly due to the control time varying on successive days, but in practice either result could have been used to maintain satisfactory control of the treatment

Further tests were done to find out if there was a difference in the delayed estimation when plasma was used instead of whole blood The specimen was obtained by spinning the blood immediately after withdrawal and, together with a sample of whole blood, posted as outlined above The results obtained were once again very similar and are shown in table II, suggesting that the extra trouble and apparatus required to obtain the plasma were unnecessary

It had previously been suggested (J A Tulloch, personal communication) that the best method of obtaining a prothrombin time, when an immediate test could not be made, was to put the plasma on ice So an experiment was made exactly as before with the samples of whole blood and plasma duplicated Two were sent through the post and two were kept in the refrigerator for 24 hours before estimation Table III shows that there was little difference in the one stage prothrombin times, which were again, from a therapeutic point of view, almost identical with those of the sample estimated immediately after withdrawal

TABLE II—EFFECT ON DELAYED ONE STAGE PROTHROMBIN TIME OF PLASMA COMPARED WITH WHOLE BLOOD

Case no	Whole blood						Plasma 24 hr later		
	On day of withdrawal			24 hr later					
	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %
1	14	34	14	14	34	11	14	31	14
2	14	30	17	14	28	18	14	29	19
3	14	28	18	14	26	19	14	31	15
4	14	28	18	15	30	18	15	30	18
5	15	25	23	15	25	23	15	26	22
6	14	32	16	15	34	16	15	33	16
7	15	29	19	15	26	22	15	30	18
8	15	29	19	15	28	18	15	24	25
9	15	30	18	15	30	18	15	27	20
10	15	38	14	15	38	14	15	34	16
11	15	23	27	15	21	25	15	24	25
12	14	25	19	14	25	19	14	25	19
13	14	20	30	15	22	28	15	21	26
14	15	27	18	15	30	17	15	34	15
15	15	33	15	16	34	17	16	36	16

TABLE IV—EFFECTS ON IMMEDIATE AND DELAYED ONE STAGE PROTHROMBIN TIMES WHEN WHOLE BLOOD IS HÆMOLYSED MECHANICALLY

Case no	Non hæmolysed						Hæmolysed					
	On day of withdrawal			24 hr later			On day of withdrawal			24 hr later		
	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %
1	15	22	26	15	22	26	15	22	26	15	24	22
2	15	28	18	15	26	20	15	30	17	15	31	19
3	15	24	23	15	26	20	15	25	20	15	26	20
4	16	38	15	16	38	15	16	36	16	16	36	16
5	14	33	14	15	33	16	14	34	13	15	34	15
6	14	26	20	14	26	20	14	26	19	14	26	19

TABLE V—EFFECT ON IMMEDIATE AND DELAYED ONE STAGE PROTHROMBIN TIMES WHEN WHOLE BLOOD IS HÆMOLYSED BY ADDITION OF SURGICAL SPIRIT

1	15	35	14	14	33	14	15	43	11	14	40	11
2	15	23	21	14	22	24	15	32	16	14	34	14
3	14	28	17	14	28	17	14	34	14	14	41	10
4	14	33	14	14	34	14	14	39	11	14	29	17
5	15	30	17	14	28	17	15	38	14	14	43	9
6	15	31	16	15	30	17	15	40	12	15	35	14

Finally the effect of hæmolysis was investigated Many of the routine samples arriving at the laboratory from the wards were hæmolysed, and it was the practice to request a fresh specimen in such cases In view of this the plasma used in the above mentioned tests was examined spectroscopically, and any specimen showing more than a faint trace of hæmolysis was discarded from the series

It was decided to study the effect of deliberate hæmolysis in the duplicate sample This was found to be very difficult to achieve, at least by mechanical means High pressure ejection from the syringe through a small bore needle followed by vigorous shaking of the tube was successful in a few cases Hæmolysis produced in this way had no significant effect on either the immediate or the delayed one stage prothrombin time (table IV) It was thought probable that contamination by either *methylated ether or surgical spirit might be responsible* for the hæmolysis commonly seen , so a group was tested in which one drop of surgical spirit had been deliberately added to the duplicate sample This produced gross hæmolysis in every case, and the close relationship noted between the two sets of results in all previous experiments was no longer found (table V)

Discussion

The care of patients on prolonged anticoagulant therapy involves far more than adjustment of their daily dose of coumarin drug, and their supervision must remain in the hands of experienced physicians It therefore remains necessary for them to report back to the main

TABLE III—EFFECTS OF ROOM-TEMPERATURE AND OF REFRIGERATION ON DELAYED ONE STAGE PROTHROMBIN TIME OF WHOLE BLOOD AND PLASMA

Case no	Whole blood						*Plasma after 24 hr in post*			*Whole blood after 24 hr in refrigerator*			*Plasma after 24 hr in refrigerator*		
	On day of withdrawal			After 24 hr in post											
	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %	Control time (sec)	Patient's time (sec)	Activity %
1	14	31	15	14	29	18	14	31	15	14	28	18	14	31	15
2	14	28	18	14	36	19	14	31	15	14	28	18	14	31	15
3	14	28	18	15	30	18	15	30	18	15	31	17	15	31	17
4	14	26	19	14	26	19	14	31	16	14	28	18	14	26	19
5	14	34	14	14	34	14	14	35	14	14	34	14	14	31	14
6	14	32	16	15	34	16	15	31	17	15	33	16	15	31	17
7	15	25	23	15	21	25	15	25	23	15	21	25	15	25	23
8	15	25	23	15	25	23	15	24	25	15	25	23	15	26	22

retina, which he described, is now generally accepted, and one may follow his classifications as follows:

(1) Changes chiefly in the central area, micro aneurysms with or without punctate hæmorrhages and punctate exudates

(2) Dot and blot hæmorrhages, confluent waxy exudates

(3) Changes in the veins (newly formed intraretinal and preretinal veins, phlebitis and phlebosclerosis, and the formation of knots, coils and loops in the distended veins), increasing hæmorrhages in the retina and vitreous, massive exudates retinitis proliferans, and detachment of the retina

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We are here concerned with the tempo of retinopathy and with the prognosis attached to the findings in any given case In Ballantyne's stage 1 the finding of micro- neurysms alone may be repeated, without deterioration nd even with transient improvement for several years The longest duration of this stage in my records is nine years In stage 2 it is usual for the changes to progress within five years to gross visual impairment Of 19 patients personally observed, in whom the entry into stage 2 could be estimated within six months, 15 were seriously hampered by reduced visual acuity after five years There are, however, striking exceptions, of which the following is a fair example

A man developed diabetes at the age of 25 At 43 he complained of poor vision. His visual acuity was corrected to 6/6 in each eye, but stage-2 retinopathy was found At the age of 48 his visual acuity was corrected only to 6/12 and the retinopathy was more extensive At the age of 50 his visual acuity was again corrected to 6 6 in each eye and the retinopathy was less obvious

Usually the younger the patient the greater is the chance of a benign course in stage 2 In stage 3 the visual prognosis is very poor, and cases like the following 2 are quite exceptional

A woman had diabetes diagnosed at the age of 25 with poor sion and stage 2 retinopathy At the age of 38 vision of her ght eye was suddenly blurred by big vitreous hæmorrhages, wo months later she had a similar episode in her left eye Both eyes cleared to visual acuity 6/12 She had no further complaint of vision At the age of 50 she is at work as a housekeeper and can read normal print and sew

A man developed diabetes at the age of 22 At the age of 34 he was found to have stage-1 retinopathy, but he had no visual impairment until he had a big vitreous hæmorrhage at the age of 47 He had two other hæmorrhages in the same year, and all of them resolved At the age of 53 his visual acuity is 6/12, and he is working as a bank cashier

The expectation of useful vision in retinitis proliferans has nowhere been clearly stated Dolger (1947) emphasised the unpredictable nature of retinopathy and the rapidity with which it may proceed to blindness Root (1952) reports the duration of retinitis proliferans in 326 cases in 124 patients who had died the average duration of retinitis proliferans was three years for males and four years for females Of the 124 deaths 66 were due to renal disease So far only 25 of the living were known to have become completely blind Root believes that associated renal or cardiac disease usually leads to death before blindness is complete This seems to be true, but exceptions are not rare, as in the following cases

A boy had diabetes at the age of 19 but maintained perfect health until at the age of 33 he began to have vitreous hæmorrhages, which left him blind at the age of 35 At the age of 41 he remains otherwise well and has no albuminuria

A woman, who had been treated for diabetes from the age of 30 became blind from retinopathy at the age of 54 She remained otherwise well with no albuminuria, and died suddenly from coronary thrombosis at the age of 62

Dolger (1947) found that 50% of his patients had hypertension and 30% albuminuria at the onset of the earliest retinal lesions Since he did not use mydriatics in examining the eyes he may well have missed minor lesions for a time, with the result that his estimates are perhaps unduly high In 50 consecutive cases in which the diabetes came on under the age of 50 (as in Dolger's series) with retinopathy but no visual symptoms, the lesions being therefore classified as early, I found hypertension in 26% and albuminuria in 14% However, with more advanced retinopathy, as Root (1952) has shown, the chances of renal disease are much increased

Course of Glomerulosclerosis

The first clinical manifestation of glomerulosclerosis is albuminuria The earliest lesions are almost certainly present for months or years before this finding but remain symptomless, like those in the retina Under the stress of ketosis an impaired capacity to adjust electrolyte balance may occasionally be noted as evidence of renal damage before albuminuria is found on routine examination The albuminuria is at first intermittent, this has been so in every one of the 17 cases observed throughout the course of the disease by me and is noted by Wilson et al (1951)

The later syndrome is subject to some disagreement Kimmelstiel and Wilson's (1936) first patients had hypertension, massive œdema, heavy albuminuria, and renal insufficiency, and several workers (Kimmelstiel and Wilson 1936, Newburger and Peters 1939, Mauser et al 1942) subsequently correlated this clinical picture with the histological findings of glomerulosclerosis though the lesions were noted by some workers to be much more common than the syndrome Henderson et al (1947) listed, as the clinical features, a long duration of the diabetes, hypertension, albuminuria, renal insufficiency, and mixed diabetic and hypertensive retinopathy The œdema was omitted In my 17 cases both pictures have been seen, but œdema appeared during the course of the illness in 14, the 3 other patients died of coronary-artery disease, perhaps before the stage of œdema On the other hand, it must be admitted that some patients with glomerulosclerosis may have escaped diagnosis because of the presence of renal infection or because of there being no necropsy The inconsistencies in description of the clinical features seem to be mainly due to difference in the patients' ages the nephrotic picture predominates in the young, whereas in the elderly there may be no distinctive signs, though diffuse changes are found post mortem

Once again we are here concerned mainly with the prognostic significance of the clinical features It seems clear that the appearance of albuminuria in a patient with long-standing diabetes, unless it can be attributed to active urinary infection or to gross cardiac insufficiency, indicates the onset of glomerulosclerosis Chronic pyelonephritis with secondary hypertension may confuse

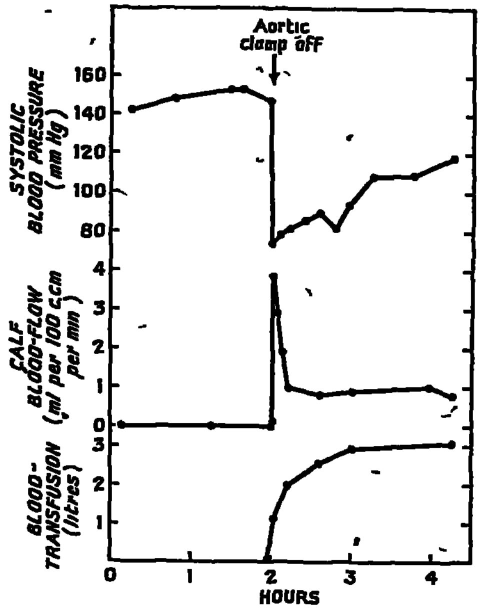

Fig 2—Systolic blood pressure, calf blood flow, and blood-transfusion during resection of aortic aneurysm Aorta clamped above the renal vessels, and bifurcation prosthesis inserted

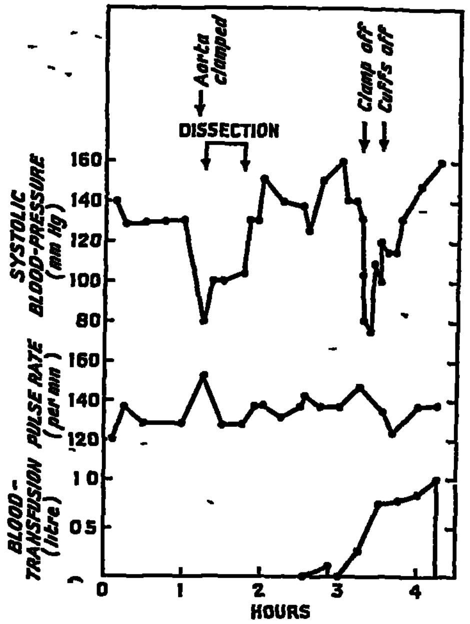

Fig 3—Systolic blood-pressure and blood transfusion during resection of high aortic thrombosis Aorta clamped below renal vessels, and Orlon bifurcation prosthesis inserted

re-established in a relatively limited area of ischæmic tissue through the internal iliac, inferior epigastric, and circumflex femoral arteries, and possibly the upper profunda femoral anastomosis When the blood-pressure has recovered from the fall so incurred, the thigh cuffs are deflated one after the other The time for this procedure seldom exceeds twenty minutes

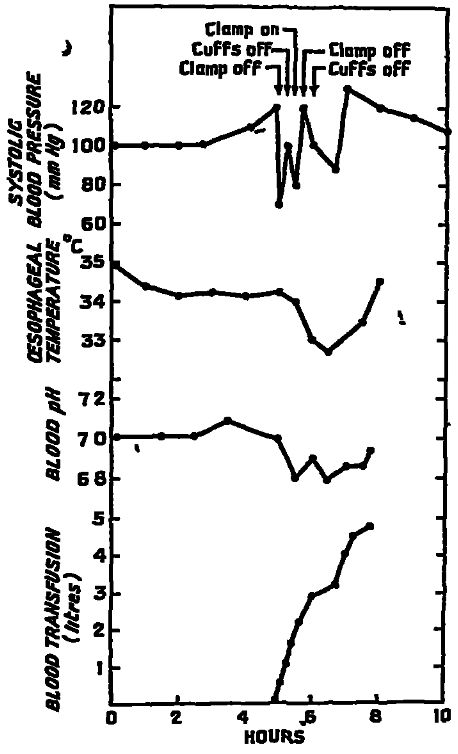

Fig 4—Systolic blood pressure, œsophageal temperature, pH of blood in inferior vena cava, and blood-transfusion in resection of abdominal aneurysm Aorta clamped below renal vessels, and bifurcation prosthesis inserted

This controlled re-establishment of blood-flow appears to limit the degree and duration of hypotension Of 7 patients so managed 1 died from coronary occlusion on the third post-operative day In addition, only 1 patient in this series has received a noradrenaline infusion during the period of hypotension

Figs 3 and 4 are representative charts of patients in this series and show the fall of systolic pressure resulting from release of the aortic clamp and the cuffs It often happens that release of the second cuff only delays the rise in pressure Fig 4 is of particular interest because samples of blood were taken from a catheter placed in the inferior vena cava The blood pH and the plasma-potassium level were estimated and recorded, The lowest pH determined was 6·79 and the highest K+ 8·5 m.eq per litre, the K+ curve being a mirror image of the pH curve This was probably due to an inadvertent rapid infusion of 3·8 litres of stored blood after an unexpected hæmorrhage Stored blood may have a pH as low as 6·4 and a plasma potassium level as high as 8·7 m.eq per litre Because of these properties of stored blood our practice is to obtain a high proportion of the total blood used in these cases fresh from the donor.

The body-temperature was recorded with an œsophageal thermocouple placed at heart level and showed the fall of temperature resulting from re-established circulation in the ischæmic tissues and the infusion of cool blood

Conclusion

Release of the circulation in operations for grafting segments of aorta suddenly increases the blood flow in the legs to two or three times the resting level and considerably more than the very small flow when the aorta is occluded There is also refilling of a partially emptied limb vascular bed This "physiological hæmorrhage" may explain the hypotension observed, but possibly the sudden addition to the general circulation of vasodilator metabolites produced by the ischæmic tissues may contribute to it Large infusions of whole blood and often of noradrenaline are required to compensate the fall in blood pressure, with a resultant increase in the blood volume in the early postoperative period, thus placing an additional strain on the heart —a matter of some consequence in patients with atherosclerosis

The use of thigh cuffs to permit a *controlled* release of the circulation appears to have limited the degree and duration of the hypotension in the cases reviewed From observation of other patients in whom the aorta has been clamped at various levels for one or two hours, the cuffs appear to be of most value in the following circumstances (1) when the aorta has been clamped proximally, (2) where a long segment of aorta is occluded, and (3) where there is little or no established collateral circulation

Summary

Release of the aortic clamp in operations for grafting segments of the aorta causes a profound fall in blood pressure

A striking increase in calf blood-flow accompanies this hypotension

A simple apparatus is described which allows a more controlled re-establishment of the circulation in such cases

Attention is drawn to the potential danger of a rapid infusion of large quantities of stored blood

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TABLE I—COMBINED RATING SCORES FOR 33 ANXIETY-NEUROTICS RECEIVING DIFFERENT DRUGS (A LOW SCORE INDICATES A FAVOURABLE RESPONSE)

Symptom or sign	How often rated	Rated by	Total score for week on		
			Reserpine	Amylobarbitone sodium	Control substance
General condition	Daily	Patient	221	155	212
	,,	Nurse	231	147	189
	Weekly	Patient	60	33	58
	Bi weekly	Physician	119	74	105
Headache	Daily	Patient	262	184	264
Indigestion	,,	,,	172	104	162
Palpitation	,,	,,	197	118	192
Sweating	,,	,,	121	78	129
Trembling	,,	,,	372	171	243
Dizziness	,,	,,	276	196	213
Drowsiness	,,	,,	360	293	272
Depression	,,	,,	352	269	336
Anxiety and tension	,,	,,	365	267	343
	Bi weekly	Physician	180	142	165
Other somatic signs	Bi weekly	,,	84	52	65
Sleep	Weekly	Patient	29	27	38
	Daily	,,	208	166	238
	,,	Nurse	722	714	829

nurse of the ward kept an independent daily record in which he assessed each patient's daily condition as "improved," "same," or "worse" (scored 0–2) The night-nurse kept a sleep chart recording the number of half-hourly periods between 10 P M and 6 30 A M that the patient was observed to be awake (scored 1 for each half-hour awake) The physician in charge of the case recorded twice weekly

(1) His assessment of the patient's general clinical condition compared with the previous period—from "much improved" to "much worse" (scored 0–4)

(2) The presence of anxiety, tension and other somatic signs—"absent," "slight," "moderate," or "severe" (scored 0–3)

(3) The patient's blood-pressure, measured under standard conditions

Finally, at the conclusion of each patient's trial but before he knew the order in which the drugs had been given, the physician rated each weekly period as better, equal to, or worse than each of the other two weekly periods

Results

Table I shows the totals of the scores obtained from 33 patients Since a low score means a good clinical response, it is clear that on the whole the patients felt better, both generally and for particular symptoms, when receiving amylobarbitone sodium than when receiving either reserpine or the control substance It is also clear that there is little or no difference between the response to reserpine and that to the control substance

Table II compares the weekly periods on the different drugs, assessed by the physician at the completion of the trial Evidently there is nothing to choose between the effects of reserpine and of the control substance The periods on amylobarbitone sodium, however, are for the most part better *than either those on reserpine* or those on the control substance, the expected proportion of "*better*" periods on amylobarbitone sodium (on the null hypothesis) lies in each case outside the 90% confidence limits of the observed proportion

TABLE II—NUMBER OF TIMES THE GENERAL CLINICAL CONDITION OF THE PATIENTS RECEIVING THE FIRST NAMED DRUG WAS BETTER, EQUAL TO, OR WORSE THAN THEIR CONDITION WHEN RECEIVING THE SECOND NAMED DRUG

Drugs	Comparative clinical response		
	Better	*Equal*	Worse
Reserpine *v* control substance	15	3	15
Amylobarbitone sodium *v* control substance	27	1	5
Amylobarbitone sodium *v* reserpine	25	1	7

Comparison of the blood-pressure readings for different weeks of the trial gave (for 29 patients only) the following mean values

	Reserpine	*Amylobarbitone sodium*	*Control substance*
Systolic pressure (mm Hg)	127 5	130 2	13[illegible] 5
Diastolic pressure (mm Hg)	72 3	76 2	79 [illegible]

The systolic pressures were lower during the reserpine week than during the control week in 24 of the 29 patients, and the diastolic pressures were lower in 21 of them These figures suggest that reserpine was exerting a definite, if slight, hypotensive effect

The principal side effects—i e, new or troublesome *symptoms—noticed by the patients* are shown below, together with the number who mentioned them while receiving the different drugs

Symptom	*Reserpine*	*Amylobarbitone sodium*	*Control substance*
Drowsiness	11	7	3
Dizziness	8	6	4
Nasal congestion	6	—	—
Swelling of ankles	2	1	1
Increased appetite	2	—	1
Dyspepsia	2	1	1
Headache	1	—	—
Nightmares	2	1	2

Objectively there were no obvious signs attributable to the drugs, no parkinsonian rigidity was observed The occurrence of side effects in patients receiving inert control substances is, of course, well recognised (Wolf and Pinsky 1954)

Discussion

The effects of drug treatment in an anxiety state are possibly best assessed by the self-observation, under controlled conditions, of a cooperative and intelligent patient making a comparative rather than an absolute assessment of the intensity of his symptoms Bias due to casual environmental factors or to apparently spontaneous fluctuations in the degree of anxiety can, to a great *extent, be eliminated by using a blind self* controlled technique and a reasonably large series of cases A further advantage of the self-controlled and *self recorded* clinical trial is that it enables the reliability of the patients' records to be checked We may summarise the evidence which tends to confirm the reliability of the patients' records in the present trial as follows

(1) The patient's scores on different drugs are closely paralleled both by those of the charge nurses and those of the physicians

(2) The sleep assessments are mutually consistent

(3) The only instance in which a score on amylobarbitone sodium exceeds that on the control substance *is for* the patients' daily rating of "drowsiness," and thus corresponds to expectation Again, although for the most part there is little difference between the scores on reserpine and those on the control substance, the reserpine scores for "drowsiness," "dizziness," and "trembling"—all recognised side effects of reserpine treatment—are much higher

As regards the duration for which the drugs were exhibited in the present trial, it might be objected that a week is not *long enough for reserpine to exert* an adequate effect However, there is ample evidence that the reserpine was exerting its action in producing side effects, as well as its probable effect in lowering blood pressure (the hypotensive effect of reserpine in normotensive people has been demonstrated by Freis and Ari [1954]) It seems unlikely that the effect of a drug on anxiety could be delayed for more than a week when its other effects are manifest within a day or two Moreover, amylobarbitone sodium, which *also* caused side effects within a day or two, could clearly influence the mental state within the same short period

A more cogent criticism of the present findings is that any possible benefit from reserpine was offset by the unpleasant side effects associated with the rather high dosage used That these side effects could be trouble-retina, which he described, is now generally accepted, and one may follow his classifications as follows:

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A woman had diabetes diagnosed at the age of 25 with poor vision and stage-2 retinopathy. At the age of 38 vision of her right eye was suddenly blurred by big vitreous hæmorrhages; two months later she had a similar episode in her left eye. Both eyes cleared to visual acuity 6/12. She had no further complaint of vision. At the age of 50 she is at work as a housekeeper and can read normal print and sew.

A man developed diabetes at the age of 22. At the age of 34 he was found to have stage-1 retinopathy, but he had no visual impairment until he had a big vitreous hæmorrhage at the age of 47. He had two other hæmorrhages in the same year, and all of them resolved. At the age of 53 his visual acuity is 6/12, and he is working as a bank cashier.

The expectation of useful vision in retinitis proliferans has nowhere been clearly stated. Dolger (1947) emphasised the unpredictable nature of retinopathy and the rapidity with which it may proceed to blindness. Root (1952) reports the duration of retinitis proliferans in 326 cases: in 124 patients who had died the average duration of retinitis proliferans was three years for males and four years for females. Of the 124 deaths 66 were due to renal disease. So far only 25 of the living were known to have become completely blind. Root believes that associated renal or cardiac disease usually leads to death before blindness is complete. This seems to be true, but exceptions are not rare, as in the following cases.

A boy had diabetes at the age of 19 but maintained perfect health until at the age of 33 he began to have vitreous hæmorrhages, which left him blind at the age of 35. At the age of 41 he remains otherwise well and has no albuminuria.

A woman, who had been treated for diabetes from the age of 30, became blind from retinopathy at the age of 54. She remained otherwise well with no albuminuria, and died suddenly from coronary thrombosis at the age of 62.

Dolger (1947) found that 50% of his patients had hypertension and 30% albuminuria at the onset of the earliest retinal lesions. Since he did not use mydriatics in examining the eyes he may well have missed minor lesions for a time, with the result that his estimates are perhaps unduly high. In 50 consecutive cases in which the diabetes came on under the age of 50 (as in Dolger's series) with retinopathy but no visual symptoms, the lesions being therefore classified as early, I found hypertension in 26% and albuminuria in 14%. However, with more advanced retinopathy, as Root (1952) has shown, the chances of renal disease are much increased.

Course of Glomerulosclerosis

The first clinical manifestation of glomerulosclerosis is albuminuria. The earliest lesions are almost certainly present for months or years before this finding but remain symptomless, like those in the retina. Under the stress of ketosis an impaired capacity to adjust electrolyte balance may occasionally be noted as evidence of renal damage before albuminuria is found on routine examination. The albuminuria is at first intermittent; this has been so in every one of the 17 cases observed throughout the course of the disease by me and is noted by Wilson et al. (1951).

The later syndrome is subject to some disagreement. Kimmelstiel and Wilson's (1936) first patients had hypertension, massive œdema, heavy albuminuria, and renal insufficiency; and several workers (Kimmelstiel and Wilson 1936, Newburger and Peters 1939, Mauser et al. 1942) subsequently correlated this clinical picture with the histological findings of glomerulosclerosis, though the lesions were noted by some workers to be much more common than the syndrome. Henderson et al. (1947) listed, as the clinical features, a long duration of the diabetes, hypertension, albuminuria, renal insufficiency, and mixed diabetic and hypertensive retinopathy. The œdema was omitted. In my 17 cases both pictures have been seen, but œdema appeared during the course of the illness in 14; the 3 other patients died of coronary-artery disease, perhaps before the stage of œdema. On the other hand, it must be admitted that some patients with glomerulosclerosis may have escaped diagnosis because of the presence of renal infection or because of there being no necropsy. The inconsistencies in description of the clinical features seem to be mainly due to difference in the patients' ages: the nephrotic picture predominates in the young, whereas in the elderly there may be no distinctive signs, though diffuse changes are found post mortem.

Once again we are here concerned mainly with the prognostic significance of the clinical features. It seems clear that the appearance of albuminuria in a patient with long-standing diabetes, unless it can be attributed to active urinary infection or to gross cardiac insufficiency, indicates the onset of glomerulosclerosis. Chronic pyelonephritis with secondary hypertension may confuse

CASES OF ACUTE PORPHYRIA

Case	Sex	Age (yr)	Medication	Neurological complications	Outcome
4 (1st attack)	M	20	0 5 g thiopentone for laparotomy	None	Recovered
(2nd ,,)			Gr 3 quinalbarbitone	Paralysis of both arms ten days later	Recovered
6 (1st attack)	F	21	Thiopentone for appendicectomy	None	Recovered
(2nd ,,)			Thiopentone for laparotomy, and gr $1\frac{1}{2}$ butobarbitone daily for six days afterwards	None	Recovered
(3rd ,,)			Gr 20 barbitone sodium and gr 4 phenobarbitone for several days in a mental hospital	Complete paralysis of both arms and legs	Died
8 (several attacks)	F	59	Large doses of various barbiturates at mental hospitals	None	Died (from carcinoma of stomach)
9	F	36	Gr 1 phenobarbitone and gr 3 quinalbarbitone daily for four days	Paralysis of arms fourteen days later	Recovered
10	F	55	Gr 1 phenobarbitone and gr 3 quinalbarbitone daily for seven days	Paralysis of both arms and legs	Died
11	F	21	0 5 g thiopentone for laparotomy followed by gr 2 phenobarbitone for fourteen days	Paralysis of both arms and legs seventeen days after laparotomy	Died, 8 weeks pregnant
12	M	58	Gr 2 phenobarbitone daily for a month before attack	None	Recovered
13	F	44	0 5 g thiopentone for laparotomy, gr $\frac{1}{2}$ phenobarbitone and gr $1\frac{1}{2}$ butobarbitone for six days after operation	None	Recovered

If it is not possible to carry out the test shortly after the urine has been passed, it should be stored in the dark and tested within twenty-four hours

In addition to porphobilinogen, the urine of patients with latent or acute porphyria may contain porphyrins, which can be detected by the 2 following techniques

Ultraviolet fluorescence—A filtered urine, preferably after standing overnight, is examined under ultraviolet light with a Wood's glass filter A distinctive red to salmon pink fluorescence indicates the presence of porphyrins To show the fluorescence more clearly, the porphyrins may be concentrated in an amyl alcohol extract of urine acidified with a few drops of acetic acid

Spectroscopic examination with the dark-vision spectroscope shows two bands at 577 and 541 mμ These are due to a porphyrin-metal complex and are very similar to the bands of oxyhæmoglobin, but if the urine is made strongly acid by adding 25% *v/v* of concentrated hydrochloric acid, a porphyrin spectrum may be seen at 597 and 553 mμ It is advisable to test various depths of urine, because a poor spectrum may be obtained with too much or too little urine

Further differentiation of the porphyrins into the various isomers and quantitative determination has proved of little value in the diagnosis of acute porphyria

During the past two years, all urines sent to the laboratory have been tested for porphobilinogen and we have been rewarded by finding 2 cases of acute porphyria case 12 was being treated at home by his practitioner for abdominal pain, and case 13 was in a surgical ward recovering from a cholecystectomy which had failed to relieve her pain

Hammond and Welcker (1948) carried out a similar investigation of the urines of 1000 patients with various diseases, but failed to find any cases of porphyria Nevertheless, the Watson Schwartz test is simple to perform, and a mass survey of a population group would provide information concerning the prevalence of latent porphyria, which is at present unknown

Inheritance

Günther (1912) recognised that porphyria was an inborn error of metabolism, and Waldenström (1937) was able to follow the transmission of acute porphyria in nine families through two, and in one family three generations He considered that the families might be descended from a common ancestor and that the defect was inherited as a dominant character not linked to either sex Gates (1946) studied Waldenström's families and other evidence of inheritance in acute porphyria, and concluded that the dominance is often irregular, and that possibly two factors are involved

Although there have been many reports of cases of acute porphyria in England, especially in the past few years, the family history is frequently stated as negative, and we have been unable to trace any family tree in which dominance could be demonstrated Markovitz (1954) reviewed all case reports published in the English language between 1941 and 1953 These numbered 69, and a proven or suspected family history was reported in 11 instances, in 17 the family history was stated to be negative, and it is not mentioned in the remaining 41

Dean and Barnes (1955) studied the genealogies of thirteen porphyric families, all of Burgher stock with many intermarriages, and showed that porphyria in South Africa is inherited as a mendelian characteristic and is not sex-linked *In these families,* however, the disease appeared in the acute form, the chronic cutaneous form (the "cutanea tarda" type), or a symptomless porphyrinuria, and in many cases one clinical type changed into the other These workers regard acute porphyria and porphyria cutanea tarda as different manifestations of the same inherited disorder but in this country Calvert and Rimington (1953) showed that it is possible to distinguish them, for in porphyria cutanea tarda during remission the fæcal porphyrin level is raised

In the present study we have found more than 1 case of acute porphyria in each of two families (fig 1) Dominance was demonstrated in family 1, but in four other affected families we have been unable to trace any inheritance of the defect

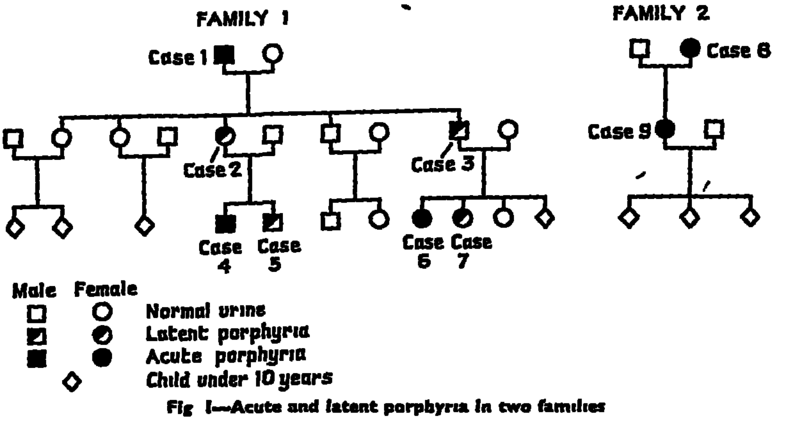

Fig 1—Acute and latent porphyria in two families

TRICUSPID VALVOTOMY

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DISEASE of the tricuspid valve is found in 22–36% of cases of rheumatic heart disease that come to necropsy but is severe in only 9–14% (Cooke and White 1941, Garvin 1943, Smith and Levine 1942), and severe tricuspid stenosis is found clinically in 3·3% of cases of mitral stenosis (Wood 1954)

Tight tricuspid stenosis can give rise to serious disability, with limitation of exercise tolerance by fatigue and angina, and in these circumstances relief of the stenosis is clearly desirable Tricuspid valvotomy has in fact been done in 18 published cases It follows from the known low incidence of severe tricuspid stenosis that this operation is likely to be done relatively infrequently

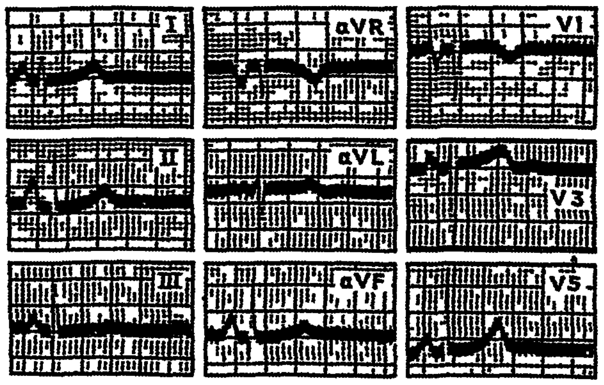

Fig 1—Electrocardiogram showing P pulmonale (II), P mitrale (V3), deep Q (aVF), and normal ventricular balance

I report here a case in which mitral and tricuspid valvotomy was done, review the published cases of tricuspid valvotomy, and discuss the problems that arise in relation to the operation

Case-report

A married woman, aged 24, complained of dyspnœa on exertion and of fatigue for five years, angina for four years, and ankle swelling for three years These symptoms had progressively worsened until she could not walk more than 100 yards Everyday activities fatigued her considerably and were accomplished only by a great effort There had been no hæmoptyses, emboli, paroxysmal dyspnœa, or rhythm change She had had doubtful rheumatic fever at the age of 5 years Her father had died from a coronary occlusion and her mother from kidney trouble

Physical Examination—She was well nourished, with no cyanosis or mitral facies The jugular venous pulse showed a dominant *a* wave 6 cm above the sternal angle The arterial pulse was of small volume, the blood-pressure was 130/70 mm Hg, and the hands were cool The apex beat was of normal quality, and there was no parasternal lift At the apex there were a loud presystolic murmur and a loud first sound, no systolic murmur, a soft opening snap, and a fairly long, low-pitched diastolic murmur of moderate intensity At the left 4th space the signs were very similar, except that with inspiration the presystolic and diastolic murmurs became much louder and longer An early blowing diastolic murmur was heard at the left 3rd and right 2nd spaces, and an opening snap too at the latter area The second heart sound was normal

RESULTS OF CARDIAC CATHETERISATION BEFORE AND AFTER MITRAL AND TRICUSPID VALVOTOMIES

—	Rt atrm	Rt vent	Pulm art	P C V	Cardiac output (litres per min)	A V O$_2$ diff	Tricuspid gradient		Mitral Rv/V
							Systole	Diastole	
Before	11/5(6)	24/0	24/10(14)	15/6(11)	3·2	6·12	10	4	0·9
After	9/2(5)	21/0	20/7 (12)	12/8(9)	4·0	5·00	6	2	1·38

Pressures in mm Hg Mean pressures in parentheses

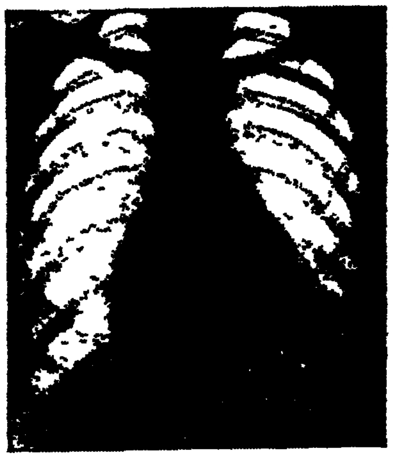

Fig 2—Radiograph showing considerably dilated right atrium

Investigations—Electrocardiography showed a 4 mm P pulmonale in lead II and a moderate P mitrale in V_3, with a normal ventricular balance There was a deep Q in aVF (fig 1) Radiography showed considerable cardiac enlargement (cardiothoracic ratio 65%) with well marked enlargement of the right atrium and moderate enlargement of the left atrium (fig 2) No valvular calcification was seen Cardiac catheterisation (see table) revealed a tricuspid gradient of 10 mm Hg in atrial systole and 4 mm Hg in diastole (fig 3) The *a* wave in the right atrium measured 11 mm Hg The pulmonary capillary venous (P C V) pressure of 11 mm Hg in the presence of a low cardiac output of 3·19 litres a minute suggested tight mitral stenosis, as did the Rv/V of 0·9 (Owen and Wood 1954) Pulmonary stenosis was absent

Diagnosis—The clinical diagnosis was mitral stenosis, tricuspid stenosis, and aortic incompetence The mitral stenosis was considered clinically to be fairly severe on the basis of a long diastolic murmur and a moderate P mitrale

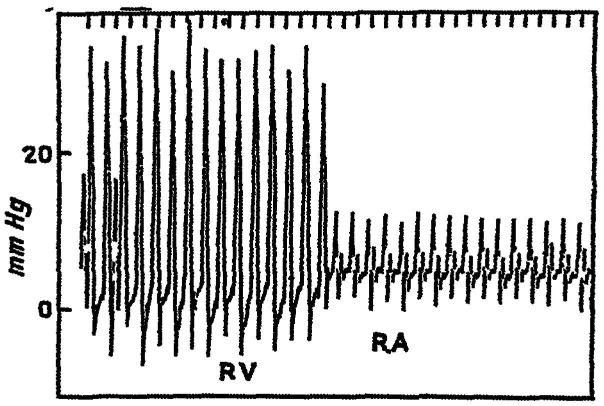

Fig 3—Cardiac catheterisation withdrawal tracing from right ventricle to right atrium showing tricuspid diastolic pressure gradient of 4 mm Hg (time in seconds)

The evidence for tricuspid stenosis was the large *a* wave in the absence of any signs of a high pulmonary arteriolar resistance, and the tricuspid diastolic murmurs Both lesions were confirmed at cardiac catheterisation and shown to be severe It was decided to undertake mitral valvotomy and, if this afforded no relief of symptoms, to proceed with tricuspid valvotomy at a later date

Mitral Valvotomy—Tight mitral stenosis was found, the valve orifice being 1 cm long, there was no incompetence It was necessary to cut both commissures, and each was split by about 1 cm thus producing moderate enlargement of the orifice Slight mitral incompetence was produced A striking feature, contrasting strongly with all other cases of mitral stenosis operated on here, was the normal size of the pulmonary artery Since the stenosis was severe, this was considered to provide good evidence, as did the absence of an opening snap over the valve at operation, that the pulmonary flow was greatly limited by the tricuspid stenosis acute porphyria After ingesting the drug she had an attack for the first time

The sulphonamide group of drugs and alcohol have also been incriminated, but the evidence against these substances is less strong than in the case of the barbiturates

The borderline between remission and relapse in acute porphyria appears to be very easily shifted, although too little is known of the factors responsible for the change in either direction

During the present study, case 9 had five attacks of acute porphyria in four years and case 4 had four attacks in two years Both patients were cooperative and intelligent, and we were able to obtain a most detailed history of the onset of the attacks, special attention being paid to any unusual physical or mental stress or any dietetic abnormalities during the fortnight preceding the attack In each case, and in each attack, the clinical manifestations were similar

The patient was in good health, carrying out the normal duties of a housewife or a factory worker The first symptom was colicky pain in the lower abdomen, which increased in intensity and often became continuous and lasted for several days The patient became constipated, but this did not precede the onset of abdominal pain by more than one day, or at most two The patients noticed that their urine became darker than usual and they became extremely apprehensive, both patients had neurological complications during previous attacks

On examination the patient's temperature was slightly raised but not above 100°F The pulse rate was increased by about 20 beats per minute, and both systolic and diastolic blood pressures were raised by about 20 mm Hg There was tenderness on superficial and deep palpation of the abdomen but no rigidity or rebound tenderness Nevertheless, these signs may easily be confused with those caused by an inflamed appendix lying in the retrocæcal position, and case 4 was operated upon at another hospital although the surgeon knew that he had porphyria

Investigations —The urine was either dark when passed or became so on standing, and contained porphobilinogen and porphyrins The serum-bilirubin level was sometimes slightly raised (1 5–3 0 mg per 100 ml), but other liver function tests gave normal results, and the rise in the serum bilirubin level remains unexplained The attacks passed off in a few days and the patients recovered rapidly Both of them have become more pigmented during the past two years, and hirsuties has developed in case 9

We are unable to suggest any precipitating cause for the recurrent attacks of acute porphyria in these 2 patients They had received no drugs, and there was no history of physical or mental stress, or of minor infections before the attacks No unusual food or drink had been taken and there was no excessive sexual indulgence No treatment was given, and we are equally ignorant of the factors which caused the attacks to subside

Rôle of Barbiturates in Acute Porphyria

In the past few years Rimington and his colleagues have made great advances in our understanding of the rôle of barbiturates in porphyrin metabolism (Goldberg and Rimington 1955)

Goldberg (1954) showed that various barbiturate hypnotics, especially those containing allyl groups, induced porphyric changes in the rabbit He also pointed out that barbiturates can inhibit some of the oxidative processes of brain tissue (Quastel and Wheatley 1933) Goldberg suggested that in addition to the possibility of a direct effect of a barbiturate drug on porphyrin metabolism, the hypnotic activity may aggravate the upset in brain and nerve metabolism described in acute porphyria by Denny Brown and Sciarra (1945)

Many reports emphasise the deterioration in the condition of patients with acute porphyria after the administration of barbiturate drugs (Prunty 1946, Jorgensen and With 1947) On the other hand, Turner (1938) and Discombe and D'Silva (1945) failed to note any relation between barbiturates and acute porphyria

All our patients were given barbiturates during one or more attacks of acute porphyria, and the complications that followed are recorded in the table It will be seen that the effect of giving barbiturate drugs during an attack of acute porphyria is unpredictable

Cases 8, 12, and 13 received barbiturates but recovered from attacks without any complications In case 4 paralysis of both arms developed after administration of gr 3 of quinalbarbitone, although in a previous attack the patient had received 0 5 g of thiopentone for a laparotomy and made an uneventful recovery Case 6 had three attacks of acute porphyria, during each of which she received barbiturates There were no complications on the first two occasions, but on the third very large doses of barbitone sodium and phenobarbitone were given at a mental hospital and she became completely paralysed in all limbs On the other hand, case 8 had received similar treatment, also in a mental hospital, and she did not have any paralysis

These data are insufficient to provide any conclusions as to the harmful effects of slow-acting, as distinct from long acting, barbiturates, or concerning those containing an allyl group, which according to Goldberg (1954) produced the greatest rise of porphyrin in rabbits' urine

In addition to our own cases, we studied many reports of other patients suffering from acute porphyria with neurological complications, and we were struck by the fact that all the patients had received some form of barbiturate medication—although in some cases paralysis of muscles was not noted until ten days after the barbiturate had been given (e g, case 4) Because cases of latent porphyria can have acute abdominal symptoms without having received any barbiturate drug (as in the later attacks in case 4 and in case 9), we suggest that the rôle of barbiturates in acute porphyria may be related more to neurological complications than to the precipitation of an acute attack

Pregnancy

Waldenström (1937) reported that 2 of his patients had died from acute porphyria during pregnancy, and he suggested that the hypnotic and other drugs given during this time might have been responsible He also thought that pregnancy itself might have precipitated an attack of acute porphyria, and Watson (1952) said that this might happen after a confinement On the other hand, Freedman et al (1952) reported that a patient with acute porphyria had improved during and after pregnancy

One of our patients was pregnant when acute porphyria was first diagnosed (case 11) and 2 others became pregnant during the course of the investigation (cases 9 and 7)

Case 11 —A married woman, aged 21, was admitted to a surgical ward with a history of abdominal pain, vomiting, and constipation for five days She had had a normal period three weeks previously, and the surgeon who examined her thought that she had a twisted ovarian cyst A laparotomy was performed under thiopentone anæsthesia, but no abnormality was found, a recently ruptured ovarian follicle was seen The abdominal pain persisted and she was treated with gr 2 of phenobarbitone daily On the day after operation the ward sister noticed that she was passing dark urine, but the significance of this was not appreciated, and it was not until she became paralysed in both legs on the twelfth day after operation that her urine was found to contain large quantities of porphobilinogen She died from respiratory paralysis a week later, an early fœtus was found in the uterus at necropsy

This patient had had no previous attacks of abdominal pain, nor any symptoms suggesting acute porphyria The urine of 6 of her relatives was tested for porphobilinogen, but none was found She had received no drugs before the onset of the pain, and we concluded that conception had played some part in the precipitation of the attack of acute porphyria

Case 9 —This patient had had two attacks of acute porphyria (with paralysis of her arms on the second occasion) when she told us that she was very anxious to have a third

Bailey (1955) points out that subvalvular fusion is much less common in the tricuspid than in the mitral valve, so this cause of difficulty, found with mitral valvotomy, should be absent from tricuspid valvotomy

In the 4 cases where details were given each of the three commissures was divided with equal frequency in 2, two commissures were divided, and in 2 one commissure was divided. In the present case the valve split naturally along the posteroseptal commissure, and in the other cases particular commissures were deliberately incised Bailey (1955) states that division of the anteroseptal commissure is to be avoided because it weakens the tricuspid valve "baffle" and is therefore likely to cause incompetence

A significant degree of enlargement was produced in all the published cases, the final valve orifice admitting $1^1/_2$-2 fingers or measuring 3 0-3 5 cm long The tricuspid-pressure gradient was measured before and after operation by cardiac catheterisation in 3 cases including the present one, and it was reduced by 1 3, and 6 mm Hg

Tricuspid incompetence is often found in tricuspid-valve surgery Anatomical study of diseased tricuspid valves led me to think that incompetence was likely to be a usual accompaniment of stenosis and to be found more frequently than with mitral stenosis, even when the tricuspid stenosis was tight (Hollman 1956) Incompetence was absent in only 2 of the 8 surgical cases in which this point was specifically mentioned After valvotomy moderate incompetence was produced in 1 case in which it had been previously absent but where incompetence was already present it was increased in only 1 case (the present one) I know, from personal communications on 2 unpublished cases that severe incompetence in 1 case fatal was produced at tricuspid valvotomy, it therefore seems important to avoid producing serious incompetence even if, as in the present case, this means only partial relief of stenosis

Associated Valve Disease—Severe mitral stenosis commonly coexists with tricuspid stenosis (Lewis 1946), and mitral valvotomy was done in all the published cases of tricuspid valvotomy except 1 (Krook et al 1955) When both valves are dealt with at one operation a sternum-splitting approach is advised (Bailey 1955) Severe tricuspid stenosis limits the mitral blood-flow and therefore decreases the symptoms and signs of mitral stenosis It may be difficult to judge the severity of the mitral lesion in these circumstances but cardiac catheterisation will prove the severity, and it is wise to assume that mitral stenosis, if present, is tight unless proved otherwise It is logical to do the mitral valvotomy first lest pulmonary œdema develop on relief of the tricuspid stenosis Disease of the aortic valve is often associated with tricuspid stenosis—in 35% of cases according to Osler and McCrae (1927) In none of the reported cases of tricuspid valvotomy, including the present one, was there serious aortic disease, but this may have been due to deliberate selection

Signs and Symptoms of Tricuspid Stenosis—Tricuspid stenosis is diagnosed clinically by observing a giant *a* wave in the jugular venous pulse in the absence of signs of a very high pulmonary arteriolar resistance (Gibson and Wood 1955) The diagnosis is confirmed by finding over the tricuspid area presystolic and diastolic murmurs which are intensified during inspiration, and according to Likoff (Bailey 1955), by turning the patient on to his right side, and occasionally by finding a tricuspid opening snap, as in the present case brought out by inspiration The symptoms of tricuspid stenosis are presumably due to limitation of cardiac output, with corresponding diminution in pulmonary venous congestion, fatigue and angina are thus prominent That these symptoms may be properly ascribed to tricuspid involvement is well shown in the present case where mitral valvotomy relieved the dyspnœa, leaving angina as the dominant complaint, which in its turn was relieved by tricuspid valvotomy

Summary

The case is described of a woman aged 24, with mitral and tricuspid stenosis, the dominant symptom of the tricuspid stenosis was angina pectoris Tricuspid and mitral valvotomy was successfully undertaken and partial relief of the tricuspid stenosis gave considerable symptomatic benefit

Among 18 reported cases of tricuspid valvotomy there were no deaths

Tricuspid incompetence is commonly associated with stenosis even when this is tight, and it is important to avoid producing serious incompetence at operation For this reason only a limited valvotomy may be possible

It is a pleasure to thank, for their encouragement and advice, Dr Kenneth E Harris under whose care the patient was, and Prof R S Pilcher who performed the valvotomies

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TREATMENT OF HAY-FEVER WITH HYDROCORTISONE SNUFF

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It is well known that hydrocortisone, in contrast to cortisone, will relieve certain disorders of the skin when applied locally It has also been used locally in chronic allergic rhinitis with some success by several workers Tuft (1954) used a hydrocortisone suspension combined with two vasoconstrictor substances acting as nasal decongestants, Rohen (1955) and Burger and Shaffer (1955) used a pure hydrocortisone suspension, and Foulds et al (1955) used hydrocortisone powder as a snuff

We present here the results obtained by treating 24 cases of pollen hay-fever with hydrocortisone acetate in the form of a fine powder applied locally to the nasal mucosa

Method

The patients, 10 females and 14 males aged 14-35 were chosen because of the severity of their symptoms and their lack of response to previous treatment, including treatment with anti-histamine substances to the limit of tolerance All gave a typical history of two years or more of continuous severe hay-fever during the summer months only All had a positive skin reaction to mixed grass pollens No case had been desensitised to pollen during the previous twelve months

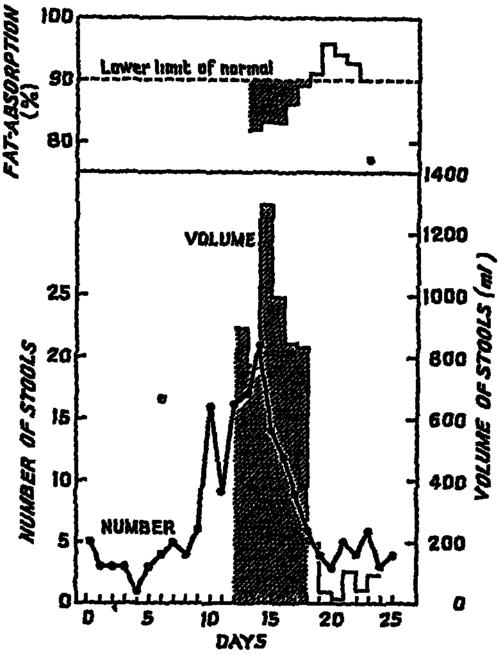

Fig 1—Fat-absorption and number and volume of stools (three-day means) of case 1 on a diet containing 50 g of fat daily hatched area, period in which phenolphthalein was detected in fæces

were any dysenteric organisms isolated A full course of antiamœbic treatment was given, the diagnosis being ulcerative colitis following amœbic dysentery Attacks of diarrhœa continued after his discharge from hospital, and, during an attack while he was visiting Birmingham, he was admitted to the Queen Elizabeth Hospital under the care of Prof T L Hardy

On examination there was no obvious wasting, and no abnormal physical signs were detected in the alimentary system Rectal examination was normal Sigmoidoscopy showed slight reddening of the mucosa, but the appearance was considered to be within normal limits, and no granularity or ulceration was noted up to a distance of 15 cm The patient appeared very concerned about his condition, gave a long and detailed account of his illness, and was obviously introspective

Laboratory Investigations—His stools were brown and semi formed or fluid, and microscopy showed them to contain an excess of fatty acid crystals but no pus or blood A barium meal ('Raybar') was normal, and a barium enema showed no ulcerative colitis or other colonic lesion A glucose tolerance test and chylomicrograph showed somewhat low rises in blood-sugar level and chylomicron counts respectively but were within the normal ranges A blood count was normal During a fat-balance test on a controlled daily intake of 50 g of fat the patient had an acute attack of profuse watery diarrhœa similar to those he had had in the past In the most acute phase twenty stools a day were passed, associated with an excessive fæcal volume Fat absorption during the early part of the attack was defective Details of the number of stools, fæcal volume, and fat absorption are shown in fig 1 At the height of the diarrhœa it was noticed that the addition of alkali to a fæcal aliquot turned it pink, and spectrophotometry of an alkaline filtered aqueous fæcal extract showed the absorption spectrum of phenolphthalein The disappearance of the pink colour on the addition of concentrated sodium hydroxide confirmed the identification as phenolphthalein When phenolphthalein had been found in the stool on four or five consecutive days, the patient was asked if he were taking laxatives This he denied, and a search of his possessions revealed none Within two days of this questioning, however, the attack of diarrhœa ended abruptly, an alkaline extract of his fæces was no longer pink, and his fat absorption became normal

Psychological investigation subsequently showed an intelligent patient, with great emotional tension and a background of incompatibility in marriage Moreover the question of attributability of his disability to Army service had been raised on several occasions In spite of this psychological background, the attack of diarrhœa observed in hospital was considered to be caused by the patient's taking phenolphthalein

Case 2—A married woman, aged 41, complained of attacks of diarrhœa and fæcal incontinence ever since anterior and posterior colporrhaphy had been done nine months earlier for stress incontinence of urine Two attacks had developed during convalescence and further attacks later with increasing frequency and diarrhœa had been almost constantly present before her admission to hospital She passed up to eight loose stools in the day time and often two at night, and she had been incontinent both by day and by night Her stools were very watery and contained mucus but no blood She appeared to give a good factual account of her disability and was regarded as a good and cooperative witness She said she was inclined to worry about small things in her home life, she had had some "spells of dizziness and sickness," but there seemed nothing abnormal in her previous history to explain her condition. She had seen a doctor only once during the nine months in which the diarrhœa appeared to have been a constant feature of her daily life

On examination no abnormality was detected apart from some pallor

Investigations—Sigmoidoscopy showed normal mucosa up to a distance of 25 cm A barium meal showed mild flocculation of the barium in the small intestine in the two hour and three hour films, and the cæcum was small and spastic Stomach, duodenum, and terminal ileum were normal A barium enema showed a normal colonic outline, but the colon was irritable, and the patient evacuated its contents on to the X-ray table A blood count showed a mild hypochromic normocytic anæmia, which subsequently responded to iron therapy Stools passed in hospital were loose and brown and were passed once or twice daily except on the first two days, when she passed five daily The fæcal fat was measured daily, with the patient on ordinary ward diet, by a modification of the method of van de Kamer et al (1949) The amount of fat excreted was within normal limits During the process of estimation it was noted that the alkaline fæcal emulsion was pink on ten days The urine passed in twenty four hours was collected on five days, and on only one of these days did the addition of alkali turn it pink The pigment was extracted from the fæces and urine and identified as phenolphthalein (see below) After phenolphthalein had been seen in the stool for about seven days, the patient was asked if she had been taking laxatives At first she denied taking any, but subsequently she admitted that she had taken two doses of a laxative since admission to hospital After questioning, her diarrhœa ceased, her stools became formed, and phenolphthalein disappeared from her stools

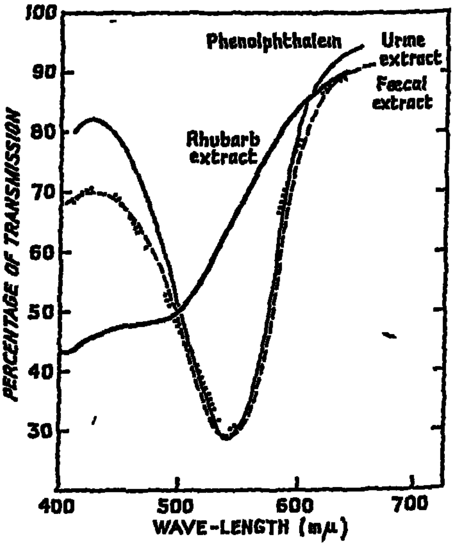

Fig 2—Absorption curves relevant to case 2

Extraction and Identification of Pigment

The pigment was identified in aqueous alkaline solution spectrophotometrically In case 2 it was extracted from was withdrawn, but all the patients who continued to take it throughout the whole season remained free, or almost free, from symptoms It is remarkable that 8 patients remained free from symptoms in spite of the withdrawal of treatment, and in spite of the fact that the season had only just started or was at its height A similar observation was made by Schiller and Lowell (1953) They gave oral cortisone 100 mg daily to 51 patients for four days This achieved complete or satisfactory relief in 42 patients, of whom 20 relapsed within a week The remainder were free from symptoms for the rest of the season It seems possible that in these cases and in ours a spontaneous partial desensitisation took place under the influence of these drugs Such desensitisation has been demonstrated experimentally under the cover of systemic cortisone (Herxheimer 1954) When some of our patients relapsed after a long interval of having no hydrocortisone, the time of their relapse did not coincide with any particular high atmospheric pollen count Possibly they had exposed themselves accidentally so heavily that the allergen broke through the protection given by a moderate degree of desensitisation In all these cases freedom from symptoms could be restored at once by resumption of the treatment

It would have been desirable to give a placebo powder during the withdrawal This would have shown us how many placebo reactors, if any, were in our series It is, however, unlikely that our very high proportion of successes could have been produced by psychological factors Moreover our patients had all had very severe hay-fever for several or many years and were very sceptical of this new treatment after the lack of success of previous efforts to relieve their symptoms The number of placebo reactors in our series can therefore be expected to be small We have been unable to observe a control series, because our supply of suitable patients with severe and uncontrollable hay-fever was limited and we did not wish to reduce our small series further

The method of treatment described here has one great advantage over desensitisation therapy in that it is safe Hydrocortisone powder in a dose of 15 mg daily applied locally to the nose for a maximum of eight weeks could not have any harmful effect even if most of it is absorbed.

Hay-fever, in severe cases, gives rise to much discomfort and disability, and any simple and safe method of treating it is welcomed by patients The subjects of this trial have been full of enthusiasm for the method, many of them stating that this was the first summer for many years they had been able to enjoy. Our experience in this small series indicates that the method is worthy of a wider trial during the next pollen season

Summary

In 23 of 24 patients with severe hay-fever who were given 15 mg of hydrocortisone snuff daily, complete control of symptoms was achieved during the first two weeks' treatment

In 17 of the 19 cases which could be followed up for the whole season satisfactory control of symptoms was achieved throughout

Of the 19 patients followed up 8 discontinued the hydrocortisone within three weeks and did not relapse thereafter

We are indebted to Messrs Upjohn of England for the supply of hydrocortisone powder and powder inhalers, and to Miss P McInroy for technical and other assistance

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RADCLIFFE RESPIRATION PUMPS

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Artificial respiration by intermittent positive pressure (I P P.R) through a cuffed tracheotomy tube was introduced by Lassen and Ibsen (Lassen 1953) for treating respiratory insufficiency in poliomyelitis This way of giving artificial respiration has proved, in competent hands, the method of choice when the throat as well as the muscles of respiration is paralysed Thus I P P R has proved invaluable in combined bulbar and spinal poliomyelitis and in conditions such as polyneuritis and tetanus (during curarisation)

Various machines have been devised to provide a respiration pump for this purpose The apparatus described here has been developed from the Radcliffe respiration pump, type A, devised by Russell and Schuster (1953) As in the original pump, the positive-pressure wave is effected by the free pressure of a weight on bellows This has proved the best method we know of, for it removes all need for safety blow-off valves and gives a square wave form which provides the maximum of ventilation in the shortest time, and so imposes the minimum of strain on the circulation (Spalding and Young 1955) Further the visible movement enables the nurse in charge to recognise any abnormality in the speed at which the bellows falls

The original pump has been greatly improved by the manufacturers (Messrs H G East & Co) and has proved in practice a reliable machine capable of operating continuously for many months with very little maintenance The use of a Sturmey-Archer bicycle gear-box provides a wide range of speeds at small cost and very little noise The Stott flutter valve (Smith et al 1954) continues to operate well, even when water has condensed in it, and its snoring sound provides an audible check of the volume of expired air with each breath The expired air can be measured with a gas-meter as it emerges from the valve The whole apparatus, complete with humidifier (Marshall and Spalding 1953) and gas-meter, is shown in fig 1 The apparatus incorporates both a 230 volt A C and a 12-volt D C motor, which provide both for continuous use in hospital and for battery operation in the case of transport by road or air

Radcliffe Positive-negative Pressure Respiration Pump

The clinical results obtained by pumps of the type shown in fig 1 cannot easily be bettered (Smith and Spalding 1955), but some physiologists argue that a negative-pressure phase is desirable in expiration to facilitate the venous return to the right heart This has therefore been incorporated in the newest design, which is therefore called the Radcliffe positive-negative pressure respiration pump (figs 2–4) Cam-operated valves have also been introduced as being more reliable than pressure-operated valves The negative-pressure phase like the positive-pressure phase, is gravity-operated and designed to provide negative pressure from 0 to –10 cm water Other features are as follows

Alternative Motors—The apparatus incorporates both a 230 V A C and a 12-V D C motor The latter is convenient for travelling or in case of prolonged electrical failure

Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

THE 56th general meeting of the association was held at Cheltenham on April 5–7 There follow brief reports of some of the papers read at the meeting

The Rose-Waaler Test

Dr C L **GREENBURY**, Dr A G S **HILL**, Dr R **SPALDING SMITH**, and Dr M S **GOOD** had had over two years' experience with a modification of the Rose-Waaler test in a series of 700 patients, including 249 with rheumatoid arthritis The test was positive in 90% of all cases of rheumatoid arthritis, and in 93 5% of those with positive X ray findings A few cases of rheumatoid arthritis were negative early in the disease, but for the most part even the earliest cases gave good positive results There was no relation between activity, judged either clinically, by erythrocyte sedimentation rate, or by C reactive protein, and a positive test

Most of the tests were done in duplicate, using saline and 2 5% sheep serum as diluents for the test sera When sheep serum was used as diluent, titres were 2–16 times higher than with saline, and a few sera were positive in serum but negative in saline Sera producing agglutination of sensitised cells in a dilution of 1 16 or higher were taken to be positive, providing that heterophile antibody was present in minimal quantity or had previously been absorbed

It was found, in common with other workers, that serum in "collagen disease" also gave positive results Two further groups of patients were found to give positive results an at present ill defined group of patients attending skin clinics, and patients with diffuse pulmonary fibrosis, finger clubbing, and arthralgia, but no arthritis It was concluded that the Rose Waaler test, at least in the modification described, was a most useful and accurate aid to diagnosis

Tubeless Gastric Analysis

Dr **JOHN HARKNESS** recalled that Segal et al [1] had recommended an azure A/cation exchange resin compound in which the quininium of the present tubeless gastric analysis is replaced by a dye which eventually colours the urine This new compound still had the disadvantages of interference by *drugs and food*, and by the need for an injection of histamine to verify achlorhydria Dr Harkness proposed that a more reliable test was to estimate the overnight urinary excretion of quinine after an oral dose of 500 mg of quinine carbonate suspended in weak alcohol or water Food and drugs did not affect the result Although histamine was not given, it was claimed that this technique could detect the false achlorhydrias missed by the standard intubation alcohol histamine fractional test meal A satisfactory test could be carried out by a patient in his own home Achlorhydrics excreted 0–100 μg quinine in eight hours (further experience might increase the upper limit slightly), patients with free hydrochloric acid in the gastric juice excreted 320–30,000 μg in eight hours

Platelet 5-hydroxytryptamine in Blood Disorders

Dr R M **HARDISTY** and Dr R S **STACEY** had conducted an investigation to determine whether the incidence of purpuric manifestations in various blood disorders was related either to the concentration of 5 hydroxytryptamine (5 H T) in the platelets or to the total 5 H T content of whole blood The platelet 5 H T concentration was estimated, and whole blood 5 H T determined, in 83 patients with various disorders of the blood and reticulo endothelial system, including leukæmias, polycythæmia vera, lymphomas, pernicious anæmia, and simple iron deficiency anæmia, and in 15 non hæmatological patients [2] Low mean platelet 5 H T concentrations were found in a high proportion of cases of all the hæmatological disorders, and these often resulted in low whole blood 5 H T Experiments on the absorption of 5 H T by platelets in vitro suggested that these low platelet 5 H T concentrations were attributable to a defect of the platelets themselves The mean platelet 5 H T concentration in these cases was unrelated both to the blood platelet count and to the incidence of abnormal bleeding All but 2 of the patients with purpuric manifestations had both thrombocytopenia and a whole blood 5 H T below normal limits, but the incidence of bleeding was less critically related to the whole blood 5 H T than to the platelet count Dr Hardisty and Dr Stacey concluded that the bleeding of thrombocytopenia cannot be attributed solely to 5 H T deficiency, and that there are no grounds for supposing that a low platelet or whole blood 5 H T concentration, in the absence of thrombocytopenia, may be a cause of abnormal bleeding

Streptococci in a Maternity Unit

Dr J D **ALLAN GRAY** described the spread of group A hæmolytic streptococci among the staff and patients of a maternity unit It began among the pupil midwives with a succession of sore throats which did not yield to sulphonamides, penicillin, holidays, or tonsillectomy In spite of strenuous efforts, the organism spread among 55 of the staff and 57 of the patients The vast majority of both staff and patients showed either no evidence of infection or at most only a trivial illness 2 infants died 1 was thought to have had a cerebral injury and the other developed his fatal illness after his discharge from hospital While a combination of penicillin and streptomycin was required to eliminate the *streptococci from the staff, penicillin alone* was sufficient to eliminate them from the patients The striking difference between the staff and the patients in the difficulty with which the streptococci could be eradicated was eventually shown to be due to the presence of penicillinase-producing staphylococci in the noses of most of the staff

Sudden Death in Infants

Dr J L **EMERY** and Dr E M **CRAWLEY** had found that in a series of 50 sudden unexpected deaths in infants the history as obtained by the coroner was consistent in only 5 cases with histories obtained after the child had been buried The histories obtained by the coroner's officer were substantially inconsistent with both morbid anatomical findings and later histories in 33 cases The follow-up histories indicated some abnormality in all infants before death, and, in the majority, symptoms of over two days' duration The inadequate histories might be due to the shock of the tragedy to the mother, and to the fear produced by the police and the coroner's investigations The procedures connected with these "sudden deaths in infancy" apparently needed revision

Salivary Tumours

Dr J M **CAMERON** and Dr A **DICK** had studied 88 cases of salivary tumours with particular attention to the pleomorphic adenomata or the so called mixed tumours The parotid gland was the most frequent site, followed by the submandibular and sublingual glands in that order They first occurred between the third and fifth decades but no age was exempt, and their growth was extremely slow The tumour recurred in about 30%, whatever the treatment Dr Cameron and Dr Dick supported the view that the cartilage like material in many of these tumours was in fact not true cartilage but a myxo chondroid substance developed by degeneration from epithelium and stroma

Acute Renal Failure after Head Injury and Operation

Dr W H **TAYLOR** and Dr J V O **REID** defined acute renal failure as a blood urea level greater than 100 mg per 100 ml and a urinary urea level of less than 2 0 g per 100 ml Such failure developed after surgical operation or head injury in 25 patients who were examined post mortem In 15 there was histological evidence of acute tubular necrosis In of the *earliest cases, casts were seen to be* produced by hæmorrhages from capillaries into tubules These hæmorrhages might be important in the process of cast formation Of the 10 patients without acute tubular necrosis, 1 had normal kidneys and 9 showed only hydropic changes in the tubules In at least 4 of these cases the duration of acute renal failure exceeded forty eight hours, and this should have been long enough for acute tubular necrosis to have become manifest

Previously described clinical features of acute renal failure were not consistently present in either the tubular necrotic or non necrotic groups All 11 patients had oliguria (less than 300 ml of urine per day) The plasma/urine chloride ratio was greater than 4/1 in all patients except 3 with acute tubular microphone, oximeter, and CO_2-meter—can be added to the trolley if required

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[1] Segal, H L, Miller L L, Plumb, E J *Gastroenterology* 1955 28, 402

[2] Hardisty, R M Stacey R S *J Physiol* 1955, 130 711

The pump is illustrated in figs 2–4 with the side plates removed Fig 5 shows the type of wave form obtained with the pump on a patient, and it is seen that the square wave form appears in both the positive-pressure and the negative-pressure phases

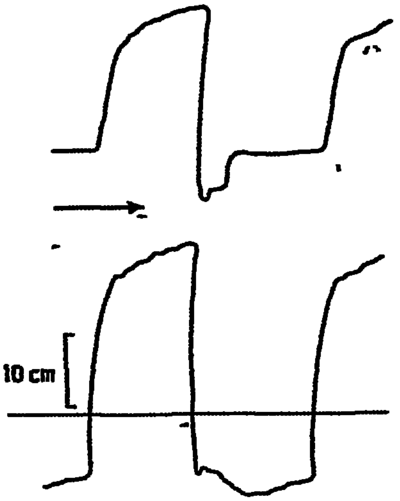

Fig 5—Wave forms obtained with positive-negative pressure pump with partial negative pressure and full negative pressure

Summary

Radcliffe respiration pumps have proved most successful in the treatment of combined respiratory and bulbar paralysis

A development of the original pump is described which includes a negative pressure phase

The design of this second type of pump has also been much improved by the manufacturers (Messrs H G East & Co, 37a, Oxford Road, Cowley, Oxford), to whom we are greatly indebted

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DELAYED PROTHROMBIN ESTIMATION IN OUTPATIENT ANTICOAGULANT THERAPY

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PROLONGED anticoagulant therapy continued over months or years must of necessity be conducted on an outpatient basis Laboratory control is essential, and patients have to report at short intervals to a hospital with laboratory facilities for accurate prothrombin-time estimations and where the medical staff is skilled and experienced in the control of such treatment This has proved difficult where patients are either fully employed or cannot travel easily, and has led to loss of work and frequent use of the ambulance service Further, the maintenance of anticoagulant therapy is restricted to patients living where these facilities exist

Freshly withdrawn samples of venous blood are requested by laboratories for the one stage prothrombin test, and this, so far as can be ascertained, is common practice It is generally stated that the specimen deteriorates fairly rapidly, and Quick (1951), describing the test, states that, though the estimation should be made within 30 minutes in research studies, up to 4 hours' storage is permissible for routine clinical purposes

Since the necessity for rapid estimation appeared to be a major factor in the problem outlined above, it was decided to put it to the test by making a pilot study of prothrombin-times estimated 24 hours after withdrawal of the samples of blood This work was done in 1953 as part of a larger investigation, and the present report is prompted by the imminence of large scale clinical trials of prolonged anticoagulant therapy

It should be emphasised that the prothrombin-time estimations were not made as a research study but were made each morning in the laboratory with large batches in the usual routine way Certain precautions were taken, however, to ensure that the identity of the specimens was unknown to the technician making the estimations

Method and Results

The one stage prothrombin test was used with fresh human brain as the source of thromboplastin A fresh thromboplastin solution was prepared and a control specimen estimated each morning The samples of blood were obtained by clean venepuncture, 4 5 ml of venous blood being run into a glass tube containing 0 5 ml of 1 34% sodium-oxalate solution and carefully mixed On reaching the laboratory the whole specimen was spun for 10 minutes at 2500 r p m, and 0 1 ml of the plasma thus obtained was used for the estimation For the purpose of the investigation enough blood was taken at each venepuncture to obtain three specimens

(1) The first was labelled by the house physician and sent for estimation in the normal way with many others from the ward or outpatient clinic It was the specimen used to control the patient s daily dose of coumarin drug

(2) The second specimen was also sent for immediate estimation under another name

(3) The third was carefully wrapped and sent through the post addressed to the sender When it returned to the department 24 hours later it was sent for estimation with that day s specimens under a different name

As a further check the first two specimens were on several occasions retrieved after estimation, relabelled with different names, and posted in a similar way for estimation the following day The technician could not

TABLE I—EFFECT ON ONE STAGE PROTHROMBIN TIME WHEN WHOLE BLOOD SPECIMENS ARE KEPT FOR 24 HOURS AT ROOM TEMPERATURE BEFORE ESTIMATION

Case no	One-stage prothrombin times						Error in delayed samples (sec)*
	On day of withdrawal			24 hr later			
	Control time (sec.)	Patient s time (sec)	Activity (%)	Control time (sec)	Patient s time (sec)	Activity (%)	
1	14	19	30	14	19	30	0
2	14	25	20	14	25	20	0
3	14	33	14	15	33	16	2
4	14	40	11	15	44	10	0
5	15	35	14	14	33	14	0
6	15	23	24	14	22	24	1
7	14	28	17	14	28	17	0
8	14	33	14	14	34	14	1
9	16	38	15	16	38	15	0
10	15	29	19	15	26	22	3
11	15	29	19	15	28	18	1
12	15	22	28	15	22	28	0
13	15	30	18	15	30	18	0
14	15	38	14	15	38	14	0
15	15	23	27	15	24	25	1
16	14	25	19	14	25	19	0
17	14	20	30	15	22	28	1
18	15	27	18	15	30	17	3
19	15	34	16	15	38	14	4
20	15	33	15	16	34	17	2
21	14	22	22	14	19	30	3
22	14	25	19	14	22	22	3
23	14	34	14	14	34	14	0
24	14	30	17	14	28	18	2
25	14	28	18	14	26	19	2
26	14	28	18	15	30	18	0
27	15	26	22	14	26	19	2
28	15	25	23	15	25	23	0
29	14	32	16	15	34	16	0
30	16	36	16	16	36	16	0

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* Where the control times differ, the error has been corrected to the first control time in simple proportion This is permissible since in the therapeutic range the curve of prothrombin activity is virtually linear

International Pharmacopœia, however, is in its infancy in the years ahead its virility will be revealed in its lists of additions and deletions

The bulk of the text is devoted to the 217 monographs Appendices, which form a supplement to those included in volume I, occupy about a third of the book They range over conventional chemical methods, biological assay, and tables of constants There is a schedule of "usual and maximal doses for most drugs," and another showing "usual daily doses for children" These are useful but they do not compensate for the omission of doses from the monographs The dosage tables also suffer because they are incomplete The *International Pharmacopœia* breaks new ground by its inclusion of a section on solutions of cardiolipin and lethicin for serological tests This "annex" was printed at the request of the subcommittee on serology and laboratory aspects of the Expert Committee on Venereal Infections and Treponematoses It creates a precedent of considerable importance to compilers of pharmacopœias

Neural Control of the Pituitary Gland

G W HARRIS, SC D, M D, F R S, Fitzmary professor of physiology, Institute of Psychiatry, Maudsley Hospital, London London Edward Arnold 1955 Pp 298 30*s*

IN this readable monograph Professor Harris describes the functioning of both the anterior and the posterior lobes of the pituitary gland As might be expected, his own work figures prominently in his account, and he admits in his preface to some bias in the presentation of material But he has produced a fascinating story which is sufficiently consistent to be readily followed and remembered yet does not belittle the uncertainties which still exist

The book begins with an account of the anatomy of the hypothalmus and hypophysis with special reference to their blood supply, and this is followed by a discussion of the mechanisms controlling secretion of the gonadotrophins, adrenocorticotrophin, and thyrotrophin In later chapters it reviews briefly but adequately the regulation of the anti diuretic factor and gives a clear and useful account of the hormonal aspects of parturition and lactation Neuro secretion receives brief but favourable mention, and the last chapter considers the hormonal influences which affect behaviour patterns in primates and other mammals

Professor Harris not only deals admirably with his special subject, but also touches informatively on many topics of general endocrinological interest

Diabetes

G F WALKER, M D, M R C P Pp 96 8*s* 6*d*

Cancer and Allied Diseases

RONALD W RAVEN, O B E, T D, F R C S Pp 121 8*s* 6*d*

Childbirth

W C W NIXON, F R C S, F R C O G Pp 106 8*s* 6*d*

London Duckworth 1955

THESE are three more volumes in the Modern Treatment series, intended for the general public Though not written for that purpose, they throw much light on current medical thought and practice They show an increasing desire to enlighten patients about normal and abnormal bodily happenings, about the medical approach to them, and about the modern medical armament—preventive and curative This rapport between doctors and patients is most desirable, but it is no easy thing to achieve To translate technical language (often, some would say, jargon) into lucid, unambiguous English is hard enough, to ensure that the translation will convey the true meaning to the lay reader is harder still, and to warn and advise without sowing fears or adding to the difficulties of the reader's own doctor is perhaps hardest of all The authors of these small books sometimes succeed in this difficult task but sometimes, perhaps inevitably, they fall short in one way or another

Diabetes contains much excellent practical advice, but the explanatory sections may not leave the reader much clearer about the nature of the disorder Unlike the other two, this book has no glossary or index

Cancer describes the nature of normal and malignant cell-multiplication and deals with radium, radiotherapy, and chemotherapy in some detail With the glossary's aid, the reader should be able to grasp what he is told In the clinical section, cancers of certain organs and regions have been chosen for relatively detailed description, including those of the pharynx, the liver, and the blood (leukæmia)—but not (rather surprisingly) tumours of the larynx, thyroid, prostate, or bladder, which usually have more specific early symptoms and are more amenable to treatment The discerning reader will find the book grim reading the absence of reliable warnings and the inefficacy of treatment for many sorts of malignant disease is all too clear Would it not have been better to concentrate on those few which an intelligent patient really can "catch in time" if he has the knowledge?

Childbirth has an admirable account of labour from the "labourer's" point of view, with effective photographs of models showing the nature of the birth process A chapter of "Any Questions?" includes a clear and comforting exposition of the rhesus situation Diet looms large in pregnancy food two hourly, no fried food, no salt at table, strict weight control, and no liquid paraffin With visits to clinics, systematic relaxing practice, and perhaps exercises, even the primigravida must have a busy time, and one imagines that the mother of one or two with a husband who fancies fried bacon would find the burden heavy

Sexual Precocity

HUGH JOLLY, M D, M R C P, consultant pædiatrician, Plymouth Clinical Area Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 276 50*s*

SOME years ago Dr Jolly started to study sexual precocity, hitherto those who wanted to know his conclusions have had to refer to an admirable but meagre paper in the *Proceedings of the Royal Society of Medicine*—that is, if they had not had the opportunity to read the thesis which won him the Raymond Horton Smith prize Now they can consult the full monograph, nicely produced in the United States and correspondingly priced

More than half the book is taken up by case-reports, many of them illustrated Sexual precocity in the physical sense, bewildering when first encountered, is seen to be resolvable into four groups constitutional (in which the child is normal in every other way, perhaps merely exemplifying how widely normal variation may extend), intracranial (hypothalamic-pituitary), gonadal, and adrenal In the first two there is premature puberty (which implies the production of ova or spermatozoa), in the others there is not To these may be added the cases produced by the administration (intentional or accidental) of stilbœstrol More of them may be seen now that potent endocrine preparations are so widely used

Until Dr Jolly's book is superseded by one written on the basis of investigations and theories yet unimagined, anyone thinking about a difficult case of sexual precocity can confidently turn to it for guidance

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Poliomyelitis (2nd ed London Edward Arnold 1956 Pp 147 16*s*)—After four important years, full of developments bearing on the treatment and prevention of poliomyelitis, the second edition of Dr W Ritchie Russell's book will be widely welcomed as an up to date survey Some controversial matters, such as the value of exercising paretic muscles to the point of fatigue during the convalescent (rehabilitation) stage, are now better explained, especially in the light of the author's further work on muscle recovery Too timid physiotherapy is still condemned, and a timely plea is made for the wider adoption of methods of actual measurement of muscle strength, as by the spring balance This aspect of the subject, like many others, is well illustrated by photographs, line drawings, fatigue records, and other graphs Changes in the treatment of the acute stage, especially in respiratory and bulbar cases, are similarly well surveyed The method of intermittent positive pressure respiration introduced by the Danish school, now falls into its natural place, not as a first choice, but for patients for whom the tank respirator is inadequate Pathogenesis is dealt with in a graphic and satisfying way, particularly the changes in the motor nerve cells It would be hard to find anywhere an account of the clinical aspects of poliomyelitis so concise and yet so comprehensive me for examination at intervals determined by the ysician-in-charge Other visits, however, simply for e estimation of the prothrombin-time, could be obviated ith advantage to both patients and staff It is not uggested that the laboratory should take over their management by post, but that the number of visits to hospital could be reduced to a minimum Patients living locally may continue to report at times to suit their working hours, but, where they live far from the centre, blood could be withdrawn either by their own doctor or at a smaller hospital (where there are no laboratory facilities) and sent by post for estimation next day

It matters little whether whole blood or plasma is sent, so long as there is no contamination with surgical spirit Such contamination is a common cause of hæmolysis and interferes with the accuracy of the results

It is hoped that estimations of prothrombin time made up to 24 hours after withdrawal of the blood, without special precautions regarding storage in the interim, will reduce the very considerable labour and time expended in dealing with such patients, particularly where large numbers are involved

It may be that the results are less accurate if there is more than 24 hours' delay, and a further study is being made to discover the effects of increasing the interval between sampling and estimation

Summary

In the control of long-term anticoagulant therapy it makes little difference whether the samples of blood used for the estimation of the one stage prothrombin-time are fresh or 24 hours old

Possible therapeutic implications are discussed

This investigation was made in the Department of Cardiology, Edinburgh Royal Infirmary My thanks are due to Dr A Rae Gilchrist for his encouragement, the staff of the Clinical Laboratory, in particular Dr Elizabeth Gilchrist, without whose coöperation the investigation would have been impossible, and Prof I G W Hill for help and advice with the paper

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CONTROL OF HYPOTENSION FOLLOWING REMOVAL OF AORTIC CLAMPS

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The operation of grafting segments of aorta, for aneurysm and thrombosis, carries a relatively high mortality, recorded by Rob (1955) as 17% in a series of 59 patients The mortality is greater when the aorta is clamped at a high level—that is, immediately below or above the renal vessels, in a consecutive series of 24 patients operated upon for aneurysms or thromboses there were 8 postoperative deaths, of which 6 occurred within the first forty-eight hours, of these latter, 3 occurred on the operating table following release of the aortic clamps, and 3 were due to coronary thrombosis occurring during the first or second postoperative day An aortogram illustrating the type of case on which these operations were performed is shown in fig 1

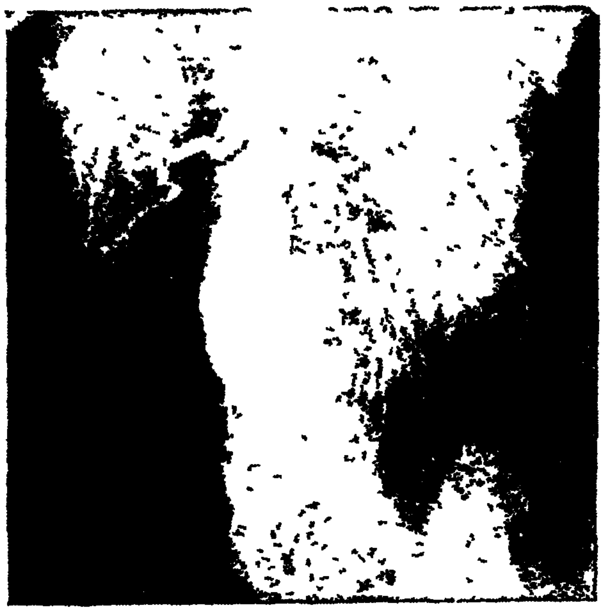


Fig 1—Aortogram showing large aortic aneurysm

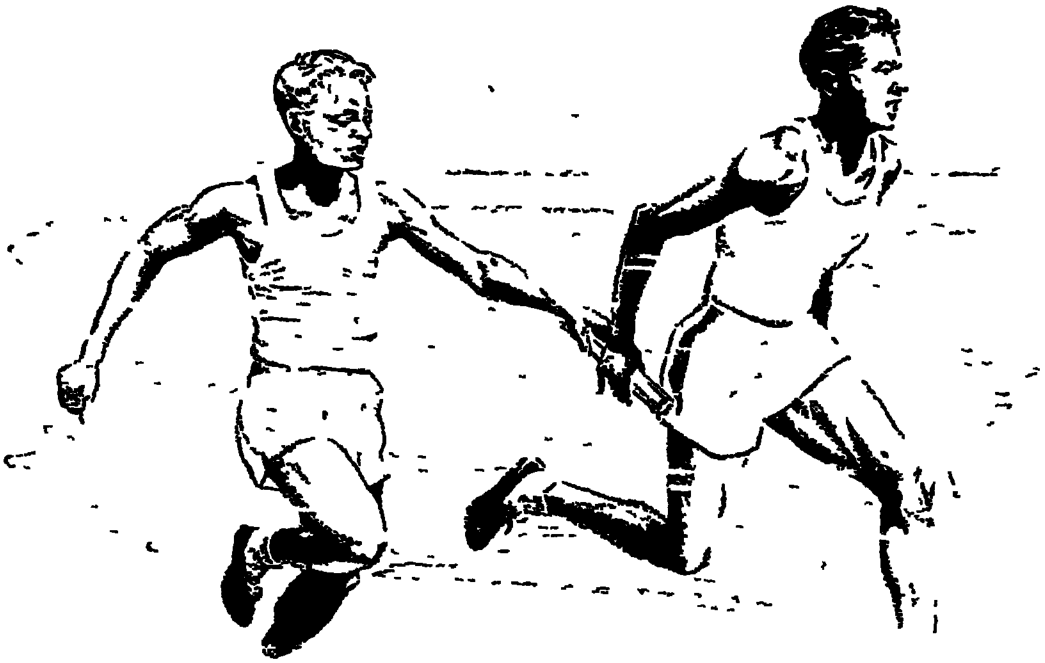
Release of the aortic clamp results in a dramatic fall of blood-pressure, which requires a rapid transfusion of blood and frequently an infusion of noradrenaline, before a satisfactory level is restored This period of hypotension may last for five to ten minutes, occasionally longer, and may result in a greatly diminished blood flow through the coronary arteries and the brain, to mention two organs whose blood-flow is greatly dependent on arterial pressure It seemed probable that the fall of blood-pressure was due to the return of blood to the previously ischæmic tissues and that it might be controlled by regulating this return This paper records preliminary results of an attempt to achieve such control

Calf Blood-flow

Calf blood-flows were recorded with a venous occlusion plethysmograph in 5 of the 24 patients, during the operation and the immediate postoperative period The plethysmograph was water-filled at 34°C, and in 2 patients operated on under hypothermia this was allowed to cool with the patient to 28°C The volume was recorded electrically (Cooper and Kerslake 1951) Ten-second inflow traces were recorded alternating with ten second periods of deflation of the collecting cuff The foot circulation was isolated with a cuff round the ankle inflated to 200 mm Hg during each three minute period of recording Fig 2 is representative of the results obtained, it shows hyperæmia in the calf on removal of the aortic clamp, coinciding with the period of hypotension The flow increases both when the patient is cooled and when he is not

Control of Hypotension

The hypotension may be partially controlled by gradual release of the aortic clamp, but in a grafting operation there is danger of thrombosis in the prosthesis if this phase is prolonged A simple apparatus has therefore been devised consisting of two arterial occlusion cuffs placed one on each thigh and connected to a mercury manometer and inflating mechanism, the valves being so arranged that the cuffs may be inflated or deflated independently The cuffs are placed as high on the thigh as possible before operation and, just before the aortic clamp is released, both are inflated to a pressure greater than the systolic blood-pressure—usually to 200 mm Hg After release of the aortic clamp the circulation is



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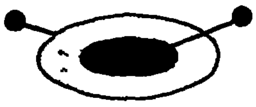

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We are very grateful to Prof C. G. Rob for advice and encouragement, Dr C. H. Cheetle, Dr H. L. Thornton, and Dr K. B. Chambers for valuable assistance, particularly in recording blood-pressure and pulse readings, and Dr D. Sutton for permission to reproduce the aortogram.

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RESERPINE IN ANXIETY STATES

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In psychiatry, where there is little agreement on basic theory and most forms of treatment are empirical, there tends to develop a definite pattern of response to the introduction of any new therapeutic drug. Firstly, there are the preliminary reports of clinical impressions; these will determine what range of dosage and what frequency and duration of administration are likely to be most suitable; and if (as is usually the case) the drug appears to be of value, further investigations are indicated. Secondly come the controlled trials; these may show that the effect of the new drug is no better than that of a placebo, or they may show that it possesses an efficacy which cannot be explained simply in terms of interest and enthusiasm. In this latter case comparative trials must be made of the new drug against a standard preparation and it is here that the new treatment stands or falls for it must be shown either to possess some new therapeutic power or to be at least as efficacious as the standard treatment.

Such a pattern can be discerned in the use of reserpine, one of the alkaloids of *Rauwolfia serpentina*. First used in the treatment of hypertension, it was found to have a beneficial effect on the neurotic symptoms of hypertensive patients (Wilkins 1954). Reports followed on its use and efficacy in various mental disorders, especially in neurotic anxiety and tension. Controlled trials of reserpine in neurotic states have produced conflicting results (Davies and Shepherd 1955, Folkson and May 1955); but, even if it were established that neurotic patients improve more on reserpine than on placebo tablets, such improvement might be due simply to a non-specific sedative action of reserpine. This possibility can be tested by comparing the effect of reserpine with that of a barbiturate (*Lancet* 1955).

The aim of the present study was to make such a comparison. We used a dose of reserpine (2 mg. t.d.s.) which is rather higher than that generally used in the treatment of neurotic patients; we did this because published reports show a clear tendency towards increased dosage and a pilot study, in which patients were given this dosage for one or two weeks, did not reveal any disturbing side-effects.

Method

The value of the self-controlled and self-recorded clinical trial in low-grade morbidity has been pointed out by Hogben and Sim (1953), and the technique has been shown to give reliable results in neurotic patients (Hare 1955). Using this technique, the present investigation was planned to compare the effect of reserpine, amylobarbitone sodium, and an inert control substance on the general clinical state and certain specific symptoms in patients with neurotic anxiety.

Case material

The patients studied were all inpatients in a neurosis unit. None was hypertensive. A patient was admitted to the trial only if his major symptoms were anxiety and tension, if he was willing and intelligent enough to coöperate, and if he appeared to be a reliable witness. 42 patients began the trial but 9 did not complete it: 2 of these 9 discharged themselves against advice for reasons unconnected with the trial; 2 refused, during the first week, to continue, saying the tablets made them much worse (both were receiving control tablets); and in 5 cases it was considered advisable to interrupt the trial and to proceed with electroconvulsion therapy, although there was no evidence that the failure to improve or the worsening of the clinical state was associated with the administration of any particular drug.

33 patients (14 male, 19 female) completed the trial satisfactorily. In 4 of these (1 male, 3 female) the dose had to be halved after three days because of the complaint of excessive drowsiness; this happened in each case while the patient was receiving reserpine. We did not feel, however, that halving the dose seriously disturbed the course of the trial; so the records of these 4 patients have been included in the analysis of the results. The average age of the 33 patients was 42.5 years (range 23–64).

During the trial the patients received a hypnotic (mostly butobarbitone gr. 3) where this was indicated but no other treatment was given.

Administration of Drugs

Each of the three drugs was administered to each patient for a week, the whole trial lasting three consecutive weeks. Thus the patient received two capsules and two tablets three times daily; and although the capsules and tablets remained identical in appearance they contained, for one week each, either reserpine 6 mg. daily, amylobarbitone sodium gr. 6 daily, or an inert control substance. Until the conclusion of the trial the order in which the drugs were administered was known only to the dispenser. It was arranged that, for the 33 patients, each drug was given an equal number of times in each of the three weekly periods and that (so far as was possible) each drug was preceded by each of the other two drugs on an equal number of occasions. This distribution eliminates any bias due to a tendency for the patients to feel better at the end of the trial period * and any bias due to the possibility that the effect of a drug might persist from one week to the next.

Assessment

Daily record charts were prepared on which each patient rated:

(1) How he felt compared with the previous day—"better," "same," or "worse" (scored 0, 1, and 2 respectively).
(2) The degree to which he had been affected by certain symptoms (see table I)—"absent," "mild," "moderate," or "severe" (scored 0–3).
(3) The quality of his last night's sleep—"undisturbed," "slightly disturbed," or "restless" (scored 0–2).

In addition, he completed a record at the end of each week indicating:

(1) How he had felt on the whole during that week compared with the previous week—from "much improved" to "much worse" (scored 0–4).
(2) The quality of his sleep during the week (scored 0–2).
(3) New or particularly troublesome symptoms.

Objective checks on the validity of the patients' records were made in the following ways. The charge-before it will be possible to decide how variations in that ratio affect the prevalence of disease

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* There was in fact a slight (statistically insignificant) tendency for the third week of the trial to be rated as better than the other two weeks.

SINCLAIR also postulates that the use of flour of low extraction-rate would significantly lower the effective content of the national diet in essential fatty acids and so predispose to atheroma and myocardial thrombosis and increase the prevalence of other diseases of civilisation, which he suggests may be attributable to relative deficiencies of these acids Here he is on very uncertain ground and can muster no direct experimental support He is right, however, in urging the need for more research on these problems, and in the present state of our ignorance it is surely rash to commit most of our population to consuming bread made from a flour about whose nutritive properties we know so little and have so many genuine doubts

Research into the origins of degenerative diseases of man is beset with difficulties Laboratory animals can be of only limited help, since in general they are much less susceptible than man It is also clear that noxious processes must persist for a long period before overt disease is manifest In this type of research the unit of time is the decade For the most part physiologists are still preoccupied by what happens in a few milliseconds, and even experimental pathologists like to get their results in a few weeks Established methods of medical research are thus not well suited to tackle the problems of the degenerative diseases The Cape Town workers are to be congratulated on the ingenuity with which they have devised an experiment which has established an important differential in the physiological effects of various dietary fats and oils They have, however, demonstrated effects lasting for only a few days clearly we should like to know that the vegetable and marine oils not only lower lipoprotein levels but can keep them low for long periods Their present findings, however, will be a stimulus to others to follow their clear lead in elucidating one of the gravest medical problems of industrial communities

A Merger?

HOSPITALS are very important and very impressive, but they ought not to dominate the medical scene, as they do now Whether people remain well and happy depends mainly on what happens to them, and is done for them, outside hospital, and we have repeatedly expressed our opinion that more of the resources of the National Health Service should be going into the kind of preventive and curative medicine that cannot be practised properly except where people live and work This view was put forcibly by Prof FRASER BROCKINGTON on Tuesday at the Blackpool meeting of the Royal Society for the Promotion of Health [1]

Last century, he said, all doctors in this country recognised that health is very largely a matter of environment, and as long ago as the 1830s disease was studied as a community problem But a hundred years later, in the 1930s, it had become customary to think of illness chiefly as a hospital episode Already the profession had retreated from its position of leadership in the challenge to environment, and "from the most enlightened of public-health pioneers, we have become the most backward, giving pride of place to the underdeveloped regions of the world To see public health in action, one must now go to Yugoslavia, Africa, Thailand, or to other and unmentionable places" One reason for this, paradoxically, is that public health has been so successful here, in eliminating the more obvious and dramatic plagues, that some people imagine it has nothing left to do, another may be that the appointment of medical officers of health has made the rest of the profession feel that public health is no longer their concern, but the principal single reason is the growth of interest in institutional care—which the National Health Service, so far from diminishing, has accentuated Under the N H S the hospitals are better organised, better staffed, and (taking it all in all) more efficiently and economically run than before, but BROCKINGTON holds that, in terms of public health, their nationalisation has been little short of disastrous, for they have been unnaturally elevated to a position of pre eminence, and are absorbing the best of the brains, and the lion's share of time and effort and money "The environment, upon whose inadequacies the whole of the apparatus of medicine is in reality constructed, has slowly receded into the background of our thoughts"

The primary need now, as BROCKINGTON and many others see it, is to shift the focus of medical care back to the community and to lessen the emphasis on hospitals "we want," he says, "a service for community health in terms of the family at home and at work, together with continuous study of disease and ill health within the community" And the obstacles, as he sees them, are not insuperable

> "Nowhere in the world has the concept of a family doctor been more firmly rooted than in Britain Nor have many countries been able to boast for so long a more complete cover of medical men trained in public health. Why should we not now bring these two great institutions together? We have the means wherewith to solve our difficulties in a merger of public health and general practice"

At present medical care for people in their homes is provided partly by the family doctor, working in contract with the local executive council, and partly *by district nurses, health visitors*, home helps, and *many other* medical and social workers employed by local authorities In BROCKINGTON's opinion this division of domiciliary services between two separate administrative machines is quite unrealistic "the general practitioner and the home nurse should work at least as closely together as the hospital consultant and the hospital nurse" As a professor of social medicine he evidently feels, too, that the family doctor's need of help from the health department is *at least equalled by* the health department's need of help from the family doctor General practitioners *should* be the *first* and *most* important agents in public health

> "Problems of care and aftercare, of the handicapped, of health education, the work of health promotion clinics, of immunisation and prevention of food-poisoning, of housing or such matters as the need to fluoridise the water-supplies, should concern them at every stage We cannot afford to leave the general practitioner working alongside, but not as part of, public health"

He believes that the right place in which, and from which, the practitioner should work is a health centre, which could give him the scientific and the social instruments for a modern approach to health, and also the advantage of team-work—not merely in the form some is shown by the fact that in 4 cases the dose had to be halved However, only one of the reserpine side effects (drowsiness) was really troublesome to the patients, and (as shown above) drowsiness often affected the patients receiving amylobarbitone sodium (also in rather high dosage) Yet, with amylobarbitone sodium, drowsiness did not stop the patients from recording that they felt improved This was not so with reserpine and at least 3 patients on reserpine specifically recorded that although they felt more drowsy and physically relaxed than before the trial began they felt no less anxious A similar " dissociated " response in a psychotic patient has been described by Tyndel (1955)

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[1] Presidential address to the Section of Preventive Medicine

It is worth noting that the patients in this trial were almost entirely new cases, many of them being recently admitted to hospital for the first time They therefore received the benefit of full initial examination and assessment on admission, together with general reassurance There was no suggestion that their treatment was experimental, the patients simply being told that they were to receive a special three-week course of tablets and capsules The conditions of the trial were such that the findings are not invalidated by any improvement due to suggestion, since the conditions were the same during the administration of each of the drugs and the experimental method was based on a comparison between different periods and not on an absolute assessment In such circumstances, especially when the periods are relatively short, this type of trial acts as a combined treatment and research project, and it is very doubtful whether (in the interests of attaining scientific objectivity) the refinement of telling the patient that this is a new treatment, and that the physician does not know whether or not it will be helpful, is necessary or even advisable

The general conclusions to be drawn from this trial are that, for a week and in the dosages given, amylobarbitone sodium caused much improvement in the general condition and in the individual symptoms of the great majority of patients with anxiety neurosis, whereas the effect of reserpine was no better than that of an inert control substance This does not mean, of course, that in smaller doses or administered for longer periods, reserpine could not be beneficial in anxiety states, but it suggests the need for caution in accepting some of the enthusiastic eports of the efficacy of this drug, and it also suggests that, at least on a short-term basis, amylobarbitone sodium is of definite value

Summary

A comparison was made of the effects of reserpine 2 mg t d.s , amylobarbitone sodium gr 2 t d s , and an inert control substance on 33 patients with neurotic anxiety Each drug was administered for a week

A self-controlled self-recorded technique was used The reliability of the records was checked by internal evidence and by objective assessment

Compared with the control week, most patients recorded much alleviation of their anxiety symptoms when they eived amylobarbitone sodium, but there was no neral tendency to alleviation when they received serpine

We wish to thank Mr E F Wellington and Mrs J Sulcock, harmacists, for their assistance, and the nurses for their oöperation with the record charts Ciba Laboratories Ltd kindly supplied the reserpine (' Serpasil ') and the matched control tablets, and Eli Lilly Ltd the amylobarbitone sodium (' Sodium amytal ') and matched control capsules

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ACUTE AND LATENT PORPHYRIA

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During the past five years we have encountered 8 cases of acute porphyria and discovered 4 cases of latent or symptomless porphyria in one family Since the area served by our hospitals is not a large one (population 150,000) we considered that acute porphyria is commoner than is generally realised We report the results of our study of the inheritance of the disorder, and discuss the factors that may precipitate an attack of acute porphyria

The clinical and biochemical classification of the porphyrias is controversial, but in this report the terms acute and latent porphyria are used to describe patients excreting excessive amounts of porphobilinogen in the urine without sensitivity of the skin

Material

The investigation is based on 6 women and 2 men whose ages ranged from 20 to 59 years (see accompanying table) Cases 4 and 6 are first cousins and case 8 is the mother of case 9 We have traced the family history of every patient and interviewed many relatives Specimens of urine were obtained from absent relatives and their medical history learned by correspondence with them and their practitioners

Examination of Urine

Colour

The urine of patients with acute porphyria, even during acute episodes, may be a normal colour, or it may be orange and dismissed as " concentrated " If the urine is left in daylight for a few hours, there is a definite alteration in colour, the urine becoming amber, particularly near the surface where it is in contact with air This simple test may be used as a preliminary test in a patient's home or at a cottage hospital where there are no laboratory facilities Urines from patients who have had blood-transfusions may also darken on standing, owing to the presence of other pigments , and therefore inspection of urine, even after allowing it to stand for some hours, is of limited value in the diagnosis of acute porphyria

In the laboratory, the darkening of the urine in cases of porphyria may be enhanced by heating it in a water-bath for ten minutes and then comparing the colour with that of an unheated control

Biochemical Tests for Porphobilinogen and Porphyrins

The urine excreted by all patients with acute porphyria (whether in the active or the latent phase of the disease) contains porphobilinogen This is the biochemical criterion necessary for diagnosis

Porphobilinogen is a colourless chromogen, but it can be identified by a simple chemical test using Ehrlich's aldehyde reagent, our technique being a slight modification of that proposed by Watson and Schwartz (1941)

To 2 ml of urine add 2 ml of Ehrlich's aldehyde reagent (0 7 g of *p* dimethylaminobenzaldehyde in 250 ml of 6 *N* hydrochloric acid) Mix and allow to stand for two minutes and then compare the colour with a mixture of 2 ml of urine and 2 ml of 6 *N* hydrochloric acid (this is a safeguard against artefacts caused by foodstuff colours excreted in the urine) Porphobilinogen gives a red colour which develops within twenty seconds, and urobilinogen gives a similar colour If a red colour is obtained, allow the mixture to stand for two to three minutes and then add 4 ml of chloroform and shake the test-tube , if the red colour remains in the aqueous layer the colour is due to porphobilinogen, but if it passes to the chloroform layer it is due to urobilinogen. Normal urines give no red colour

Gilchrist and **Tulloch** have treated 321 patients with a mortality of 18·1% and an incidence of thrombo-embolic episodes of 10·6% It is interesting to see that the mortality-rate has improved from 22·9% with the first dicoumarol treated series reported in 1950 to 14·4% in the phenylindanedione treated patients reported in 1954 With figures such as these, many people will wonder why anyone should oppose routine anticoagulant treatment for all patients, yet there is still much disagreement among cardiologists on this question

The reason, shortly, is that the mortality of coronary thrombosis depends largely on the extent of the initial lesion, the shock it causes, the medical history of the patient, and the occurrence of subsequent thrombo-embolic episodes **Russek** and **Zohman**[7] proposed an initial classification into "good risk" and "poor risk" cases, and they believed that anticoagulants should be given only to the poor risk group, comprising about 30% of patients In their experience the mortality-rate of untreated good-risk patients was only 2% and the incidence of thrombo-embolism less than 1% Since anticoagulant treatment itself is not without risk, they argued, there appeared to be no good reason for using it for so slight an improvement **Gilchrist** and **Tulloch** counter this view with several telling points They say that the doctor is faced with the individual patient and his family, and if 2 or 3 in 100 good risk patients can be saved by anticoagulant treatment when they would otherwise die, the slight risk is justified Moreover, it is hard to judge, six to twenty-four hours after the onset of an acute infarction, whether the patient is, in fact, a good or a poor risk, and they quote the experience of **Halpern** et al[8] who found it necessary, within forty-eight hours of the onset of the attack, to revise the grouping of about a third of their series of 117 patients But to delay a decision about anticoagulants for twenty-four or forty-eight hours is to deny a patient the benefits of early treatment **Halpern** et al therefore gave every patient anticoagulants, but they stopped treatment after forty-eight hours in all those who could then be regarded as good risks **Gilchrist** and **Tulloch** consider that this is too soon to stop treatment, and they recommend a minimum of ten days for the patient assessed as a good risk on the first day, should there be any unfavourable change, such as thrombo embolism, the course of treatment can then be extended by three weeks In the more severe cases they adhere to their previous recommendation of four weeks' treatment, extended if necessary by three weeks from the date of any subsequent thrombo embolism This programme means that *every* patient admitted to hospital is given anticoagulants, and this course can now be confidently adopted because the risk of therapeutically induced hæmorrhage has been so much reduced by present-day methods and drugs **Gilchrist** and **Tulloch**, using phenylindanedione, with efficient laboratory control, have had no serious hæmorrhagic complications in their last 120 patients If bleeding does occur, 10–50 mg of the oral vitamin K_1 emulsion will stop it

Gilchrist and **Tulloch** also discuss other possible effects of anticoagulant treatment They refer to the investigation of **Helen Payling Wright** and her co-workers[9] which showed that the rate of recanalisation of thrombosed arteries and veins is more rapid when the "prothrombin activity" of the blood is kept low Another point is that pulmonary infarcts are much less frequent in patients who have had anticoagulants, even though the patients ultimately die, thus, in 88 treated but fatal cases, there were 3 pulmonary infarcts, whereas in 160 control necropsies in untreated cases, pulmonary infarcts were found 27 times—a striking difference Prevention of pulmonary infarction is important because there is evidence, such as that provided by **Cole** et al,[10] that these incidents diminish the immediate and later chances of survival

The observations of **Gilchrist** and **Tulloch**, and all the arguments about anticoagulant treatment concern, almost exclusively, those patients with myocardial infarction who are admitted to hospital for treatment But not all patients with myocardial infarction are admitted to hospital, indeed, as **Morgan Jones**[11] puts it, "it is very doubtful whether any community will in the future be able to provide enough hospital beds for the treatment of all cases of coronary thrombosis, even if this were desirable" **Morgan Jones** reminds us that recovery is the rule if the patient is still alive when the doctor arrives If the patient is still alive, then the decision to recommend removal to hospital or treatment at home has to be made, and this decision often turns on whether or not he needs anticoagulants This brings us back once more to the assessment of prognosis, the decision between "good risk" and "poor risk" If the verdict is "good risk," then the relatively small advantage to be obtained from anticoagulants must be set against the risk of transport to hospital, if the assessment is "poor risk," then the patient should be got to hospital for anticoagulant treatment as soon as possible The responsibility for this decision rests usually with the consultant called to see the patient, and he may be fortified by **Morgan Jones**'s opinion that "there must be few serious conditions in which we can at onset separate off clinically as large a proportion of cases with so hopeful and encouraging a prognosis" Thus, **Morgan Jones** believes that good-risk patients can be treated at home without anticoagulants, and many cardiologists agree with him, but **Gilchrist** and **Tulloch** might not The alternative is to give anticoagulants to all good risk patients, comprising perhaps two thirds of the total number, and to do so, some means must be provided for practitioners to get prothrombin-time estimated on blood samples taken in the patient's home **Owren** and others have used long-term anticoagulant treatment for myocardial infarction[12], but in the domiciliary control of treatment from the start, blood samples must be collected at home and delivered to the laboratory and the result sent to the doctor as soon as possible In his article this week, Dr **Watson** records his inquiries into the possibilities of organising such a service, with results that, so far, seem encouraging

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[12] See *Lancet*, 1954 ii 742

Case-reports

FAMILY I

CASE 1.—The grandfather of cases 4 and 6. This man died in 1940 at the age of 64, and unfortunately we lack proof that he had acute porphyria. Nevertheless, we have questioned his widow and his doctor, and think that the attacks of abdominal pain from which he suffered during the later years of his life (and for which no cause was found) were symptoms of acute porphyria. In addition, the records of his last illness describe extensive paralysis, which his widow asserts was very similar to that of her grand daughter. Members of his family state that his urine was sometimes very dark, but, as far as we can trace, it was never tested for porphyrins.

CASE 4.—A man, aged 20, and a first cousin of case 6. While he was serving in the R.A.F. his urine was found to contain moderate amounts of porphobilinogen. He was in good health and had not had abdominal pain or other symptoms suggesting acute porphyria. We therefore classified him as a case of latent porphyria and warned him of some of the inherent dangers of the disease. A few weeks later and shortly after the death of his cousin, he had a severe attack of abdominal pain associated with constipation and was admitted to a hospital in another part of the country as a case of suspected appendicitis. He informed the surgeon that he had porphyria, and the presence of porphobilinogen in his urine was confirmed, but laparotomy was performed under thiopentone anæsthesia and a healthy looking appendix was removed. He made an uneventful recovery from the operation, but was discharged from the R.A.F. on medical grounds. Three months later he had a further attack of severe abdominal pain. We had asked his practitioner not to give him any barbiturate drug, but he was attended on this occasion by a locum practitioner, who prescribed gr. 3 of quinalbarbitone (Seconal). On his admission to hospital the next day an increased amount of porphobilinogen was found in his urine, and his systolic and diastolic blood pressures were raised 20 mm. Hg above the usual levels. The attack of abdominal pain subsided in a few days, but ten days after the onset he complained of weakness of both arms and fairly extensive paralysis of the muscles of both shoulders and arms developed. He made a slow but good recovery during the next few months. During the past two years, this patient has had four further bouts of abdominal pain, but barbiturate drugs have not been prescribed and there have been no neurological complications. Porphobilinogen has been found in his urine whenever it has been tested, and the amount is greatly increased during an attack of abdominal pain.

CASE 6.—A married woman, aged 21, was admitted to hospital with complete paralysis of all limbs and some weakness of the intercostal muscles (fig. 2). Her urine was a port wine colour and the diagnosis of acute porphyria was confirmed by finding that the urine contained large quantities of porphobilinogen and porphyrins. During the previous three years the patient had had several attacks of abdominal pain for which two laparotomies were performed; on the first occasion a healthy looking appendix was removed, and on the second some adhesions were divided. The attacks of abdominal pain continued and she underwent a course of psychiatric treatment, including sedation with large doses of barbiturate drugs, after which weakness in both legs developed and she became completely paralysed in all limbs. Despite many forms of treatment the patient died five months after admission to hospital.

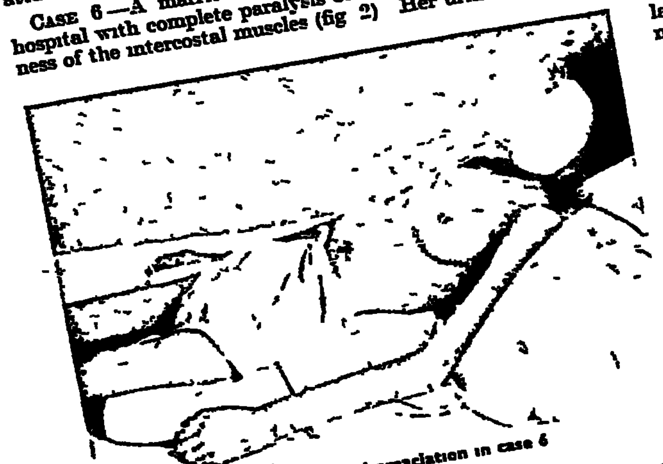

Fig. 2—Advanced emaciation in case 6.

Latent Cases

CASE 2.—The father of case 4, aged 45. He has no symptoms of acute porphyria, but his urine is often pink and contains a moderate amount of porphobilinogen.

CASE 3.—The mother of case 6, aged 43. She has no symptoms of acute porphyria; her urine is a normal colour but contains porphobilinogen.

CASE 5.—The brother of case 4, aged 19. He has no symptoms of acute porphyria; his urine is a normal colour but contains porphobilinogen.

CASE 7.—The sister of case 6, aged 20. She has no symptoms of acute porphyria. This patient has had two confinements without complications. Her urine is normal in colour but contains porphobilinogen.

FAMILY II

CASE 8.—The mother of case 9. She was treated for "plumbism" at the age of 35, and had a severe attack of abdominal pain for which a laparotomy was advised when she was 40. She refused operation and the pain subsided in a few days; she was free of attacks between the ages of 40 and 59 when they recurred several times a year. Despite numerous investigations, including radiography, no cause to account for the pain was found and she received psychiatric treatment, including electroconvulsive therapy, in mental hospitals. After her daughter had had an attack of acute porphyria, her urine was examined and found to contain much porphobilinogen. She died at the age of 64 from carcinoma of the stomach.

CASE 9.—A married woman, aged 36, was admitted to a surgical ward with lower abdominal pain and constipation. She was treated with enemas and given gr. ½ phenobarbitone twice daily and gr. 3 quinalbarbitone at night; the abdominal pain was relieved in a few days and she was discharged from hospital. She was readmitted to a medical ward fourteen days later with weakness of both arms; her urine was dark and contained porphobilinogen. During the next few days, paralysis of the extensor muscles of both wrists developed, and tests confirmed weakness of several other muscles in both arms and forearms. With active physiotherapy she eventually made a complete recovery but she has continued to pass varying amounts of porphobilinogen in the urine for the past four years. During this time she has had occasional attacks of abdominal pain and has twice been admitted to hospital for observation. No barbiturate drugs have been given and there have been no further paralytic episodes. She became pregnant last year and gave birth to a healthy girl; her urine contained moderate amounts of porphobilinogen during the confinement.

OTHER CASES

Our 4 other patients with acute porphyria (cases 10–13) came from different families; but although we investigated many relatives, including the parents of cases 10 and 12, we found among them no cases of latent porphyria.

CONCLUSIONS

The inheritance of the defect in acute porphyria as a dominant was confirmed in family I. In view of the negative family histories in many well authenticated cases, we think it possible that more than one factor is involved, or that affected members of the family excrete porphobilinogen intermittently or in such small amounts that it cannot be detected by the Watson-Schwartz test.

Precipitation and Features of Acute Attacks

Watson (1954) states that the mechanism by which the latent disease becomes manifest is unknown, and he suggests that there are various precipitating factors.

Günther (1912) referred to "toxic" porphyria because of the frequency with which acute attacks followed the ingestion of sulphonal and 'Trional'.

Waldenström (1937) administered a barbiturate to a woman who had never had an acute attack but whose sister had had study revealing the pitfalls which may trap those who make deductions from such an investigation (and also the means of avoiding them), they have proved that pulmonary tuberculosis is not related to the operation but rather to the standard of nutrition before operation The attack-rate is high in men 15% below their standard weight before partial gastrectomy, contrariwise, if the preoperative chest radiograph and weight are normal there is little to fear They point the moral every attempt should be made before partial gastrectomy to raise the weight of undernourished patients, since the chance of restoring nutrition after the stomach has gone is remote

CHILDREN NEED FAMILIES

FAMILY disruption undoubtedly contributes to juvenile delinquency Evidence of this has been impressively adduced by Bowlby,[1] in confirmation of earlier workers, including Healy and Bronner[2] and the Gluecks[3] Attention must therefore be given to the special problems of emotionally deprived children in any programme of delinquency prevention which claims to be comprehensive This is the theme of a second report,[4] recently published by the City of New York mayoral office, with the significant title Children Need Families The earlier New York report[5] dealt with broad preventive measures, the new one is concerned with the needs of children deprived of a normal home life It emphasises the fundamental principle, in the rehabilitation of these dependent and neglected children, that they should be cared for on the basis of a family group

The cornerstone of the New York programme is the provision of adequate numbers of suitably trained and professionally qualified social workers and counsellors, to augment existing child-welfare services within the city Their chief rôle would be to conduct intensive field work among families otherwise likely to break up in disharmony By providing close support and encouragement for emotionally inadequate, unstable, and often demoralised parents, the precarious family structure can be preserved and strengthened, thus reducing the load of emotionally deprived children for whom the community might otherwise become responsible This is sound preventive medicine it is also sound economics, since the cost of these expanded services is broadly balanced by the saving in keeping children out of trouble When the family has already broken down, or when breakdown proves inevitable, the aim is to reinstate the child, wherever possible and as soon as possible, within his own family, by a sustained effort directed towards the parents, or, failing that, to find him at least a secure substitute home with enlightened foster parents, or parents by adoption if that is appropriate This is, in essence, the reconstructive aspect of the programme It is good to see the increasing recognition of these principles, and the decline of the earlier policy of accommodating such children in homes and institutions where their healthy emotional development was often endangered by the starched and impersonal atmosphere As Mr Epstein's report puts it, "children well fed, well groomed and clothed, substantially sheltered (in these homes), may still be miserable children A chef in a stainless steel kitchen can hardly ladle mother love into the soup"

In this country, similar considerations are steadily gaining ground, as illustrated by the 7th report on the work of the Children's Department of the Home Office[6] In London, the health committee of the London County Council proposes to employ some 50 additional whole-time home helps, with the object of trying to keep together, at home, families whose children might otherwise have to be received into care, through illness or incapacity of the mother[7] A proportion of these home helps, after training, will also work with and teach housecraft to mothers who need help of this kind As in New York, the aim is to prevent family dissolution rather than cater for its aftermath

While applauding the expansion of these social services, we must temper our support with caution The help given by welfare workers to families in need of readjustment and rehabilitation, involves encroachment upon emotional conflicts and intimate personal problems which demand tact, technical training, and enlightened understanding for their satisfactory resolution It is of vital importance to ensure that the additional social workers to be recruited in this sphere have had the necessary training, and are imbued with a sense of responsibility that matches their rôle as home savers Children do need families, but they must be stable and emotionally intact ones

EKIRI

FOR a long time Japanese physicians and pathologists have been claiming that a form of acute infantile disease, *ekiri* (also known as *hayate* [typhoon] and as *kyusho* [acute illness]), though possessing many affinities with bacillary dysentery is not strictly speaking a shigellosis As most of the work has been carried out in Japan it has not attracted much attention in other parts of the world It has, however, aroused much local interest—so much so that a special study of it was made in the summer of 1947 by an American research team, and last April a symposium was held at Kyoto during the annual meeting of the Japanese Association for Infectious Diseases

A report from Japan[8] on the ætiology of *ekiri* from the clinical, pathological, bacteriological, and biochemical aspects leaves many questions unanswered The *ekiri* state, though acknowledged to be related to bacillary dysentery, resembles peripheral vascular failure due to anoxia in small children Deinbee Naito observes that the syndrome occurs only in Japanese infants, it is common among those aged 2–7, but no sucklings suffer from it The syndrome consists in disturbances of the central nervous and circulatory systems in combination with disorder of the intestinal tract It is thought to be due to some toxic product which acts mainly on the vascular system It is stipulated that the toxin is non bacterial—for instance, one of the toxic amines, which it is impossible to detect in the blood, though in the acute period there is a remarkable increase of blood ammonia (0 84 mg per 100 ml) Amine formation is presumably due to the intestinal flora, the majority of tyramine producing strains are *Escherichia coli* and *Aerobacter aerogenes* Sakamoto and Suzuki assert that the syndrome is not fulminating bacillary dysentery It is distinguished by intense circulatory disturbances Sakamoto has brought forward evidence that it is a typical shock manifestation in response to a food allergy, for which he holds *miso*, a kind of soybean, responsible

Despite the involved and often conflicting arguments it is difficult to escape from the suggestion that organisms of the dysentery groups are the chief factor In Japan bacillary dysentery is widespread and severe, the fatality rate in infants in the Kyoto Municipal Hospital, despite chemotherapy, is still over 10% Confusion may have arisen because of the difficulty of culturing the dysentery group from the necrotic mucosa, where these organisms are swamped by other bacilli child In consultation with Prof C H Gray we strongly advised her against such a course, but nevertheless she became pregnant a year later and was safely delivered of a baby girl with the aid of pethidine During pregnancy, she had two mild attacks of abdominal pain and passed moderate amounts of porphobilinogen in her urine, but the amount was not increased at delivery or during the puerperium.

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[1] Bowlby, J Maternal Care and Mental Health, W H O, Geneva 1952

[2] Healy W Bronner, A New Light on Delinquency Newhaven Conn 1936

[3] Glueck S Glueck, E Unravelling Juvenile Delinquency Cambridge Mass 1950

[4] Children Need Families By HENRY EPSTEIN deputy mayor City of New York Office of the Mayor 1955

[5] Perspectives on Delinquency Prevention City of New York, Office of the Mayor 1955 see *Lancet* Jan 7 1956 p 34

[6] 7th Report on the Work of the Children's Department H M Stationery Office 1955

[7] See *Lancet* Feb 25 1956 p 307

[8] Advances in the Study of Ekiri in Japan Edited by Kozo Ogasawara, M D, professor of bacteriology Nagoya University, Japan Tokyo Japan Society for the Promotion of Science 1955 Pp 101

CASE 7 —This patient, aged 20, is a case of latent porphyria belonging to family 1 She has had two normal confinements without an acute attack of porphyria developing, and she hopes to have more children. Apart from avoiding barbiturate drugs, no special precautions were taken during her pregnancies. The amount of porphobilinogen passed in the urine was not increased during her last confinement

Comments

The factors which cause a patient with latent porphyria to have an acute attack are unknown but many instances between the ages of 18 and 30 (when pregnancy is most likely) have been reported. Possibly the bad reputation which pregnancy has acquired as a precipitating cause of acute porphyria is in part due to the coincidence of the period of greatest fertility with the age-group which is most susceptible to acute porphyria

Mental Symptoms

It is well known that mental disturbance is a common accompaniment of acute porphyria, and Markovitz (1954) reported that mental changes were noted in over three-quarters of the 69 patients in his review In the present study, cases 6, 8, and 12 had spent periods in mental hospitals, and cases 4, 9, and 11 had psychological upsets during porphyric attacks Cases 6 and 11 died, but the other patients recovered and their mental state became normal as the attack subsided In addition, we observed no mental disturbances in 4 cases of latent porphyria (family 1), and we suggest that the so-called porphyric temperament is not a common feature of the disease The histories of many patients with acute porphyria is a lamentable tale of wrong diagnoses, unnecessary operations, and sedation or shock treatment, possibly these vicissitudes may have caused the " nervous constitution " mentioned in some reports This should not be confused with the mental symptoms that often accompany attacks of acute porphyria

Treatment

The efficacy of any treatment is notoriously difficult to assess in acute porphyria in which spontaneous remission and rapid improvement are common (Rimington and Goldberg 1954) During the past five years, we have treated ten attacks of acute porphyria in 7 patients with one or more of the following drugs neostigmine, potassium and calcium salts, corticotrophin, cortisone, 'Eucortone,' and large doses of vitamin B_{12} and other vitamins No beneficial effect was noted, and rational therapy must await a clearer understanding of the chemical pathology of the disease

On two occasions acute attacks were accompanied by a striking decrease in the serum sodium level (to 103 m eq per litre in case 12, and 118 m eq per litre in case 13) Both patients were considerably improved by infusions of normal saline, and we agree with Davies (1949) that careful control of the electrolyte balance is essential during acute attacks

When abdominal pain is severe or during a confinement we use pethidine, and paraldehyde is preferable to barbiturate drugs as a sedative for patients with mental symptoms although the pathogenesis of porphyria is at present unknown, barbiturate drugs should not be prescribed We treated 3 patients in artificial respirators, but they all died

Cases 4 and 9 survived an attack during which the muscles in the shoulders and arms were paralysed and we were agreeably surprised by the full recovery of function that they achieved with physiotherapy—and in a shorter time than is usual for a similar paralysis caused by poliomyelitis

Summary

In five years 8 cases of acute porphyria have been found in a population of 150,000

Inheritance by mendelian dominance has been demonstrated in one family

The precipitation of an acute attack and the influence of barbiturates and pregnancy are discussed

Mental disturbance is a common accompaniment of acute porphyria

We thank Prof C Rimington, F.R S, and Dr A Goldberg for their help and interest in this investigation, and Dr A I Cheyne for allowing us to study case 10

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DIARRHŒA DUE TO PHENOLPHTHALEIN

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THE exact diagnosis of many cases of chronic diarrhœa often remains in doubt, they may be labelled " colitis," nervous or lienteric diarrhœa, and so on Further elucidation of this ill-defined group will depend on more complete and accurate methods of investigation Routine use of fat-balance tests to assess the function of the small intestine has, for example, already shown that idiopathic steatorrhœa is the cause of many such cases (Cooke et al 1953) The technique for the fat-analysis of the stools that we now use is essentially that of van de Kamer et al (1949), by which the total fatty acids excreted are estimated daily The two following cases of diarrhœa due to phenolphthalein were discovered accidentally by this method Such a cause was quite unsuspected, and the diagnosis would otherwise have been missed

Case-reports

CASE 1 —A man, aged 30, complained of attacks of intermittent diarrhœa for nine years He said they had begun in 1943, when he started to pass frequent bloodstained stools after being captured in Germany while serving as a commando His weight fell during imprisonment from 12 st to 7 st in six months Although the diarrhœa improved it continued until his release in 1945 After treatment in a British hospital it gradually improved until 1951 Between October, 1950, and November, 1951, he had ten attacks of abdominal pain and vomiting with diarrhœa Investigation in another hospital in November, 1951, included sigmoidoscopy, which showed ulcers suggesting old amœbiasis No amœbæ were seen, nor authorities in order to have heroin back The A M A is still vigorously opposed to its return

In Germany, the heroin fatherland, it has not been used for a considerable number of years, it has practically disappeared from legal and illegal traffic alike For the time being the drug is suppressed by administrative means in anticipation of a prohibition by parliamentary Act The German Pharmacological Society and the Association of Chambers of Physicians have been consulted and have raised no objection

No better illustration of the change of opinion can be given than that of Switzerland At the 1931 conference the Swiss delegation declared that heroin was considered "indispensable for the treatment of certain diseases, in particular for certain cases of tuberculosis"[11] Twenty years later, however, Switzerland promulgated a new federal narcotic law in which the importation and manufacture of heroin, and trade in the drug, were prohibited[12] This time, as the Swiss Federal Council stated in its message, the medical profession accepted the complete prohibition of diacetylmorphine[13] Thus, although the same types of diseases have to be treated as twenty years ago, the medical profession can now do without heroin Not one voice against this regulation has been raised in the Swiss medical journals, nor, as far as I could see, in the daily press In the same message, the Swiss government said "It should not be forgotten that the problem is of primary importance from the social and health points of view, and that in taking the initiative of this decision, the country will fulfil a humanitarian task which is in keeping with its traditions" There was no addiction to heroin of any importance in Switzerland which would have required suppressive measures, and the decision may have meant some commercial disadvantage since orders from foreign countries for other pharmaceutical products may be lost when the export firms are unable to supply heroin as well This action by Switzerland therefore seems to me a particularly impressive example of international cooperation Several countries where heroin has been abolished, retain a small stock of heroin *for scientific purposes or for the use* of any doctor who feels that in a particular case its administration is indispensable

There are reasons to expect that at least one of the four countries which remain in favour of the use of heroin in medical practice will presently change its attitude

British Opinion

I have followed with attention the development of the "heroin case" in Great Britain within the last few years, and particularly what has been written in the medical journals during the last fifteen months

There is no doubt that, within the obvious limits set by public health, the doctor should be free to prescribe the drug of his choice this is one of the necessary and fundamental rights in the conscientious practice of medicine It is also clear that a drug which has been used for several decades to the satisfaction of many colleagues should not be abolished without the agreement of the medical profession On the other hand, we all have some conservative tendencies in the use of medicaments As has been mentioned, opinion has changed in Switzerland, and the same is true of Canada where it was formerly divided but where now (according to the Canadian delegate at the meeting of the Commission on Narcotic Drugs held in New York last spring) "the prohibition of heroin would not cause any difficulties in medical practice"[14]

When, on the recommendation of the British Pharmacopœia Commission,' the monograph on heroin was deleted from the 1953 edition of the *British Pharmacopœia*, there was in the medical press no relevant discussion When it became known in the House of Commons in February of last year that the Government intended to abolish the use of heroin from Jan 1, 1956 the voices raised in the important medical weeklies were much less numerous than might have been expected.

The discussion at the annual representative meeting of the British Medical Association last June[15] showed, if I understood it correctly, that there was some misunderstanding as to the reason for the proposed abolition of heroin, although Dr E A Gregg, the chairman of council, referred quite *correctly to the dreadful picture* of heroin addiction Similarly, in some of the letters to the medical press doubt has been expressed whether the disappearance of heroin from medical practice would help in the suppression of illicit traffic of that drug I am sure that it would do so, indirectly, for, as THE LANCET has said,[16] "the more countries that impose the ban the easier would be the task of those checking illicit traffic, for wherever the ban operates any heroin found is certainly illicit" But the World Health Organisation is not responsible for controlling the illicit traffic in drugs It is a medical body and the purpose of its proposal was and is simply to try to prevent the *creation of heroin addicts in medical practice*

The official figure of only 54 heroin addicts at present known in the United Kingdom is small—though it forms a fairly high proportion of the total of about 300 recognised drug addicts It is not, however, negligible if I am right in supposing that at any rate the great majority of the 54 developed their addiction through therapeutic administration of the drug Many of them, perhaps would never have become addicts if they had been given another, less dangerous, drug instead of heroin with its great euphoric potency

Reference has been made to "political pressure" from the World Health Organisation for the banning of heroin[17] As a retired medical officer of W H O, I can say that no such pressure was ever in question A resolution of the World Health Assembly, which is composed of delegates of the Member States, the overwhelming majority of whom are physicians or (if not) advised by physicians, cannot properly be characterised as "political pressure"

Alternative Drugs

What is quite clear from this correspondence is that some doctors still regard heroin as a most valuable drug for which there is no complete substitute[18] *One of them* writes[19] "It seems inescapable that many of the depreciatory remarks about heroin emanate from people who do not know its value, rather like the Russian gentleman who said whisky was not such a good drink as vodka because he had never tried it" For my part I should say just the opposite—namely, that many insist on the irreplaceability of heroin because knowledge of the alternatives is not yet widespread enough

In discussing the possibility of replacing heroin fully by less dangerous (though also addiction-producing) drugs, we have to consider both its antitussive and its analgesic action

Antitussive

Besides codeine and dionine, which are not always strong enough and can have undesirable side effects, hydrocodone (e g, 'Dicodid'), acetyldihydrocodeinone (e g, 'Acedicone'), and dihydrocodeine (e g, 'Paracodine') have been used for a long time Among the fæces and urine first with amyl alcohol and then redissolved in aqueous sodium hydroxide Phenolphthalein 65 mg given to another person was readily identified in the stool by the same procedure The extraction of rhubarb with amyl alcohol yielded solutions which became red when redissolved in sodium hydroxide, owing to chrysophanol (also present in senna), but the colour was different to the eye from that of phenolphthalein and its absorption-curve was different (fig 2)

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[11] League of Nations Conference for the Limitation of the Manufacture of Narcotic Drugs Geneva, 1931 XI 10, Records vol 1 p 142
[12] Oct 30 1951 which came in force on June 1, 1952
[13] Message of the Swiss federal council to both chambers of parliament April 9, 1951
[14] United Nations Commission on Narcotic Drugs 10th session 1955 E/CN 7/SR 268 p 4
[15] *Lancet*, 1955 i 1220
[16] *Ibid* p 1311
[17] Douthwaite A H *Brit med J* 1955 i 907
[18] See for instance *Lancet* 1955 i 1220
[19] Mulvany, J H *Brit med J* Jan 14, 1956 p 114

Discussion

Though both patients denied taking laxatives at the material times, diarrhœa ceased abruptly after they had been questioned about this The disappearance of diarrhœa coincided with the disappearance of phenolphthalein from the stools There seemed therefore to be good reason to believe that the diarrhœa was due to the phenolphthalein, and that their word could not be accepted Although in both patients there was some psychopathic background malingering could not be ruled out

Most of the average dose (60–240 mg) of phenolphthalein is excreted in the fæces because phenolphthalein is rather insoluble (von Vamossy 1902), and some of the absorbed portion is excreted in the bile Phenolphthalein excreted in the urine is in the free form (after large doses only) and conjugated as sulphate and glycuronate, mainly the former, in which state it does not turn pink on the addition of alkali unless it is first liberated by hydrolysis by boiling with hydrochloric acid It may be excreted for several days in the conjugated form after a single dose (Fantus and Dyniewicz 1937) A simple confirmatory test would therefore seem to be examination of the urine for free and conjugated phenolphthalein

In the present cases diarrhœa was possibly initiated by either a single large dose or several smaller doses but the urinary investigations were too few to indicate the dosage

It is difficult to estimate how often this type of case occurs, but in a review of 1000 consecutive gastro-intestinal cases Soper (1938) found 177 habitual takers of purgatives containing phenolphthalein, 152 of these cases had been diagnosed as catarrhal colitis Soper noted that symptoms of colitis disappeared when the offending drug was withdrawn, but he did not state in how many this sequence of events was seen Ease of detection must vary with the purgative used. In the present cases detection was made simple by the readiness with which phenolphthalein appeared when the fat-balance was being estimated by the method of van de Kamer et al (1949)

The steatorrhœa seems worth recording Phenolphthalein effects purgation primarily by preventing the absorption of water from the large or the small intestine or both, it does this directly by stimulating the motor mechanism and indirectly by increasing the intestinal secretion and thus the bulk of the contents, to which the intestine responds by increased peristalsis (Fleig 1908, Ott and Scott 1908, Blick et al 1942) The presence of excess fat in the stool indicates that the small intestine is involved in the process The fat-absorption defect may thus be the result of an acute diarrhœa due to small-intestine hurry

Summary

Two cases of diarrhœa due to self-medication with phenolphthalein are described and the methods of detection outlined

Attention is drawn to the possible importance of self-induced diarrhœa as a clinical syndrome and a further cause of steatorrhœa

We wish to thank Prof T L Hardy and Dr C F Hawkins for permission to publish cases 1 and 2 respectively, Dr H G Sammons and Mr John Taylor for help with the analyses in case 1, and the United Birmingham Hospitals Endowment Research Fund, the Mackenzie Mackinnon Trust, and the Medical Research Council for financial assistance

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Preliminary Communication

TREATMENT OF HYPOPHOSPHATASIA WITH CORTISONE

We have previously reported[1] certain metabolic abnormalities in a female infant with hypophosphatasia

The patient presented at the age of 5 months with markedly defective skeletal calcification, particularly in the metaphyseal regions The total serum calcium level was elevated, the inorganic phosphorus was normal, and the alkaline phosphatase activity was considerably below normal The patient has been under our observation for the past sixteen months, and until seven months ago the skeletal lesions were becoming more pronounced, though slow linear growth of the long bones was taking place

In June, 1955, we were led to postulate that a disturbance in adrenal cortical function was producing the skeletal lesions in this child In consequence we administered cortisone to suppress adrenal function The administration of 100 mg, and later 50 mg, of cortisone for a total period of two months did not alter the radiographic picture and produced toxic side effects However, a reduction in the serum-calcium level and an elevation of the serum-alkaline phosphatase activity to low normal values encouraged us to administer a somewhat lower dose of cortisone Within three weeks on 37 5 mg of oral cortisone daily, radiographic evidence of mineralisation appeared in the long bones at the zones of provisional calcification, and within the next seven weeks very considerable calcification took place in the metaphyseal, diaphyseal, and subperiosteal regions The bones were continuing to grow and their appearance was approaching normal During this second period of cortisone therapy the total serum-calcium and alkaline phosphatase levels again became normal

Schlesinger et al[2] have shown that spontaneous and sometimes rapid improvement can occur in hypophosphatasia, and for this reason we have withdrawn cortisone on three occasions In each instance the alkaline phosphatase activity fell to pre treatment levels within two weeks Moreover, during a two-month period without therapy we have observed a recurrence of defective calcification in the new matrix which was laid down at the growing ends of the long bones

From these findings we believe that cortisone produced a remission of many or all of the pathological features in our case of hypophosphatasia At present we do not know whether the beneficial effects of cortisone were mediated indirectly through suppression of abnormally functioning adrenal tissue or whether they were due to a direct pharmacological action on the disease process

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[1] Fraser D Yendt E R, Christie, F H E *Lancet*, 1955, i, 286

[2] Schlesinger, B, Luder, J, Bodian, M *Arch Dis Childh* 1955, 30, 265

conclusion that only about 10%—rarely up to 15%—of the served food went into the pig-bin.

Results

Tables I–V summarise briefly the results.

Calories

The energy value of the average intake (table I) compares favourably with the recommendations of the British Medical Association (1950): 2750 calories daily for men on light work and 2500 calories for women, with 80 and 73 g. of protein. Incidentally our figures are slightly lower than those cited in the last report of the Ministry of Food (1953). Thus the calorie intake of the patients appeared to be satisfactory, and their diet contained sufficient animal and total proteins.

TABLE I—AVERAGE DAILY INTAKE OF FOODS PER PATIENT *

Month (1951–52)	Calories	Protein (g.)	Fat (g.)	Carbohydrate (g.)
October	2930	77	105	430
November	2800	73	98	406
December	2725	71	94	398
January	2700	71	93	393
February	2850	73	102	408
March	2775	72	99	399
April	2800	70	102	390
May	2715	71	101	388
June	2965	87	104	420
July	2770	72	99	397
August	2825	84	98	401
September	2875	76	101	41[illegible]

* Calculated from all food delivered to the kitchen (after McCance and Widdowson 1946).

Hæmoglobin

The hæmoglobin estimations (table II), performed only as a sideline and always by the same experienced observer, show considerably lower values than those found by Olbrich (1947) for elderly people living in institutions (13.9 g. per 100 ml. for males and 13.2 g. per 100 ml. for females). It is perhaps pertinent to refer here to the many other causes of anæmia, such as chronic infection, occult bleeding due to peptic ulcer, colitis, and cirrhosis of the liver, which are so commonly found in patients with chronic ill health.

Prothrombin-time

A pilot survey of prothrombin time gave normal values (table III) (normal clotting time was standardised at 25 seconds).

Carotenoids and Vitamin A

As table IV shows, the level of blood carotenoids in our patients was less than half that of other patients from London, and the blood vitamin A level was similarly much lower. Incidentally in 1945 we found similar low carotenoid levels in a boys' institution (Moore and Leitner 1949). On the other hand when 50 Claybury patients chosen from those with the lowest carotenoid levels, were given daily a good helping of carrots or spinach (170 g.) their blood carotenoid level was trebled within forty-four days, and the blood vitamin A level rose even higher than that of controls (Leitner et al. 1954). This demonstrated clearly that in certain aspects the hospital diet was far less satisfactory than that of the general population.

TABLE II—HÆMOGLOBIN ESTIMATIONS*

Group	No. of patients	Age (yr.)		Hb	
		Range	Mean	%	g. per 100 ml.
Males	178	16–89	59.5	82.3	12.2
Females	136	21–92	62.2	72.4	10.72

* Evans photo-electric hæmoglobinometer calibrated 100% = 14.8 g. per 100 ml.

TABLE III—PROTHROMBIN-TIMES

Group	No. of patients	Mean age (yr.)	Mean prothrombin time (sec.)
Males	57	58.5	[illegible]
Females	19	61.4	[illegible]
Males and females	76	59.2	26.[illegible]

Vitamin C

The vitamin-C status (table V) seems at first sight satisfactory. The gross average of the mean time necessary for saturation with ascorbic acid in our patients, from estimations throughout the year, was a little more than four and a half days. Only one similar investigation has been made in a mental hospital (Horwitt 1942) and in this the vitamin-C status was expressed as plasma ascorbic-acid levels. The comparison of results by these two methods is not easy (Prunty and Vass 1944), but our four and a half days' mean saturation time certainly does not compare unfavourably with the low plasma ascorbic acid levels obtained by Horwitt in the U.S.A.

The purpose of the saturation test is to show whether the ascorbic acid intake has been above or below some accepted standard of intake, and, if below, how much below (Harris 1943). We agree with Harris (1942) that in persons who are on the borderline of scurvy (or have scurvy) saturation usually takes seven to ten days.

In the Claybury patients the time needed for saturation varied widely, and this is consistent with the well known seasonal variations (Harris and Olliver 1943). More than 10% of all our patients became saturated only on the seventh day of loading or later. In most cases the delayed saturation was found between March and July. A similar delay was present in our patients during three successive years. In fact of 117 men and 122 women patients examined during the "spring periods," 24 and 18 respectively fell into this group, while the corresponding numbers in 118 men and 103 women patients between July and March ("autumn period") were 2 and 4 respectively. Most of these patients with delayed saturation had obvious clinical signs of the scorbutic state. Nearly all had follicular hyperkeratosis with or without perifollicular hæmorrhages over the gluteal area,

TABLE IV—BLOOD-LEVELS OF CAROTENOIDS, VITAMIN A, AND VITAMIN E *

—	Patients in Claybury Hospital				Control patients		
	No. of patients	Mean age (yr.)	Mean stay in hospital (yr.)	Mean values	No. of patients	Mean age (yr.)	Mean values
Carotenoids (I.U. per 100 ml.)	179	59	16.5 (range 2–52)	88	220	45	219
Vitamin A (I.U. per 100 ml.)	159	„	„	118	219	„	150
Vitamin E (mg. per 100 ml.)	175	„	„	1.15	64		1.31

* Leitner et al. 1952.

TABLE V—ASCORBIC ACID SATURATION TESTS

Group	No. of patients	Mean age (yr.)	Mean body weight (lb.)	Mean stay in hospital (yr.) (range)	Mean saturation time (days)
Males	235	48.9	129.9	17.7 (2–44)	4.8
Females	22[illegible]	52.6	125.6	11.0 (2–5[illegible])	4.5

necrosis, so that unregulated tubular loss of chloride with a plasma/urine ratio of about 2/1 was not a characteristic feature The specific gravity of the urine was fixed between 1008 and 1014 in only about a quarter of the cases

Dr Taylor and Dr Reid concluded that after head injury and operation acute renal uræmic failure may be present in the absence of histological tubular necrosis, and that when there is tubular necrosis its characteristic clinical features may be absent, thus causing confusion in diagnosis

The "Buffy Coat" in Anæmia in Pregnancy

Dr H B **Goodall** described how microscopic examination of the "buffy coat" from the hæmatocrit had been applied to the investigation of anæmia in pregnancy By giving a remarkably true reflection of the type of erythropoiesis in the marrow, it had enabled the diagnosis of "pernicious anæmia of pregnancy" to be made even when the rest of the peripheral-blood picture was not characteristic During this investigation it was also found that erythrophagocytosis is not uncommon in the blood of pregnant, parturient, and puerperal patients The possibility that the ingested red cells were fœtal had in one case been confirmed by differential agglutination, but in other instances the phenomenon might merely indicate a hæmolytic process affecting the maternal erythrocytes

Pituitary Necrosis in Raised Intracranial Pressure

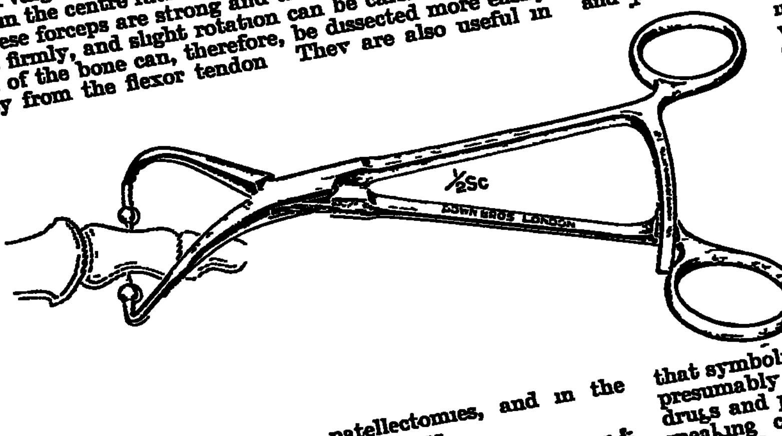
Dr Lionel **Wolman** said that among 270 patients dying with a tentorial pressure cone resulting from a unilateral space occupying lesion, 12 instances of recent necrosis of the anterior lobe of the pituitary were found The necrosis due to infarct ranged in extent from a small solitary area to as many as five discrete areas occupying most of the pars glandularis, but separated from each other and from the capsule by a zone of intact tissue The age of the infarcts, histologically assessed, could be correlated with the probable duration of tentorial coning The blood supply to the anterior lobe passing down the hypophyseal stalk was considered to be impaired by the distortion of the optic chiasma, hypothalamus, and infundibulum The mechanism which produced these infarcts seemed to be quite distinct, and Dr Wolman separated this group from postpartum necrosis of the pituitary and from various other causes

New Inventions

HALLUX FORCEPS

The forceps here portrayed are designed to hold the proximal end of the 1st phalanx in Keller's operation for hallux valgus (The diagram shows the forceps holding the bone in the centre rather than more proximally)

These forceps are strong and they grip the base of the bone firmly, and slight rotation can be carried out The base of the bone can, therefore, be dissected more easily away from the flexor tendon They are also useful in other procedures such as patellectomies, and in the operative treatment of certain fractures



The instrument is made by Messrs Down Bros and Mayer & Phelps, and I am indebted to Mr V G Carter of that firm for his help in their design and construction

W E **Tucker**
C V O , F R C S

London

Reviews of Books

Outline of Orthopædics

John Crawford **Adams**, M D , F R C S , consultant orthopædic surgeon St Mary's Hospital, London Edinburgh E & S Livingstone 1956 Pp 423 32*s* 6*d*

This is a book for students, and a very welcome one It aims to give "an easily read account of our present knowledge and thought on orthopædic surgery in the shortest possible compass consistent with accuracy, and without resorting to the style of a synopsis" Orthopædics is now so vast a subject that the success of such a book depends as much on the author's choice of what to leave out as of what to put in, and on the whole Mr Adams has done admirably

Nearly a third of the book is a general survey of orthopædic disorders, this is necessarily superficial, but it probably covers the irreducible minimum which the student must know The later chapters on specific regions contain very useful and orderly sections on history taking and physical examination, and throughout the book there is constant and admirable emphasis on the clinical side Some may wish to see more stress laid on the need always to have the other limb exposed for comparison The diagrams are clear and most of the radiographs are outstandingly good

The individual surgeon may find many points open to criticism, and he might reasonably say that some of the text particularly that dealing with the ætiology of certain conditions, is rather old fashioned—but perhaps this is good for the examinee If the student cannot feel with his hands that one trochanter is higher than the other, will the construction of Bryant's triangle really help him to decide the point? Some will be disappointed that there is so little indication of where manipulative methods of treatment may be helpful

On the whole, however, Mr Adams succeeds splendidly in his difficult task, and his book should be in steady demand by medical students

Pharmacopœia Internationalis 1955 Vol II

Geneva World Health Organisation Pp 350 35*s* Also published in French

The first volume of the first edition of the *International Pharmacopœia* was published three years ago, and it is gratifying to learn from the preface to volume II that its predecessor was given a good reception and is now in wide use The origins and scope of volume II are stated succinctly by the editorial committee

"The urgent need for the publication of volume I, which arose from the developing activities of the World Health Organization in co ordinating and unifying the health activities of its Member States, led to the omission from that volume of certain drugs concerning which rapid advances in knowledge and practice were being made Volume II supplies these omissions and deals with various forms of insulin, with tubocurarine chloride, and with the antibiotics chloramphenicol, chlortetracycline, dihydrostreptomycin, oxytetracycline, penicillin and streptomycin. Some synthetic chemical drugs of recent introduction to therapeutics are included and an attempt is made to complete the information given in volume I by including, in appropriate instances, monographs on compressed tablets, sterile injections, and tinctures"

The scope of the work is now comparable to that of the older national pharmacopœias Here and there, however, there are signs of compromise—which is perhaps as well in a work that symbolises international cooperation This attitude presumably explains the inclusion of a number of drugs and preparations which are in eclipse in English-speaking countries When, in 1955, monographs are published on bismuth subnitrate, bismuth salicylate, amidopyrine, aconite, sodium barbitone, and tincture of digitalis, some people may wonder whether national fashions have got the better of good judgment The suggested that the urge to have children was too strong ever to be suppressed, and that easy and effective birth control would simply enable a family or a population to cut its coat according to its cloth

A lively argument arose over the morality of "artificial" versus "natural" birth-control The panel agreed that birth-control should operate before, not after, conception, but disagreed on the permissible ways of preventing conception Mrs Stocks could not see the ethical difference between any methods of contraception once the motive of sexual intercourse with the deliberate intent of not having children was approved To restrict intercourse to the safe period with this intent seemed to her to be no different from mechanical or chemical contraception at the same or any other time, except that it was less effective, it was the motive behind the act that was the key to the ethical problem Lady Pakenha could not agree

Doctors were hardly mentioned The participants clearly held that the determination of national and individual policy on birth control was the province of biologists, economists, statesmen, and churchmen Mrs Stocks thought that *the doctors' job was to devise and* disseminate contraceptives

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Symposia

THE NEUROHYPOPHYSIS

In Michael Foster's textbook of physiology of 1894 it is stated that nothing is known of the function of the posterior lobe of the pituitary gland By 1898 the gland was recognised to contain a vasopressor substance Three years later Magnus and Schafer described the diuretic action of extracts, and in 1906 Dale noted their oxytocic properties These facts were recalled by Sir Henry Dale in his opening address at the Colston Symposium on the Neurohypophysis, held in Bristol on April 9–12 The subsequent communications made it clear that the posterior lobe has not only three recognised functions—the control of water excretion by the kidney, of movements of the uterus during parturition, and of the ejection of milk as a result of suckling—but also almost certainly other just-glimpsed activities In fact the posterior lobe may be one of the conductors of the endocrine orchestra of which the anterior lobe is the first violin

The posterior lobe is part of a system which in vertebrates is old in the evolutionary sense, and which also has its homologues in many invertebrates It is probably *part of a neurosecretory system*—i e, *the neurones* manufacture active substances which are normally liberated from the ends of the axons In invertebrates such as worms, crustacea, and insects a number of such systems are known, the secretions are stored in gland-like structures and are concerned with growth, metamorphosis, and reproduction amongst other functions (B Hanstrom) In higher vertebrates the active substances are made in the supraoptic and paraventricular cells of the hypothalamus and are stored in the posterior lobe of the pituitary There is evidence that the histological appearance of this hypothalamic/posterior-lobe system varies in the manner to be expected if the granular stainable material in the cells and their processes is indeed related to hormonal activity The gland is equivalent to only part of the invertebrate system, so possibly other neurosecretory areas may exist (W Bargmann) The form in which the hormones are present in the gland is not certain The full activity of vasopressin and oxytocin resides in *two* octapeptides, but before release into the circulation these are probably attached to a large protein molecule which may be a "carrier" substance Oxytocin may be removed from storage more rapidly than vasopressin, as is seen after parturition and during lactation, *also, oxytocin does not appear to* be made so early in life as vasopressin Thus the two hormones show some measure of independence (C Fromageot) and are remarkable for the apparent rate at which they can be removed from and rebuilt in the gland

Excess of vasopressin is believed by some workers *to* be a factor in causing toxæmia of pregnancy One difficulty in obtaining definite evidence for this view is that several antidiuretic substances can be extracted from blood, or formed from its proteins by enzymes natural to the body These antidiuretic substances are not made by *the posterior pituitary since they can appear* in animals from which the posterior lobe has been removed (H *Croxatto*) A *further difficulty* is that both vasopressin and oxytocin are so potent that they exist in blood in very low concentrations Their estimation is a challenging problem The obvious line of attack would be to collect blood flowing from the gland, since presumably there the hormone concentration would be at its highest Owing to the situation of the pituitary this is more easily said than done, but in cavernous sinus blood more oxytocin than vasopressin is found, which bears out the observation that oxytocin is the more *mobile of the two hormones* There *is a remarkable* interchangeability between the hormones of different and widely separate species of animals, any oxytocin so far examined has always had the same chemical structure Vasopressin is known in two forms In most animals arginine is one of its amino acids, but in the hog this is replaced by lysine Hog vasopressin has far less antidiuretic activity in dogs than arginine vasopressin, but the other activities of the two types of vasopressin are equivalent (H B van Dyke) This fact may ultimately help to unravel the chemical processes whereby the antidiuretic action is triggered The rate of disappearance from the circulation of injected vasopressin is rapid (about three minutes) Once released from the gland the *hormones are destroyed by organs* such as the kidney and liver, and *they are also* partly excreted in the urine (H Heller) The estimation of vasopressin in the urine—*usually as antidiuretic hormone* (A D H)—is one way of determining the conditions under which the endogenous hormone is liberated, thus it appears in *greatly increased* amounts in dehydration, fainting due to blood loss, and emotional disturbances A D H *appears* in the urine of those suffering from motion sickness, *but* not of those who *do not* experience motion sickness, despite swinging and other stimuli, nor is it found as a result of blackout due to acceleration (R L Noble) Thus the pattern resembles that in many experimental conditions, an increase in the osmotic pressure of the blood, excitement, and certain types of volume or pressure change of the circulation, such as may be induced by changes in posture, induce antidiuresis

There is little modern evidence that *vasopressin* ever except during anæsthesia, has the vasopressor action which gave rise to the name it still bears Accordingly it is generally believed that its power to raise blood pressure is pharmacological rather than physiological, but, in rats at least, it may be a factor in causing compensatory vasoconstriction and maintaining blood *pressure after severe* hæmorrhage (M Ginsburg)

Closely allied to the question of *polyuria* is *that of* polydipsia, since in some conditions the *former* is primary and the latter secondary, or vice versa It must be asked, therefore, whether there is a thirst centre comparable *to the hunger and satiety* centres which have been shown to exist in the hypothalamus In goats electrical stimulation of defined areas in the anterior hypothalamus induces immediate and voluminous drinking, whereas destruction *at* certain sites produces complete adipsia *As yet it is not clear whether* the drinking area is an *entity in its own right, but it is* possible to cause simul

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been discussed by Best et al,[9] Hench and Ward,[10] Thorn et al,[11] and others *It is now becoming apparent* that the adrenocortical steroids are not the only factors determining the level of the blood eosinophils on the one hand, eosinopenia could be produced in adrenalectomised mice by injecting the plasma of adrenalectomised dogs[12], on the other, "glucocorticoid" eosinopenia could be prevented by giving large doses of heparin[13] But the response of the eosinophils to the administration of adrenocortical steroids can nevertheless be used not only as a method of assay,[12] but also to define the range of biological activity of new compounds Thus, aldosterone is stated to have one third of the activity of cortisone in the eosinopenia test,[14] whereas deoxycortone is inactive[11]

It is apparent, therefore, that an explanation of corticosteroid eosinopenia might well help in understanding the mode of action of adrenocortical hormones Several possible explanations have been advanced Dustin and de Harven[15] suggest an inhibition of eosinophil production in the bone-marrow, and Gordon[16] considers that there is a direct effect on the circulating eosinophils, but recently another interesting hypothesis has been put forward by Esseller et al[17] On the strength of experiments in which the reticulo-endothelial system (R E S) was "blocked" by trypan-blue, they concluded that the "glucocorticoids" acted partly by inhibiting the release of eosinophils from the bone-marrow, and partly by increasing the extent of destruction of these cells by the R E S The possibility that the R E S was at least partly responsible had already been envisaged by previous workers (Thorn[18] for instance), and since the spleen is the most accessible part of the R E S, much attention has been paid to the relation between the spleen and the eosinophils Biggart[6] refers to several workers who believed that eosinopenia is caused by overactivity of the spleen An important observation was made by Opie[3] in 1904 when he noted that the spleen of the guineapig contained a considerable number of eosinophils, which were particularly abundant in the periphery of the pulp but were absent from the malpighian corpuscles The more eosinophils there were in the circulating blood, the more there were in the spleen When, however, the guineapig was starved for five to eight days, the number of eosinophils both in the blood and in the spleen was greatly reduced, but no decrease could be seen in the bone-marrow

Opie's observations have been largely confirmed by later workers, but their significance was not fully appreciated for some time In 1938 Klemperer[19] drew attention again to the fact that the spleen of reptiles, amphibia, and birds (he examined the flamingo) contained many eosinophils, as did the spleen of several humans of varying ages who had all died a sudden violent death, the number of eosinophils in the spleen was proportionately greater than in the circulating blood —partly owing, he thought, to selective migration from the blood stream Allen[20] and Enos et al[21] have noted the disappearance of eosinophils from the human spleen when the patient survived some catastrophe, such as coronary occlusion, for a longer period Enos et al used the presence or absence of splenic eosinophils, in conjunction with changes in the adrenals and in the liver to estimate the approximate survival time of battle casualties in Korea

This phenomenon has now been studied in greater detail by Sevitt[22] By counting the number of eosinophils in sections of the spleen of people who had either died relatively suddenly or whose spleens had been removed within 3–7 hours of an injury, he established a baseline value for eosinophils in the normal spleen The normal spleen contained many more eosinophils per unit volume than the blood, thus confirming the observations of Klemperer[19] Within 24 hours, often even within 12 hours, of severe "stress" in the form of burns, infection hepatic necrosis, &c, the number of eosinophils in the spleen fell progressively, splenic eosinopenia might then persist for several days The accuracy of Opie's observations has thus been fully borne out half a century later

By correlating the changes in the spleen with histological changes in the adrenal cortex and with the level of eosinophils in the blood, Sevitt found that splenic eosinopenia often preceded the loss of lipids from the adrenocortical cells, and that the splenic eosinopenia was in turn preceded by eosinopenia in the blood Since the blood eosinopenia can, with certain reservations be taken as a sensitive index of adrenocortical stimulation it follows that splenic eosinopenia can be similarly interpreted Splenic eosinophilia, however, does not necessarily denote adrenocortical failure Caution is clearly required in drawing conclusions about a dynamic state such as the life of the eosinophil, from a static histological picture, and Sevitt himself noted some apparent exceptions Moreover, the depletion of adrenocortical lipids, the criterion used by Sevitt to denote adrenocortical activity, although useful, is nevertheless only an indirect index As Symington et al[23] have again pointed out, what is seen is variations in the lipid and not in the steroid pattern Despite these limitations, however, it is possible to draw useful conclusions, as Sevitt and Enos et al have shown, and it is probable that splenic eosinopenia, used in conjunction with histological changes in other organs, such as the pituitary and the adrenal glands,[24] will remain of interest and value, particularly perhaps to the forensic pathologist

These observations also raise the question of whether the spleen plays an active part in the production of the eosinopenia—a question of great theoretical interest At present no conclusive answer can be given, but certain experimental and clinical findings are relevant The presence of necrotic eosinophils in the spleen suggested to Sevitt the possibility that this organ either destroyed viable eosinophils or removed degenerate cells from the circulation Degenerative changes in circulating eosinophils had in fact been described in laboratory animals as well as in man[16-5] Padawer and Gordon[25] considered that subsequent ingestion of these cells by the macrophages of the R E S was the normal mechanism of disposal Although the presence of neither the pituitary nor the adrenal glands is necessary for this *destructive process, "stress" or adrenocortical hormones* considerably enhance it An accumulation of eosinophils, under the influence of cortisone, in the spleen of mice has been recorded by Spain and Thalhimer,[26] but the finding has not been confirmed in the rat[27] The fact

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THE LANCET

LONDON SATURDAY APRIL 28 1956

Fats and Disease

SINCE the time of THUDICUM,[1] chemists have been systematically engaged in elucidating the complex structures of the lipids found in biological materials Present knowledge of the subject is summarised in simple language in a small monograph by LOVERN[2] and set out more fully in the new edition of HILDITCH's authoritative treatise[3], and these clearly show that the variety of the lipids and the specificity of their chemical constitution is second only to that of the proteins Physiologists have been slow to unravel the biological significance of these differences in chemical structure and only in the past few years have attempts been made to assess their importance in pathology, and especially to appreciate the possible rôle of different fats in the ætiology of degenerative diseases Three weeks ago SINCLAIR[4] indulged in some fascinating speculations arising from the view that the sophisticated diets of modern urban man are relatively deficient in the fatty acids linoleic and arachidonic These acids contain 2 and 4 double bonds and BURR and BURR[5] showed many years ago that they were essential in the diet of rats if growth was to be maintained and dermatitis prevented Most nutritionists have held that human diets are never significantly deficient in these acids, but SINCLAIR thinks that relative deficiencies associated with a high intake of saturated fatty acids and a low intake of vitamin B_6 may predispose to a variety of degenerative disorders including atheroma and myocardial infarction In their article this week Dr BRONTE-STEWART and his colleagues in Cape Town provide evidence, from trials on man, that the nature of the dietary fat affects the lipid content of the serum · oils in which a high proportion of the fatty acids are unsaturated—i e most vegetable oils and those derived from fish and marine mammals—consistently depress serum-cholesterol levels

As ANFINSEN[6] points out, lipids are transported in the plasma and through the extracellular fluids in three forms

1. As chylomicra which are large particles, usually visible under the microscope They are mostly composed of triglycerides, but their detailed chemical architecture remains a mystery
2. As β-lipoproteins, which contain about 25% of protein per particle and include varying proportions of cholesterol triglyceride, and phospholipid
3. As α-lipoproteins, which contain relatively more protein and less lipid and so have a higher density.

It is now established that patients who have had a recent infarction of the myocardium have a high level of β-lipoproteins in their plasma and this is associated with high levels of cholesterol[7] The fact that atheromatous plaques contain large quantities of cholesterol adds circumstantial evidence that the infarction and the disorder of fat transport in the blood are causally related Moreover, studies of the blood-clotting mechanisms have shown that some of these may be intimately connected with fat transport KORN[8][9] has demonstrated that the clearing of fat from the blood after a fatty meal is brought about by a lipoprotein lipase which is a tissue enzyme The enzyme is present in heart muscle and in adipose tissue, and its high degree of specificity of action on the triglycerides of lipoproteins and chylomicra apparently depends on the presence of heparin indeed heparin may possibly be a component prosthetic group of this enzyme ROBINSON and POOLE[10] have been studying the effect of chylomicra, present in the blood after a fatty meal, in making the blood more coagulable, and adduce evidence that this effect is specifically due to the presence in the chylomicra of ethanolamine phosphatide—a substance which resembles lecithin in chemical composition except that the choline base is replaced by ethanolamine Normally ethanolamine phosphatide probably constitutes only 5–10% of the total phospholipid in chylomicra and studies of the factors which may increase this percentage may well provide a clue to chemical processes responsible for pathological thrombosis The specific chemical properties of lipids are now beginning to be related to pathological processes

The great importance of the work of BRONTE-STEWART and his colleagues lies in the assumption that any dietary factor that raises or lowers the level of β-lipoproteins in the blood will also, by implication raise or lower the liability to myocardial infarction. In their experiments on volunteers it was shown that ingestion of beef dripping, butter, hydrogenated ground-nut oil and eggs in large numbers was followed by rises in β-lipoprotein levels in the plasma on the other hand ingestion of olive oil, ground-nut oil, sunflower-seed oil, arachis oil seal oil or pilchard oil was associated with falls in or low levels of, serum-β-lipoproteins Food fats and oils thus seem to fall into two classes whose effects on plasma-lipids are antagonistic to each other If these results are substantiated coronary-artery disease becomes in part a preventable disorder—but at the cost of a complete revolution in our present-day dietary habits The hydrogenation plants of our modern food industry may turn out to have contributed to the causation of a major disease To preserve the unsaturated fatty acids in vegetable oils and marine oils and to make these oils palatable and acceptable to industrial populations would be a herculean task for those who would seek to change people's eating habits All the principles of the modern margarine industry might have to be put into reverse However, comments on Dr SINCLAIR's hypothesis from Professor YUDKIN in our last issue and from Prof ANCEL KEYS this week indicate that systematic knowledge of the ratio of essential to total fatty acids is far from complete for single artificial dietary fats and it is almost non-existent for the total fats consumed in the diets of any large group of persons Thus more knowledge of actual fatty acids in the diets of populations is needed

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TABLE I—REPLIES BY 1361 WOMEN IN CHARGE OF CHILDREN ATTENDING CHILD WELFARE CLINICS

Question	No	% of total
Main advantage of attending		
Check on progress	1018	74·8
Expert advice	926	68
Relieve anxiety	128	9·4
Better than doctor	36	2·6
Cheap foods, &c	216	15·9
Companionship	37	2·7
Regular supervision	28	2·1
Can service be improved?		
Yes	208	15·3
No	1030	75·7
Regular attendance?		
Yes	1170	86
No	131	9·6
Reason for first attendance		
Advice of health visitor	139	10·2
Advice of hospital midwife or antenatal clinic	77	5·6
Advice of doctor	9	0·5
Advice of neighbours, friends	42	3·1
Advice of foster mother	7	1·0
First baby	219	16·1
Premature baby	19	1·4
To use service	63	4·6
Belief in child welfare service	46	3·4
Mother's advice	10	1·0
Child not progressing	19	1·4
Vaccination or immunisation	7	0·5

council's clinics at which no Ministry of Food preparations were sold No other specific statement was made by more than 10% of the respondents as a whole Very few mentioned the general practitioner—2·6% said that the clinic service was better than that given by their own doctor

To the fourth question—"*reasons for first attendance*"—the replies were few and varied 16% said they first attended on the health visitor's or midwife's advice, and another 16% because they wanted help with their first baby Otherwise only 1–2% of the respondents gave any particular reason, but many mentioned their ignorance as to how to bring up a baby

On the third question 86% of the women claimed that they attended "regularly" In reply to this question, 136 reasons were given for not attending regularly (table II)

76% of respondents stated that the service could *not* be improved, while 15% said *that it could* There was no appreciable difference in the replies from voluntary and council clinics, but, as was to be expected, criticisms were far fewer when the clinic was held in suitable premises than when a church hall was used

TABLE II—REASONS GIVEN BY 136 WOMEN FOR IRREGULAR ATTENDANCE AT CLINIC

Reason	No
Only when requiring special advice	9
Child doing well	21
Child older	38
Ill health of mother	7
Other children	12
Children of school age	3
Mother at work	6
Loss time	18
Child ill	8
Times inconvenient	7
Clinic too far away	4
First visit	1
Weighs baby at home	2
1 or first baby only	1
Total	136

Specific suggestions for improvement numbered 114 (table III), these suggestions were made, not only by the 204 respondents who said they thought improvement possible, but also by others who did not The only suggestions made by more than a handful of respondents were (*a*) more frequent sessions and longer hours ([illegible] *respondents*), (*b*) *more staff* (*20 respondents*), and (*c*) less queueing and waiting (*15 respondents*) These suggestions would all seem to amount to the same thing and while they can hardly be regarded as constructive in any detail they merit careful investigation

SAMPLE SURVEY

A random sample of households was visited by the interviewers Of the 306 respondents, 288 were mothers *10 were fathers, and 8 were grandmothers*

The sample was obtained from the records of the housing *authority, which gave the names and addresses of all the* families in these estates with young children Some [illegible] households were originally drawn as the sample, owing to the shortage of interviewers the final sample consisted of [illegible] names and addresses Of these, 8% proved impossible to contact, 7% refused to answer because they were too busy 2% had moved or were on holiday and in 3% of the cases there was no adult female or other suitable person present *This left 80% of the final sample, or 306 cases, as completed* replies

In answer to the question whether the respondent thought child-welfare clinics were a good idea, over 8[illegible]% of respondents, both in those families where there were children under 5 years old and in those where the children were now older, answered "yes," and less than 15% "no" *Of 198 mothers of children under 5* years of age who were questioned, 170 approved of child welfare clinics, and of these, 115 gave reasons (table IV)

TABLE III—SUGGESTIONS FOR IMPROVEMENT OF CHILD WELFARE SERVICE

Suggestion	No
Open more frequently longer hours	[illegible]
More friendly atmosphere, canteen teas, &c	9
More weighing scales, less delay in weighing	7
More staff	20
Warmer premises	4
Less queueing and waiting	15
Better sanitation cleanliness	5
Better seating	3
More regular visits by health visitors to homes	4
Stamps at food centres	6
Orange juice to be paid for in cash	1
Children's old clothes to be on sale	3
Compulsory X ray examination	1
Foot X ray machine	1
Specialists from children's hospitals to attend	1
Sewing classes	1
Cheap foods at each session	3
Other	[illegible]
Total	114

About 35% *of all the mothers* who responded (whether they approved of the clinics or not) thought it was worth while taking the children for expert advice Only [illegible]% said that their reason for approval was the opportunity to get a general check up on the child's progress, and that it enabled them to get the child weighed, this contrasts with the 75% of mothers *at clinics* in the first part of the investigation who gave "check on progress" as their reason for attendance 10% thought the clinic worth while for the inexperienced mother, which agrees with the 16% of attenders at the clinics who said they originally came with their first baby

Thus 86% of mothers approved of welfare centres, but when they or the father or grandmother were asked

TABLE IV—REASONS FOR APPROVAL OF CHILD WELFARE CLINIC NAMED BY 115 MOTHERS OF CHILDREN UNDER 5 YEARS

Reason	No	Reason	No
For advice	37	For welfare foods	4
For inexperienced mothers	11	Doctors are specialists	3
Weighing	10	Better than G P or hospital	9
General check up	7	Hearsay	[illegible]
For first child	7	Other	

of group practice but as a partnership of doctors with home nurses, midwives, health visitors, and home helps. "In uniting public health and general practice we could create something much greater than either separately," and the "new service for community care would become the friendly rival of the hospital service." One of its main objectives, indeed, would be to reduce calls on the hospital, and BROCKINGTON suggests that, except in emergency, it should be responsible for all admissions to hospital, which would enable it to give priority to those patients in greatest social need. The hospital would be used "as a very special instrument rather than a universal salve", and apparently the bed bureau, besides procuring hospital admissions, would arrange for the domiciliary medical teams to give most attention to the people who require it most. As the senior administrative officer, the M.O.H. would coordinate the team, operate the bed bureau, and organise health education. "The records of medical teams and the hospitals, which should be made available to him, would guide the conduct of the community service. In this work he would be immensely aided by the closer association with general practitioners." The problems of community health would be under continual discussion by the doctors themselves in the local medical committee, and BROCKINGTON sets great store by the preservation intact of this statutory body, which has maintained the professional freedom of practitioners under the executive councils and could do the same under local government. "There would be no need to alter the present machinery for payment and appointments, and for dealing with the fortunately few complaints which arise."

One can agree with Professor BROCKINGTON's diagnosis without entirely approving his plan of treatment. In support of his proposal to transfer to local authorities the work now done by executive councils he can quote Sir JOHN MAUDE,[2] who considers such a transfer desirable as a first step towards administrative integration of our tripartite N.H.S. But the other members of the Guillebaud Committee differed from Sir JOHN about this and thought the suggestion would not commend itself to the medical profession.[3] If there were really such a thing as the "general-practitioner service" to which BROCKINGTON refers, the arguments for merging it with the public-health service might be unassailable; but in point of *fact* general practice is conducted not by a service but by individual doctors who have made a personal *contract* with individual patients. The provision of this kind of personal care is perhaps the main contribution of general practice to a world increasingly full of impersonal organisations; and we must beware of even so innocent and rational-sounding a measure as the "coördination of medical teams" should it seem likely to impair the family doctor's sense of personal responsibility. But if there is danger in the organisation of general practice by anyone other than the practitioner himself, it is also true that his patients nowadays often need the help of the various kinds of skilled people whom the M.O.H. can alone provide; and the Society of Medical Officers of Health is obviously right when it says that "medicine in the future can gain immeasurably from a collaboration between the general pract Medical Officer of Health and his staff". can collaboration be further promoted? eral-practice review committee of the British Medical Association thought that "until there is at least a closer and more general administrative liaison between these two branches of the Service some difficulties and misunderstandings will persist".[5] The majority of the Guillebaud Committee, on the other hand, was not persuaded that changes in the machinery were the answer. "The problem of cooperation," they said, "has been tackled more effectively in some areas than in others and ... where integration is lacking the reasons are probably to be found more in the personalities concerned than in any defects of organisation."[3] What is now needed most, we should guess, is more practical demonstrations of what can be done to improve the quality of general practice and public health by the collaboration of people who really care about both. This is the kind of invaluable experiment which does not necessarily depend either on health centres or on more money, but on vision and good feeling. Even a small merger by those keen enough to achieve it under difficulties could be more instructive than a large one imposed by statute; and we hope that Professor BROCKINGTON's arguments will lead many to think further about their local possibilities.

Treatment of Coronary Thrombosis

SCOTTISH *institutions* die hard, and the threat to the future of the *Edinburgh Medical Journal*, first published in 1805, has happily been averted by a union with the *Glasgow Medical Journal* to form a new *Scottish Medical Journal*. It is supported by the four Scottish medical schools and it is appearing monthly. The Edinburgh and Glasgow medical journals have in their day recorded the work and opinions of a great many famous men. In carrying on this task, the editor of the *Scottish Medical Journal*, Dr ALEXANDER BROWN, and his colleagues have the good wishes of doctors in many parts of the world.

The first article in the first issue of the new journal deals with a subject that has engaged the attention of more than one Scottish medical school—the anticoagulant treatment of acute myocardial infarction. GILCHRIST and TULLOCH,[6] of Edinburgh, set out their views after seven years' experience which has convinced them that efficiently controlled treatment with oral anticoagulants has halved the death-rate during the first six weeks of hospital care; and they also believe that the incidence of thrombo-embolic episodes over the same period has been reduced even more. They point out the difficulties of obtaining really comparable treated and untreated groups of patients; but when proper precautions are taken and alternate cases are allotted to treated and untreated groups there is, they say, "a uniformity in the findings which is difficult to challenge". The mortality in a control untreated group from four large investigations works *out* at 29·2%, and the combined mortality for treated patients comes to 16·6%. In the seven years, times, may be largely to blame Undoubtedly there are considerable differences between clinics in respect of progress in health education and the use of visual aids and group discussions This inquiry has, perhaps, suggested some of the ways in which improvements may be possible

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[2] Report of the Committee of Enquiry into the Cost of the National Health Service. Cmd 9663. H.M. Stationery Office, 1956, p. 285.

[3] *Ibid*, p. 60.

[4] Functions of the Medical Officer of Health. Published by the Society of Medical Officers of Health, Tavistock House South, Tavistock Square, London W.C.1.

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I acknowledge my indebtedness to Mr T David, formerly statistician to the London County Council, for the statistical analysis, and for planning and organising the sample survey My thanks are due also to the medical students of Guy's Hospital who showed such keen interest and gave such valuable assistance, and to Dr J Crammond, late of the London School of Hygiene and Tropical Medicine, and to the health visitors and staff of Division 7, L C C I am grateful to Dr J A Scott, medical officer of health, London County Council, for his interest

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Neonatal Mortality

In 1955 the neonatal-mortality rate in England and Wales was 17 3 per 1000 related live births[1] This is the lowest annual rate recorded in this country, the previous record low rate was 17 7 in 1953 and 1954

Parliament

QUESTION TIME

Maternity Services Inquiry

Replying to a question, Miss PATRICIA HORNSBY SMITH, parliamentary secretary to the Ministry of Health, said that the members of the committee set up to inquire into the maternity services were as follows

The Earl of Cranbrook (chairman) Mr G F Gibberd, F R C O G, Mr H J Malkin F R C O G Dr A Beauchamp, Dr W V Howells, Dr J Forest Smith, Dr Jean Mackintosh Miss M Williams, S R N Miss V Shand S R N Lady Pakenham, Mrs Geoffrey Wilson, and Sir Basil Gibson

Chairmen of Health Executive Councils

Replying to a question, Miss HORNSBY SMITH, said that in England and Wales on March 31, 1956, 27 members of the medical profession were chairmen of local health executive councils

Mr CHARLES ROYLE Does not the Minister regard the appointment of doctors as chairmen of executive councils as a rather undesirable practice ? No education committee would appoint a teacher to the chairmanship Will not the Minister make representations to executive councils along these lines ?—Miss HORNSBY SMITH There are 13 lay and 12 professional members on such a committee and they elect their own chairman If in special circumstances they believe that one of their number who happens to be a doctor, or for that matter a dentist, is outstanding for the chairmanship, they are free to elect him Mr ROYLE Does that reply alter the principle ?—Miss HORNSBY SMITH I think that the answer in many cases is that if lay members attended as regularly as some professional members, they would be in a better position to vote for someone else

Mr ARTHUR BLENKINSOP Does not the hon Lady appreciate that there is a point of substance here at which she might well look again ? At the outset of the scheme the Minister appointed the chairmen That was then changed I think that it is highly desirable that executive committees should consider whether they should not appoint a lay person in many cases, unless there are exceptional reasons for the contrary Miss HORNSBY SMITH The vast majority, of course, are lay chairmen

Young Children in Remand Homes

Replying to questions Mr W F DEEDES, under secretary of State for the Home Department, said that the statistics of admissions to remand homes were not kept in a form which would enable him to say how many children were detained in such homes for truancy, and how many were detained between the ages of 8 and 11 years These homes were used mainly for the temporary accommodation of children pending their appearance in court, or while arrangements were made for admission to an approved school

Miss JOAN VICKERS Does the Minister consider it desirable to keep children from truancy in remand homes ? Last year in the home in which I am interested there were 55 such children Will the Minister try to ensure that the young children between the ages of 8 and 11 are not included in the remand homes with the older children who have committed many offences for which they have been brought before the courts on a number of occasions ?—Mr DEEDES The second point in the supplementary question will certainly be borne in mind

Prison Hospital Accommodation

Mr FRANK ALLAUN asked the Home Secretary if he was aware that in the 88 year old Strangeways Gaol, Manchester prisoners confined to bed for long periods with tuberculosis had to be kept in the ordinary prison cells, and that in the hospital of this gaol, holding 1100 prisoners, there were only four one bed rooms for men who must be isolated because of mental or physical sickness, and what steps he proposed to take to provide adequate hospital accommodation in the prison —Mr DEEDES replied The hospital at this prison is admittedly inadequate, but the only solution is to build a new one This will involve substantial reconstruction of other parts of the prison, and will be undertaken when funds can be made available The present accommodation in the hospital proper comprises three wards with thirty two beds and four single rooms In addition there is an extension of the hospital on one of the prison landings of twelve rooms These are not ordinary cells but properly equipped hospital rooms with large windows At present there are 5 cases of tuberculosis in the rooms on the prison landing These cases are under the treatment of a tuberculosis specialist from outside, and are under the immediate supervision of the medical officers and hospital staff of the prison

Mr ALLAUN Would the Minister agree that, whatever a man's prison sentence, his health should not be damaged by it ? Will the Minister therefore ensure that sufficient hospital beds are made available at Strangeways for tuberculous patients and others with serious illness, particularly since as I saw last week, it is extremely difficult for prison officers to carry sick prisoners into the four single bedrooms, two of them padded cells, because of the narrowness of these archaic corridors ?—Mr DEEDES The difficulty is a structural one The grounds of Manchester Prison are completely built up and to build a new hospital it will be necessary to remove a branch of the prison to a site adjacent to the prison, which is now available

Air-pollution Measurements

Replying to a question, Mr J R BEVINS, as representing the Lord President of the Council, said that, under the aegis of the fuel research station of the Department of Scientific and Industrial Research, about 3000 measurements of air pollution were made throughout the day and night during the fog, from Jan 4 to 7 last, in the areas of London, Birmingham Leeds, Manchester, Salford, and Sheffield In the London area the averages of the results for pollution by smoke and by sulphur dioxide were about three quarters of the average during the severe fog of December, 1952, and between three and four times the concentrations in normal winter weather The average concentrations of smoke and sulphur dioxide in the other areas of investigation were about the same as in the London area The concentrations of carbon monoxide in the several areas were not much greater than in normal winter weather The observations were made by more than 500 volunteers, including many from the Civil Defence Corps

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[1] Registrar General's Weekly Return for the week ended April 14, 1956 H M Stationery Office Pp 20 1s 3d

Annotations

A NEW MUSCLE RELAXANT

MUSCLE relaxants have so far been used mainly in anæsthesia, where a short duration of action and the need for parenteral injection are not disadvantages A new preparation, zoxazolamine (2 amino 5-chlorobenzoxazole), is active by mouth and has a relatively long action [1-3] It seems to act centrally and to depress the subcortical and spinal polysynaptic pathways It has essentially no action on the monosynaptic arcs, motor nerves, myoneural junctions, or striated muscle Zoxazolamine thus resembles mephenesin rather than the peripheral neuromuscular blocking agents such as tubocurarine or suxamethonium Given to animals, zoxazolamine can produce a flaccid paralysis lasting several hours without a significant change in consciousness, blood-pressure, or respiration Repeated daily, oral doses in rats and dogs produced no cumulative or toxic effects[3]

This new drug has been used in the treatment of spasticity caused by neurological disorders, and some preliminary reports have appeared [4-6] Many conditions have been studied and the results have been variable Clinical observation and electromyographic studies have confirmed that zoxazolamine is a mild muscle relaxant in some spastic states, but its action varies from case to case and even in the same patient at different times Unfortunately reduction of spasticity does not necessarily mean improved voluntary control of limb movements, and it is often achieved at the expense of reduced muscle strength A diminution in muscle tone has been noted, chiefly in patients with spinal cord lesions, and this has been associated with abolition of uncontrolled mass flexion movements and considerable subjective improvement The benefit in patients with spasticity of cortical origin and in paralysis agitans has been inconsistent and indefinite The drug has also been used in patients with muscular stiffness and aching due to rheumatic diseases [7] Side-effects have not been unduly troublesome with doses up to 0 5 g four times a day The commonest have been nausea, vomiting, epigastric discomfort, and dizziness Fever and transient skin rashes have occasionally been noted No blood abnormalities have been recorded

There is no doubt that zoxazolamine has pharmacological properties as a muscle relaxant that make it suitable for long continued administration Chief amongst these are its effectiveness by mouth, duration of action, and low toxicity But the benefit to be achieved by its use in spastic and rheumatic states cannot yet be assessed Zoxazolamine can do nothing to the underlying disease, but by reducing spasticity it may aid physiotherapy and reablement Conditions such as disseminated sclerosis and rheumatoid arthritis are notoriously variable in their course and this makes assessment of the drug difficult, and it seems itself to be rather irregular in its behaviour after oral doses No further conclusions can be drawn on the evidence we have seen so far

MENTAL DEFECT AND HYPSARRHYTHMIA

Prof R S Illingworth [8] has described twelve children in whom severe dementia and convulsive disorders developed rapidly between the ages of four and eight months The striking feature was an abrupt change in social responsiveness, motor and manipulative development were retained to a surprising degree The initial fits were of various types, but later most of the children had salaam attacks Neurological examination revealed no physical signs, but electro-encephalography showed the pattern which Gibbs et al [9] call hypsarrhythmia This pattern consists in bursts of very-high voltage slow waves, together with spike activity which shifts rapidly from site to site the abnormalities are diffuse, and normal patches of record are not found The hypsarrhythmic pattern is common in young epileptic children with massive damage involving the subcortical masses

The disorder described by Illingworth may be less unusual than is supposed because the characteristic epilepsy does not last long, nor does the E E G pattern endure One of the most striking features of the epilepsies of childhood is their sensitivity to maturation Ounsted [10] has shown that the phenotypic expression of the convulsive genotype is rapidly overcome by maturation, and he has pointed out that this is true also of those epilepsies which go with hypsarrhythmia, and which stem from gross anatomical lesions "The anatomical lesions remain, the mental defect remains, the characteristic E E G pattern lingers on, but the fits themselves are inhibited by quite a slight advance in maturity"

Research into the epileptic diseases of childhood has been much neglected in this country Children of the type that Professor Illingworth has described formerly died young They now live on, a burden of hopeless pity to those who care for them

TUBERCULOSIS AFTER PARTIAL GASTRECTOMY

DURING the past decade all too many defects have been attributed to partial gastrectomy, and it seemed that an increased incidence of pulmonary tuberculosis might prove to be one Forsgren [11] was one of the first to show that after partial gastrectomy patients were more liable to pulmonary tuberculosis and that the risk to them might be ten times greater than to the general population In this country Pulvertaft,[12] reviewing Visick's cases, found that of 23 intercurrent deaths from a total of 632 patients 7 had been due to pulmonary tuberculosis and 1 to tuberculous meningitis Bruce Pearson [13] reported 11 cases, 4 of which were found in a follow up of 93 patients, the other 7 were seen as cases of tuberculosis and could not therefore be measured as a proportion of a definite gastrectomy series Tanner [14] was unable to demonstrate a prevalence of more than 5 per 1000 in the 403 patients submitted to mass radiography two to seven years after partial gastrectomy—the rate to be expected in the general public But there were also 2 deaths from tuberculosis and 8 patients under treatment in the 611 consecutive cases of gastrectomy from whom the 403 were selected for mass radiography These last figures are rather against Tanner's view that there is no increased proneness to tuberculosis Allison [15] described 21 cases but gave no indication as to incidence, he suggested that "the faulty assimilation of nourishment together with metabolic imbalance brought about by chemical factors in the body, so lower a person's resistance that tuberculosis is a likely sequel in a certain proportion of patients" Thorn et al [16] have now been more specific They followed 955 patients in whom an X-ray examination of the chest was performed as a routine before partial gastrectomy, and they found that 6 3% had evidence of pulmonary tuberculosis before operation In an admirable

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Letters to the Editor

DEFICIENCY OF ESSENTIAL FATTY ACIDS

SIR,—Dr H. M. Sinclair's engaging essay in your issue of April 7 merits more detailed comment that I can supply at this distance from my home laboratory. However, some notes may help your readers appraise the situation in a field unduly beset with conflicting claims and feverish competition.

Besides solving the coronary heart disease problem, Sinclair disposes of lung cancer and leukæmia for good measure, but these latter minor problems I shall leave to others. The central issue of Sinclair's speculations is atherogenesis and the regulation of the concentration of cholesterol in the blood. His thesis is that our present plight in Britain, the United States, and other countries where coronary heart disease is so alarmingly frequent, is due to dietary deficiency of the "essential" fatty acids—linoleic and arachidonic—largely ascribable to the evils of hydrogenation and deficiencies of vitamin E and pyridoxine.

While I join in deploring the increasing use of hydrogenation and many other methods of "improving" our natural foods, I think it can be shown that even in the United States hydrogenated fats are only a small fraction of the total fat consumption, which provides, moreover, a per-capita intake of linoleic acid at least as high as that of many populations, as in Japan, who suffer relatively little coronary heart disease.

The idea that a deficiency of essential fatty acids (E.F.A.) in the diet may be related to atherogenesis is not new; it was suggested a dozen years ago by Dr George Burr, then at the University of Minnesota, and it has been discussed in the United States for several years, notably by another Minnesotan, Dr Ralph Holman of our Hormel Institute. Last year Dr B. Bronte Stewart developed this thesis in South Africa and recently he discussed the question in England. It is well known that animals fed diets extremely deficient in E.F.A.—and such diets are not easy to prepare—often have increased amounts of cholesterol in the liver, but I know of no demonstration of the production of atheroma in these experiments. Moreover, I am unaware of any evidence that a low intake of E.F.A. in the human diet will, by itself, produce either hypercholesteræmia or atherosclerosis. Indeed, even the possibility of E.F.A. deficiency in adults is debated vigorously, and there is not yet unanimity of opinion about the situation among infants, where the best case for the essentiality of E.F.A. has been made—by another former Minnesotan, Dr Arild Hansen.

It is easy to show, as we have been doing for half a dozen years in controlled experiments on man, that merely changing the proportion of calories supplied by ordinary food fats (not hydrogenated) in modern Western type diets promptly results in corresponding changes in the serum cholesterol concentration, even when the intake of calories, cholesterol, proteins, and vitamins is constant. In such experiments, each lasting from four to six months and involving twenty or more men, isocaloric substitution of carbohydrates (sugar, potatoes, and bread) for a large part of the dietary fats involves a sharp reduction in the intake of E.F.A.—and the serum-cholesterol falls and stays down so long as the low fat diet is continued. But when the reverse substitution is made, using lard, butterfat, cottonseed oil, olive oil, coconut oil, or mixed food fats, the serum cholesterol concentration rises. Supplements of vitamin E or of protein (casein) do not alter the result.

These several food fats do not produce quantitatively the same degree of elevation of the serum cholesterol, and a few fats, which do not bulk large in our diets, may have no cholesterogenic effect. We have observed this as well as others, including Kinsell in California, Ahrens in New York, and, recently, Bronte Stewart in South Africa. But the point for the present discussion is that with most of the common food fats an increase in the fat consumption produces an elevation of the serum-cholesterol at the same time the intake of E.F.A. is being increased.

Now it is conceivable that E.F.A. may have no cholesterogenic effect and that large amounts of E.F.A. may counter some of the cholesterogenic tendency of fats containing no E.F.A. But even if this were true it seems unreasonable to ascribe to a "deficiency" of E.F.A. the result of increasing the total intake of fats *and* of E.F.A. (for none of our ordinary food fats are devoid of E.F.A.). I believe it is difficult to ignore the impressive body of evidence leading to the conclusion that our present prevalence of hypercholesteræmia and coronary heart disease would be much altered if we simply reduced the general level of fat in the diet, and that we got into our present plight, at least in part, because we have adopted an increasingly fat rich diet. We are rapidly approaching the time when we must ask seriously what is to be done about it. Dr Sinclair's argument obviously suggests that we solve the coronary problem, without retreating from our high-fat diet, by taking a daily swig of linoleic acid and a few vitamin pills. I wonder whether this is a responsible answer to a serious question.

There are other difficulties with Sinclair's thesis and the facts he adduces in its support. He indicates that Eskimos and "some Norwegians" consume high fat diets but escape atherosclerosis because they eat marine foods in a diet unsullied by the chemist. He forgets that recently[1] he argued persuasively that Eskimos have long since ceased to eat high fat diets. And he seems to be unaware that large amounts of hydrogenated whale oil are eaten in Norway, which is, nevertheless, not among the countries eating the largest amount of fats. (The latter are, more or less in order of decreasing fat as a percentage of total calories: U.S.A., Finland, Australia, New Zealand, Denmark, Canada.) In any case no one knows what may be the freedom, if any, of the Eskimo from atherosclerosis; it *is* known that *coronary-heart disease is a serious problem* in Norway.

Sinclair makes a good deal of cholesterol esters as the villain in the piece. Two facts should give pause here. In the first place, pathologists tell us that the cholesterol esters, as a fraction of the total, are relatively low in newly formed atheroma and that the percentage of esters rises with the age of the lesion. And in the second place, the proportion of ester to free cholesterol in the serum is substantially the same in hypercholesteræmia as in normal or hypocholesteræmia, in coronary patients and in their clinically healthy controls. Further, the amount of cholesterol esters in the liver and in the skin may be interesting, but I do not know that anyone has suggested this as a measure of atherosclerosis.

I feel strongly that a most important clue to the solution of the coronary problem is in the differing frequency of the disease in populations that differ in their modes of life. And I am pleased to learn that Dr Sinclair is agreeing with me that the diet plays a most significant rôle in this. Consideration of the dietary fat and the rôle of cholesterol in the blood transport of this (as lipoprotein) seems to resolve the striking contrasts in the burden of coronary heart disease we have observed in comparing Americans and some Europeans with southern Italians, Sardinians, African Bantu, and Japanese on their native diets. Climate is not the answer, and no more than a minor role can be given to the frequency of obesity in the several populations. If serum cholesterol is the criterion, dietary fat far outweighs differences in physical activity as a causative factor, and we observe that there are plenty of physically inactive men in Italy and here in Japan but,

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[1] *Proc. nutr. Soc.* 1953, 12, 69.

Special Articles

HEROIN
FROM THE INTERNATIONAL POINT OF VIEW*

P O WOLFF
M A M.D Ph D
HONORARY PROFESSOR OF PHARMACOLOGY IN THE FREIE UNIVERSITÄT OF BERLIN, LATE CHIEF OF THE ADDICTION-PRODUCING DRUGS SECTION OF W H O

DIACETYLMORPHINE or heroin the "wonder drug" of 1898 has been recognised, for several decades as the most dangerous of the opiates—because it so easily induces addiction and because the treatment of that addiction can be so difficult and even perilous

International Action

As long ago as 1923 the Opium Advisory Committee f the League of Nations proposed an inquiry into the uppression of this drug[1] but the main effort began with the conference which in 1931 prepared the Convention for the Limitation of the Manufacture of Narcotic Drugs. A group of four experts including the late Prof W E Dixon and myself, were asked a number of questions[2] In reply we said that heroin was particularly likely to produce addiction because it is "more powerful than morphine and its dose is smaller." because "heroin euphoria is much more pronounced than that of morphine" and because troublesome "constipation does not occur in the addict" We regarded heroin as at least equal to morphine in its pain-relieving action, and as more effective in the relief of cough But we also stated that its addiction-producing properties from the medical point of view, are "much worse" than those of other addiction-producing drugs; we referred to the rapidity with which addiction is induced, to the change in personality with weakening of all the higher mental faculties and to the difficulty of cure We added that we had "evidence that a large majority of the eminent pharmacologists and physicians in various countries are definitely opposed to the employment of heroin in medical practice," and when asked whether the drug is indispensable we said that it "can be entirely dispensed with"

At this 1931 conference unanimity concerning abolition of the production, sale, and medical administration of heroin could not be reached; but Article 10 of the convention contained certain special restrictions on the export of heroin[3]—thus indicating the necessity for particular supervision—and the delegates passed the following recommendation[4]

> The Conference Recognising the highly dangerous character of diacetylmorphine as a drug of addiction and the possibility in most if not all, cases of replacing it by other drugs of a less dangerous character Recommends that each Government should examine in conjunction with the medical profession the possibility of abolishing or restricting its use and should communicate the results of such examination to the Secretary General of the League of Nations"

Year by year the Permanent Central Opium Board and the Drug Supervisory Body (which started their work under the League of Nations and continue it under the United Nations) collected and analysed information on the licit movement of the drug—manufacture, import export, consumption, &c[5] and in 1949[6] and 1950[7] the World Health Organisation's Expert Committee on Drugs Liable to Produce Addiction expressed alarm because production was still on the increase

On the basis of the work of the expert committee and the information collected by the Director-General of W H O, the Sixth World Health Assembly in May, 1953 unanimously expressed its conviction that heroin is not irreplaceable for medical practice, and that the abolition of legally produced heroin by member States would facilitate the struggle against its illicit use It accordingly recommended first, that campaigns should be undertaken to convince doctors and governments that heroin is not irreplaceable, and secondly that member States which had not already done so should cease to produce or import the drug[8]

Having received these recommendations and also one from the Commission on Narcotic Drugs the Economic and Social Council, on July 12 1954 urged all governments to prohibit the manufacture import and export of heroin and asked the Secretary-General of the United Nations to communicate this resolution to all Governments for such action as they might be in a position to take[9]

The Response

How has the situation developed? Whereas in 1949 only 25 countries and 27 non self governing territories had given up the use of heroin in medical practice of the 20 States which have still supplied estimates for heroin consumption in 1956 only 4—leaving aside for the time being the United Kingdom—are not prepared to renounce its use As the World Health Organisation counts some 80 members it is clear that the overwhelming majority of governments are in favour of abolition The Expert Committee on Drugs Liable to Produce Addiction concluded last October that more and more physicians throughout the world are finding it possible to substitute less dangerous drugs for diacetylmorphine in accordance with the committee's repeatedly expressed view on the replaceability of this dangerous addicting agent"[10]

In the U S.A, where the import export and production of heroin has been forbidden since 1924 the government maintains a small stock in case a doctor wants to administer this drug to a patient, but during all these years there have been only two requests for its use In fact the American Medical Association never opposed the ban on heroin rather they recommended its abandonment before the Act was passed In 1917 the Council on Pharmacy and Chemistry of the A M.A deleted heroin from its *Handbook of Useful Drugs*, saying

The Council holds that heroin has no advantage over morphine that it shares every disadvantage of morphine, and that, on the whole its introduction has been harmful, in that it furnished a specious means for avoiding the well founded popular fears of morphine by substituting another habit-forming drug, In 1920 the house of delegates of the A.M.A resolved "That heroin be eliminated from all medical preparations, that it should not be administered, prescribed or dispensed, and that the importation manufacture and sale of heroin should be prohibited in the United States"[10a]

Although there have been sporadic expressions of dissent in the years since there has never been any concerted move to restore the drug Furthermore, contrary to rumours which apparently have spread in London there has been not one request to the American

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* From a paper read in part to the Society for the Study of Addiction on Feb 21, 1956 Author's present address is 1 rue de Contamines Geneva

[1] League of Nations advisory committee on traffic in opium 5th session Geneva 1923 Minutes p 121 (Doc C 418 M 184 1923 XI)

[2] League of Nations Conference for the Limitation of the Manufacture of Narcotic Drugs Geneva, 1931 XI 10, Records vol 2 p 120 (annex 7)

[3] Text of the 1931 Convention as amended by Protocol of 1946 United Nations (1947 XI 6) Article 10

[4] *Ibid* p 41

[5] Drug Supervisory Body Report (E/DSB/13) Geneva 1955 XI 3

[6] *Off Rec Wld Hlth Org* 1949 19 31

[7] *Tech Rep Wld Hlth Org* 1950 21 5

[8] *Off Rec Wld Hlth Org* 1953 48 22

[9] United Nations Economic & Social Council E/Resolution (XVIII)/S 1954 resolution G

[10] *Tech Rep Wld Hlth Org* 1956 102 5

[10a] *J Amer med Ass* 1920, 74 1324

ECZEMA VACCINATUM

SIR,—I discussed the pathogenesis of Kaposi's varicelliform eruption in a paper[1] which described the virological investigation of 9 cases, including 3 of those reported by Sommerville and his colleagues[2] which were referred to by Dr Napier (Jan 14) in comment on the paper by Dr de Salles Gomes and his colleagues (Dec 17)

Since then I have isolated herpes simplex virus from another 16 cases, including children involved in two outbreaks in dermatological wards, but have not encountered another case of eczema vaccinatum In my experience, in mild cases the eruption may remain confined to areas of skin which *have been* affected by eczema, though it may spread beyond the boundaries of dermatitis active at the time The disease may develop on a basis of unbroken skin in a phase of remission of eczema[1 3]—an observation which supports the hæmatogenous as against the surface contamination theory of pathogenesis Although secondary enlargement is to be expected in lymph-glands draining areas of skin affected by the pustular eruption, another point in favour of the hæmatogenous theory is that adenopathy may not only precede the appearance of the rash but may even be the presenting feature[2 4] The general pattern of the classical case with its incubation period and sudden onset of febrile illness before the development of the eruption resembles that of other virus exanthemata in which viræmia is recognised as an essential stage

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N R GRIST

A NEW WAY OF TREATING FLAT FEET IN CHILDREN

SIR,—Mr Sayle Creer has long been an authority on this subject and consequently I read his letter (April 7) with interest and great care—perhaps more carefully than he read my article (Feb 11) For though we agree in broad principle and in objective, it is a personal preference that condemns my conception of "flat feet," and there is no foundation for his claim that the device of Mr Charlesworth[5] is similar to my heelseat

He finds with me, though he states the case differently, that if the forefoot is left prone one can correct flat foot by inverting the heel Mr Charlesworth effects this by an admirable heel and arch support which extends to the heads of the metatarsals It is an effective appliance, but to me it has the disadvantage of all arch supports in that it takes weight under the longitudinal arch The original virtue of the *heelseat* is that it produces an arch while the foot bears weight only on the normal three points—viz , the heel and the heads of the first and fifth metatarsals In this way the child's foot is allowed to develop normally, and once the arch is formed the foot is strong Moreover it is important that the floor of the heelseat should not be wedged, for it is the weight of the child on the level surface which keeps the walls of the heelseat vertical and therefore maintains the position of the heel If the base is wedged the heel slides to the outer side and produces the problem that Mr Charlesworth discusses

Mr Sayle Creer has quite reasonably given himself the prerogative of limiting the definition of "flat foot" to the foot with a flattened longitudinal arch To all other flat feet in children he refers as pronated, everted, or valgus feet With many other orthopædic surgeons, I am content to say that the feet are flat in any child that walks on the inner borders of the feet—whether the condition is due to a congenitally flat longitudinal arch or acquired by "everting the heel of an otherwise normal mobile foot" The difference is one of terminology only, and perhaps for the purpose of the article, which is to describe a method of treatment, Mr Sayle Creer will permit both types to be called flat feet—for if he will try the heelseat with persistence he will find that even the congenital flat foot can so be treated

Judging by the number of queries that I have had from many parts of the world, I am happy and relieved to find that the "heelseat" seems to be regarded as both original and useful by orthopædic surgeons, pædiatricians, and specialists in physical medicine

Newlands Cape,
South Africa

ARTHUR J HELFET

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[1] Grist N R *Glasg med J* 1953 34, 1
[2] Sommerville J , Napier, W , Dick A *Brit J Derm* 1951 63 203
[3] Snyder W *Arch Derm Syph Chicago* 1951, 64 789
[4] McLachlan A D Gillespie M *Brit J Derm* 1936, 48 337
[5] Charlesworth F Chiropodial Orthopædics Edinburgh, 1951

MYASTHENIA GRAVIS

SIR,—Your editorial last week reveals a remarkable failure to understand the significance of recent investigations into the defect of neuromuscular transmission in this disorder Thus, you state that the conclusions we drew from the response of myasthenics to the administration of decamethonium are opposed to those of Grob et al ,[1] which are based on the effect of the intra-arterial injection of acetylcholine It is with the intention of correcting the confusion of thought that must have been created that we should like to re-state the generally accepted interpretation of these results

Decamethonium (C10) has been shown to act at the myoneural junction in a similar manner to acetylcholine[2] but with the difference that because it is not rapidly destroyed by cholinesterase its actions can be readily studied Using this drug in cases of myasthenia we demonstrated[3] that, whereas in normal subjects it acted as a pure depolariser, in myasthenics it acted by *a fleeting depolarisation followed* by a more prolonged non-depolarisation (i e , curare like) block—the so called dual response The fact that in myasthenics, as in normal subjects, decamethonium can be recovered unchanged from the urine indicated that the abnormal response to *decamethonium* was a *property* of the motor end plate. On the basis of these results we put forward at that time the theory that the underlying mechanism at fault in myasthenia was an alteration in the manner in which the motor end plate responded to acetylcholine or one of its breakdown products

In 1955 Grob and his colleagues reported the results of their work using the intra arterial injection of acetylcholine In essence, they found that the response in both normal and myasthenic subjects was in two phases first, a prompt depression of muscle activity (depolarisation block) which lasted about a minute and was soon followed by a secondary depression which persisted for thirty to sixty minutes This late depression was found to be identical with the effect of the injection of choline—a breakdown product of acetylcholine Furthermore they noted that, whereas acetylcholine produced a rapid depolarisation block in both normal and myasthenic patients, choline gave rise to a depolarisation block in normal subjects and a non-depolarisation block in myasthenics In other words, the injection of acetylcholine in myasthenic subjects gives rise to a "dual block"—i e , a fleeting depolarisation block (due to acetylcholine) followed by a *prolonged non* depolarisation block (due to choline) On the basis of their results these authors were unable to say "whether this abnormal response was due to a change in the myasthenic end plate itself, or to the formation in myasthenic patients of a product of choline which is a *competitive* blocking agent" However, after comparing our results with their own they conclude "this suggests that the myasthenic end plate may react abnormally " ecently developed drugs are methadone ('Physeptone' inctus) pholcodine (which has to be classed with codeine) and dextromethorphan (known as 'Romilar') This last product is said to have no side effects, to maintain its efficiency over long periods, and not to induce addiction t does not prevent the coughing up of phlegm or alter the consistence of the sputum[20] and it has no analgesic action It seems to be much used in the U S A

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[1] Grob D Johns, R J Harvey A M *Amer J Med* 1955, 19 684
[2] Burns B D Paton W D M *J Physiol* 1951 115, 41
[3] Churchill Davidson H C , Richardson A T *Ibid* 1953 122,

Analgesic

Besides the more familiar drugs such as hydromorphinone ('Dilaudid') pethidine methadone ('Physeptone'), and phenadoxone ('Heptalgin') I should like to draw attention to levorphan (which in Great Britain formerly had the generic name methorphinan and is known as 'Dromoran') In chemical structure it is closely related to morphine but its analgesic effect lasts longer than that of morphine, and consequently much longer than that of heroin—which is helpful in the treatment of chronic pain Its side-effects, including constipation, are less than those of morphine and it also has the advantage of being effective when given by mouth Other synthetic analgesics including pethidine and methadone are also effective by mouth but often cause nausea and vomiting whereas levorphan is generally well tolerated (For many years I have insisted on the need to avoid injection of analgesics, so as not to create a "needle habit" in potential addicts[21]) At the New York session of the Commission of Narcotic Drugs in April–May, 1955 Dr N B Eddy, chief of the section on analgesics, National Institutes of Health Bethesda, Maryland described levorphan as "as effective an analgesic as heroin" and "as effective as morphine in the treatment of cancer[21 22] Therefore it seems to me that this drug deserves more consideration

Conclusion

On a question so complex as that of heroin, there cannot easily be unanimity Personally I have always recognised that in Great Britain there will be no danger to the public if heroin remains available in the future under the same conditions as at present The British physicians and surgeons—probably mainly the older generation—who are accustomed to administering heroin after surgical operations or otherwise know how to manage this dangerous tool On the other hand reliable sources have repeatedly confirmed to me that the younger colleagues, as in other European countries, do not use heroin any more Moreover, when it is given to relieve cough, there is no great risk that heroin addicts will drink whole bottles of linctus or cough mixture for what they really look for is an intravenous injection or a chance to sniff their drug If there were not a world-wide danger and an urgent request for coöperation by all countries—including the very few which have not yet agreed to abolish heroin—nobody would bother about the availability of heroin in the U K

On the other hand, the history of therapeutics has shown repeatedly that remedies held in great esteem are rejected when better ones have been found I believe that heroin is now ripe for replacement

I am hoping therefore that the British medical profession will agree to give up the use of this drug I ask those doctors favouring heroin to re examine the truly practical possibility of relieving extreme human pain without it As the Home Secretary said last July, there is certainly a "need for an international effort to mitigate the heroin problem"[23] and in my view it is important to continue the efficient international coöperation over addiction-producing drugs which was started under the League of Nations To abolish the use of heroin even where there is no national necessity to do so would be a valuable contribution to the idea that nations should work together for the common good.

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[20] See for instance Tünnerhoff F K Schwabe H K *Klin Wschr* 1955, 33 576

[21] Wolff P O *Bull Hlth Org L o N* 1945–46 12 513 and earlier

[22] Eddy N B United Nations Commission on Narcotic Drugs 10th session 1955 E CN 7/SR 273 p 8 See also Wolff P O *Ibid* 9th session, 1954 E 2606 E CN 7 283 p 15

[23] *Brit med J* 1955 ii 199

NUTRITIONAL STUDIES IN A MENTAL HOSPITAL

Z A LEITNER
M.D Berlin
L.R.C.P.E

I C CHURCH
M.R.C.S D.P.M
LATE PSYCHIATRIC REGISTRAR

From Claybury Hospital Woodford Green Essex

In general hospitals the turnover of patients is quick, and during their stay their diet often depends on their ailment In mental hospitals, on the other hand because patients stay longer the diet is often even more important We briefly describe here some of the results of nutritional studies at Claybury Hospital

Material and Methods

During the greater part of this investigation patients in Claybury Hospital numbered about 2300, with a preponderance of females About half of the women and a third of the men patients were over 65 years of age The admission-rate is about 1300 per annum and each year just over 1000 patients are discharged

The main part of our investigation was carried out between May 1951, and May 1954 As far as possible we selected ambulant cases in apparently good physical health (all patients with recent feverish illnesses were excluded) who had been inpatients continuously for at least two years but we also included some newly admitted patients

A general nutritional survey was carried out during the whole time of the study including control of nutritional intake and body weight and a larger proportion of the ambulant hospital population was regularly examined with special regard to symptoms and signs of early deficiency states (Leitner 1948)

All laboratory investigations were carried out after careful study of the case history and after clinical examination In many cases estimations were made of total carotenoids vitamin-A reserves (Kimble 1939), vitamin E reserves (Quaife and Harris 1944), vitamin-C reserves (Harris and Abbasy 1937), hæmoglobin level (Evans photo-electric hæmoglobinometer) prothrombin-time (Quick 1936) and petechiae counts (Hess and Fish 1914)

The greater part of this investigation was carried out while essential foods were still rationed At first we were tempted to follow the conventional quantitative food survey—to weigh and analyse sample meals and to deduct the remains on the plate But apart from the fact that the resources were insufficient for such an investigation we felt that it would only have specious precision and singling out one particular ward for weighing and analysing meals for, say, a week might yield a misleading result as regards the hospital in general or even the selected ward in another week

We therefore adopted a seemingly less exact method. The amount of food delivered to the central kitchen was carefully measured Milk, meat and fish (fresh and made up) and cheese were always weighed again before being sent to the wards Fat and sugar were rationed, bread and potatoes were plentiful Marmalade jam, green vegetables, and fruit were scarce and they were therefore fully consumed. Our practice was to instruct repeatedly the ward sisters in several wards simultaneously to collect and preserve daily all the waste from the plates for consecutive periods of two to three weeks The remains were carefully measured We came to the by any method, due to the difficulties of following up a series of cases in a moving population, and determining the frequency of complications which may arise many years after the original injury. Further, the disease is primarily a disease of the active years of life and does not occur in children or in the elderly, with the sole exception of epileptics. It is, therefore, not so easy to collect even in a busy clinic an adequate number of cases, for an essential part of the investigation must be a study of the mode of treatment employed in the reduction of the dislocation. This you do not mention.

It is quite probable that in the past Kocher's manœuvre as carried out under insufficient anæsthesia contributed a considerable quota of cases. Since the use of thiopentone and modern relaxants, the ease with which a shoulder can be reduced has been so increased that no additional capsular damage need be done in the majority of cases, and it is my impression that the frequency of recurrence is slowly declining.

Even if one could collect a group of cases in the appropriate age group reduced by the same method and treated by alternate fixation and immobilisation, one's conscience might trouble one, as one cannot suggest a method of investigation which would not impose a hardship on the patient. Even if the recurrence-rate were as high as one in ten, an individual, faced with the choice of three weeks' immobilisation to avoid that risk and the certainty that if a recurrence did occur a straightforward operation followed by three weeks' immobilisation and perhaps a further three weeks' rehabilitation would cure it, would prefer to take his chances of having to be immobilised later rather than immediately.

I have tried to make some comparisons between the methods in the past and have been defeated by the almost instinctive resistance of the patient who when he feels his shoulder is right will take it out of his sling and use it regardless of the advice given to him. In my experience one of the surest ways of losing a young patient from the clinic is to immobilise him for three weeks after a dislocation. Only a few of the more phlegmatic patients will continue under this régime without raising question.

This is an interesting clinical problem but it appears it will only be solved by central registration of dislocated shoulders, uniformly treated, and a further registration of their recurrence. When the answer would appear to warrant this, I have no doubt somebody will find the necessary energy to answer your questions.

London, W.1. J. G. BONNIN.

BREAST CHANGES IN FIBROCYSTIC DISEASE OF THE PANCREAS

SIR,—Dr. Stroud and Dr. Heppleston, in their letter last week, illustrate the changes in the breast of a 6-week-old child, and conclude that the enlargement was due to "mastitis neonatorum." With this conclusion I entirely agree (though I dislike the term), and there is no need to invoke "mucoviscidosis" or antibiotic therapy.

I have examined histologically the breasts of many infants aged 0–6 months, and in a series of 115 such infants the histological picture illustrated by Stroud and Heppleston was found 15 times. This series was collected in the immediate post-war period, when the only antibiotic in general use was penicillin. This particular histological picture was not the only one responsible for enlargement, although the largest breasts usually showed this appearance. A secretory picture similar to that of the lactating adult breast is also common, and may produce quite considerable enlargement. The cystic change illustrated by Stroud and Heppleston may be a stage in the normal progression from the secretory to the resting (prepubertal) phase, since it was found to have a maximal incidence about the 2nd–3rd week, while the secretory picture was found maximally in the first 7 days of life. The prepubertal picture does not appear until the 4th week onwards. The oldest case showing the cystic appearance was 18 weeks. Pictures intermediate between secretory and cystic, and between cystic and prepubertal, were found in 14 of the 115 cases.

I have no details of antibiotic therapy in these cases, but there appeared to be no correlation with any particular disease process, and the sex-distribution was equal—8 boys and 7 girls.

Department of Pathology,
Bedford General Hospital. J. C. VALENTINE.

⁂ Through a misunderstanding of ours it was stated in the letter by Dr. Stroud and Dr. Heppleston that case 1 was one of Dr. Jolly's three cases (*Lancet*, 1955, ii, 1136). In fact cases 1 and 2 were seen in the department of child health of the Welsh National School of Medicine.—ED. L.

FLUIDS FOR INTRAVENOUS INFUSION

SIR,—For some years I have used a brand of vacuum-bottled sterile intravenous infusion fluids and have felt able to rely on these products. Within six months I have found a faulty vacuum in four bottles (isotonic saline three, isotonic saline/glucose one) and in one of each the pressure was a little above atmospheric. Apparently complaints of this kind are rare. I have heard of no similar experiences. Every bottle that I use I open myself, and I wonder if such faults are missed when nurses open bottles and either do not appreciate or do not report the defect.

The method of bottling used by this firm makes it hard to see how the vacuum can fail, and no one so far has given a satisfactory explanation of the origin of a pressure above atmospheric (around 10 cm. of water in one case). I would urge anæsthetists and others setting up "drips" to watch for a lack of bubbling (or for frank squirting out of the solution) when the caps are removed from such bottles, and not merely to discard them but to report such events to the makers.

London, E.11. JOHN BARNARD.

HÆMATEMESIS

SIR,—I feel that Dr. Bancroft's comments (April 14) on my article (April 7) are reasonable and should be answered.

The method was used, in the first instance, only on the very late case of hæmatemesis—the case that almost invariably ended fatally. It was used, therefore, as an alternative to emergency gastrectomy and was found to give better results. The only remaining procedure for obtaining direct controls would have been to retain 50% of these patients on a régime which had already failed.

The most positive proof I can offer is the way in which patients who have failed to respond to routine medical treatment cease bleeding after the administration of adrenaline and 'Stypven.' This statement can be confirmed or discredited only by an actual trial of the method. We found at an early stage in the investigation that gastric lavage and stypven in doses of up to 20 ml. were often ineffective, yet when repeated in conjunction with adrenaline the bleeding was immediately controlled—though, as I discovered subsequently, only temporarily in a proportion of cases of true "surgical" hæmatemesis.

The main point at issue for the physician and surgeon alike is to recognise "surgical" hæmatemesis early. As a rule patients are transferred to a surgical ward for one of two reasons: either because they comply with the standard criteria for surgery, or because they will not respond to medical treatment after the most patient and persistent endeavour. In the first instance we observed a 30% error in diagnosis, and in the second the results of operation were not encouraging.

on the outer side of the arm, or in the clavicular region gingivitis and stomatitis with hypertrophy of the dental papillæ were common, but boggy, tender, bleeding gums were restricted to the few patients who had retained their teeth. Petechial hæmorrhages and ecchymoses, with extensive bluish purplish discoloration on the lower legs and ankles and occasionally on the forearms, were found in a group of male patients working in the gardens, but in none of the women who had a prevalently sitting occupation.

Petechiæ counts were performed in 278 of these 460 patients. As has been repeatedly noted (Medical Research Council 1953) the number of petechiæ was unrelated to the vitamin-C reserves.

Discussion

The nutrition of the patients in the hospital was such that gross deficiency states were uncommon. This is the more gratifying because several patients included in the investigation had been continuously at Claybury for fifty years or more. Only just over a decade ago, as many as 10 cases of frank pellagra were found in a few months in a single mental hospital (Hardwick 1943) (and 5 further cases were found within the same period in two general hospitals [Rimington and Leitner 1945]). During the present investigation only 3 cases of fully developed pellagra were seen, and 1 of these was in a newly admitted patient with florid scurvy.

While clinically obvious gross deficiency states were infrequent, detailed study disclosed "latent" deficiencies. In old people mucous membrane changes are usually more or less readily detected, but skin changes, gingivitis in edentulous elderly patients with neglected mouths and with atrophied and shrunken structures are more difficult to recognise, and they may occasionally be absent even in cases of advanced deficiency. Although the food was calorically sufficient and contained enough protein the nutritional status in carotenoids, vitamin A, and vitamin C was unsatisfactorily low, leading in many cases to deficiency states which were bound to impair general health.

The urgent need to reorganise catering arrangements in mental hospitals has been emphasised by Harington Hawes (1955). We support this timely proposal, although we are not convinced that fulfilment of such a programme would necessarily eliminate all the inadequacies found in the diet of our patients. We suggest that meanwhile the present scanty supply of vegetables (such as carrots, spinach, kale, leeks, turnip greens, tomatoes) should be enhanced by increasing the yield of the farms attached to many mental hospitals, and that each patient should be given routinely one 50 mg tablet of ascorbic acid daily. We are aware that 30 mg of ascorbic acid in the daily food provides a satisfactory margin of safety for the average person (League of Nations 1938). In mental hospitals, however, some patients, although without obvious symptoms and signs of disease, and perhaps only with occasionally recurrent mild attacks of diarrhœa or steatorrhœa, are far below average health, and may even be unable to absorb or to utilise nutrients satisfactorily (Boscott and Cooke 1954).

In our opinion any addition to the diet of a purified vitamin (such as ascorbic acid) is at best only a poor substitute for proper food, and this practice ought to be eliminated as soon as circumstances permit. But in our large mental hospitals we are faced with an unusually difficult and complex problem: many of the kitchens are old and their equipment obsolete, the financial allowance for food is limited, and often the patients, because of their mental disorder, are uncoöperative. Our studies have convinced us that even the most appetising diet will not be taken by some of these patients at all regularly without supervision and coaxing by specially allocated nursing staff. This supervision seems to be out of the question while the prevailing shortage of personnel persists, even if the financial resources were forthcoming. Addition of ascorbic acid seems to be the only immediate remedy for the poor vitamin-C intake in our mental hospitals.

Summary

A three year nutritional survey in a mental hospital, combined with laboratory investigations, showed that the food provided sufficient calories, but the patients' hæmoglobin levels and their nutriture in carotenoids, vitamin A, and vitamin C were low.

It is suggested that all patients in mental hospitals should be given 50 mg of ascorbic acid daily, and that the supply of leafy green vegetables should be substantially increased.

We thank Dr J S Harris, physician superintendent, for his help throughout this investigation, and Dr George Graham for suggesting it. Our thanks are also due to the medical, nursing, and laboratory staff of the hospital, especially Mr F C Radley and Mr G W Swyers. The part of the work dealing with vitamins A and E was planned and carried out in constant cooperation with Dr T Moore and Dr I M Sharman, to whom we are particularly grateful for much advice and help. Dr Margaret Briggs, of Roche Products Ltd, kindly supplied the ascorbic acid needed in the investigation.

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FAMILY PLANNING ASSOCIATION

On April 17 the Family Planning Association held in London an "Any Questions" meeting on Parenthood by Choice or by Chance, with Mr C H Rolfe, of the *New Statesman*, in the chair, and Mr J D Bronowski, PH D, Mr Julian Huxley, D SC, F R S, Lady Pakenham (who represented a Roman Catholic viewpoint), Canon Mervyn Stockwood, and Mrs Mary Stocks answering the questions.

The questions ranged widely from the need for birth-control to combat the effects of death control to the ethical dilemma of the stage at which "interference" with reproduction might be allowed to take place. Most members of the panel thought that some degree of birth-control was inevitably necessary in all parts of the world, because the world population was increasing more rapidly than any possible increase in food production. With one exception they agreed that the discovery of a simple and infallible contraceptive would not be a danger to the human race. Dr Bronowski thought that the birth rate depended on the economic stability of a country, and the ability of parents to have a feeling of fulfilment in their children; when they felt able to do so they tended to have enough or more than enough children to maintain the population. Canon Stockwood

Obituary

ARTHUR HUGH McCULLOCH EATON

M B Belf, F R C S E

Mr Eaton, senior surgeon to the Tyrone County Hospital, died on April 1 The youngest son of the late Mr and Mrs J C Eaton, Altnagelvin, Derry, he was educated at Foyle College and Queen's University, Belfast He served in the 1914–18 war as a surgeon probationer in the R N V R, and on demobilisation he returned to Queen's and graduated with honours in 1922 After taking the F R C S E in 1927, he was appointed as surgeon in the Tyrone County Hospital, Omagh As a Territorial officer he was called up in 1939 and he served in Boulogne until the evacuation in 1940 At the request of the Tyrone hospital committee he was recalled to his civilian post before the end of the war He served as president of the Northern Ireland branch of the British Medical Association, of the Omagh branch of the British Legion, of the Tyrone branch of the British Red Cross Society, and of the Tyrone County Club He was also a member of the Tyrone Grand Jury

W S B writes "Mr Eaton was one of the small band of surgeons working in country hospitals in Ulster who bore the brunt of surgery for so many years until the introduction of the health service The fact that his hospital, from small beginnings, became one of the largest Ulster hospitals outside Belfast was due to his continued efforts, administrative skill, and personality, as well as his surgical skill He was a quiet and unassuming man who, despite the early age at which he took up his appointment, foresaw the possibilities of development in country-hospital work Such were his sound common sense and the confidence that he inspired in his hospital committees that he was able to build up outpatient clinic organisations and form a nucleus of a fuller medical staff, so that when the consultant and specialist services were introduced at the beginning of the health scheme his hospital was already well developed and able to take a full part from the beginning in the new era In a provincial hospital the tie between staff, patients, and local people is, in many ways, stronger than in any of the larger city institutions, and Mr Eaton will be sincerely missed, not only as their medical adviser but as their friend, by the great numbers of people who had benefited from his ceaseless hard work and kindly advice"

He leaves a widow and two daughters

ALEXANDER GIBSON

M A, M B Edin, F R C S E

Dr Gibson, consulting orthopædic surgeon to the Winnipeg General Hospital, whose death at the age of 73 has been announced, was one of the many distinguished emigrants whom Scotland has sent to Canada

He was born in Edinburgh and educated at the university there, graduating M B with first-class honours in 1908, and winning the Vans Dunlop and Ettles scholarships He held a university demonstratorship in anatomy before he came to London to continue his surgical and anatomical studies After taking the F R C S in 1913 he was appointed to the chair of anatomy in the University of Manitoba During the first world war he served with the Canadian Forces in India and Egypt, and during the late war he was in charge of a Canadian Red Cross unit in Scotland He was a past president of the Canadian Orthopædic Association and surgeon in charge of orthopædics at Winnipeg Military Hospital

An English colleague who had met him at meetings in London and Quebec writes

"For many years Alexander Gibson's name has been familiar to orthopædic surgeons in this country from his publications, particularly in connection with the surgery of the hip joint, though for many of the younger generation the first chance of the pleasure of his personal acquaintance came on his visit to Britain in 1952 for the Orthopædic Meeting of the English speaking World—and it was a real pleasure He had the gift of friendship His writings were lucid and he was a most admirable speaker, forceful and clear in the best Scottish tradition With our colleagues in Canada we share a sense of deep loss of a fine surgeon and a fine man"

Diary of the Week

APRIL 29 TO MAY 5

Monday, 30th

Manchester Medical Society
4 30 P M (Medical School, Manchester University) Prof A Stampar (Zagreb) Public Health in Underdeveloped Countries

Postgraduate Medical School of London, Ducane Road, W 12
4 P M Dr Ian Gilliland Exophthalmos

Tuesday, 1st

Royal College of Physicians of London, Pall Mall East, S W 1
5 P M Dr A H Douthwaite *Pitfalls in Medicine* (First of two Croonian lectures)

University of London
5 30 P M (London School of Hygiene and Tropical Medicine Keppel Street, W C 1) Prof L Kreyberg (Oslo) Ætiology and Occurrence of Lung Cancer in the light of Pathological Anatomy

Royal Society of Medicine, 1, Wimpole Street, W 1
8 30 P M *Orthopædics* Sir Reginald Watson Jones Treatment of Bone and Joint Injuries—past, present, and future (Presidential address)

Institute of Child Health
5 P M (Hospital for Sick Children, Great Ormond Street, W C 1) Dr J H Ebbs (Toronto) Changes in the Stature of School children in the last Half Century

Wednesday, 2nd

University of London
5 P M (St Thomas's Hospital Medical School S E 1) Dr S W Kuffler (Johns Hopkins Hospital) Patterns of Innervation and Contraction in Striated Muscle

Royal Society of Medicine
4 30 P M *Proctology* Dr Neil Swinton Mr Bryan Brooke, Mr Stanley Aylett Ileostomy
5 15 P M *History of Medicine* Dr Douglas Guthrie The Hippocratic Oath

Postgraduate Medical School of London
2 P M Dr Henry Haber *Clefts, Vesicles, and Bullæ*

Institute of Diseases of the Chest Brompton, S W 3
5 P M Dr Paul Wood Physiological Classification of Pulmonary Hypertension

Manchester Medical Society
4 15 P M Dr T F Fox The Medical Empire

Medico Chirurgical Society of Edinburgh
8 30 P M (Royal College of Surgeons, 18, Nicolson Street, Edinburgh) Dr I W B Grant Chronic Bronchitis

Thursday, 3rd

Royal College of Physicians of London
5 P M Dr Douthwaite Pitfalls in Medicine (Second of two *Croonian lectures*)

Institute of Laryngology and Otology, 330, Gray's Inn Road W C 1
11 30 A M Dr H C Andersen (Denmark) Diagnosis and Screening of Deaf Children in Denmark
12 15 P.M Dr Ole Bentzen (Denmark) Auditory Training in Denmark

St John's Hospital Dermatological Society, 5, Lisle Street W C 2
5 P M Prof W Montagna (Rhode Island) Reappraisal of the Phenomenon of Hair Growth

Honyman Gillespie Lecture
5 P M (University New Buildings, Teviot Place, Edinburgh) Dr J H Ebbs Medical Services in the Canadian Arctic

University of St Andrews
5 P M (Queen's College Small's Wynd, Dundee) Dr A A Douglas Birth Injuries of the Eye with particular reference to Congenital Squint

Friday, 4th

University of London
5 P M (St Bartholomew's Hospital Medical College, E C 1) Prof F A Simeone (Western Reserve University) Post denervation Supersensitivity

Royal Society of Medicine
10 30 A M *Otology* Dr Hans Engstrom (Sweden) The Organs of Corti Dr Jan Wersäll (Sweden) The Structure of the Vestibular Sensory Apparatus
2 30 P M *Laryngology* Mr K Harrison Dr *Helen* Russell Ectopic Salivary Adenomata Mr F C W *Capps* Prof George Cunningham Four Cases of Identical Tumour Associated with the Infra orbital Nerve and its Sheath
5 30 P M *Anæsthetics* Dr Robert Virtue (Colorado) *Dihydroxy* corticosteroids of Blood during Anæsthesia and Surgery

Postgraduate Medical School of London
10 A M Dr Edward Hamlin, jun (Harvard University) Thyroid Biopsies

St Mary's Hospital Medical School *Paddington*, W 2
5 P M Mr G W Williams Uterine Abnormalities and their Clinical Significance

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A memorial service for the late Sir Morton Smart is to be held at the Savoy Chapel, London, on Wednesday, May 2, at 11 45 A M neous drinking and antidiuresis owing to the overlap the two regions (B Andersson) Pituitary resistant abetes insipidus is known to occur in man, and for this ason among others it is of interest to discover just where the kidney A D H acts to cause water reabsorption the rat, urine can be collected by micropuncture from me parts of the distal convolution of individual ephrons In all instances, whatever the concentration f the bladder urine, tubular urine from the first part of he distal convolution is hypotonic to plasma , the final rocess of concentration must therefore occur distal to his point—i e , in the latter part of the distal convolution nd perhaps also in the collecting duct (H Wirz) A imilarly hypotonic urine is found in the distal con-olution of certain anurans which lack a thin segment of he loop of Henle, though the kidneys of these animals an concentrate under the influence of posterior-pituitary ormone (W H Sawyer) There is agreement, then, that oncentration of urine due to vasopressin occurs in the istal part of the distal convoluted tubule, but it is ncertain whether concentration also takes place in the ollecting ducts

It is in relation to oxytocin that a number of new ossibilities are appearing So far this substance is nown to affect uterine activity and milk ejection only, et it is released from the gland in many circumstances nd in greater quantities than is vasopressin , and it is ormally present in the gland in equal amounts in males nd females It can be shown that the administration f oxytocin by itself may greatly affect blood-flow hrough, and sodium excretion by, the kidney and that hen both vasopressor and oxytocic hormones are given together, in proportions in which they may well be released in the body, they have effects on sodium excretion not seen when either is given alone (F P Brooks and M Pickford) It is unknown whether the action on the kidney is direct or dependent on an intermediary For functional as well as anatomical reasons it is possible that oxytocin has some action on the anterior pituitary For instance, although after parturition total absence of suckling allows mammary involution, in rats, if some mammæ are used and some are not, the unused ones do not involute, suggesting that suckling is the stimulus to a reflex release of prolactin which maintains alike the used and unused glands Moreover, if oxytocin is given to rats with diabetes insipidus (i e , with no endogenously produced oxytocin) the expected mammary involution does not occur Suckling undoubtedly stimulates the posterior lobe to release oxytocin, which may then reach the anterior lobe via capillary vascular connections (A T Cowie and S J Folley)

Another important function of oxytocin may be in aiding the transport of spermatozoa from vagina to fallopian tubes The known rate of movement of spermatozoa cannot account for the speed with which they reach the upper end of the genital tract , and there is good evidence for increased uterine movement in response to coitus Now comes the observation of an apparent increase in the oxytocin content of jugular blood in cows when the uterus is stimulated manually Taken in conjunction with the known action of oxytocin on the uterus, this suggests that coitus causes a reflex liberation of oxytocin which in turn induces coordinate movements of the uterus so that the sperms are swept rapidly along the genital tract towards the ovum (R J Fitzpatrick) Confirmation of this will depend on a suitable method for extracting oxytocin from blood, and there is some hope that a satisfactory method may be perfected Already there are indications that oxytocin is present in jugular blood in greater amounts than vasopressin This would agree with van Dyke's findings on the content of cavernous sinus blood, and with the many functional studies which point to an always greater liberation of oxytocin than of vasopressin (J M Walker)

Finally, if the posterior lobe can influence the anterior lobe it may indirectly affect the adrenal cortex Some link between them is suggested by the fact that certain types of stress known to affect the adrenal cortex at the same time deplete the posterior lobe of its A D H Further, hydrocortisone seems either to speed the replenishment of the posterior lobe or to inhibit the release of A D H In adrenalectomised rats hydrocortisone also protects the posterior lobe against the severe effects of dehydration (R Gaunt, J J Chart, and C W Lloyd) There are still other pointers to the interaction of the posterior lobe and the adrenal cortex Thus, an adrenalectomised rat with diabetes insipidus has an almost normal plasma-sodium concentration, but if the animal is treated with A D H its plasma sodium falls , and a rat with diabetes insipidus shows less loss of ascorbic acid from its adrenal cortex in response to a stress stimulus than does a normal animal, but it can be made to react in an almost normal manner by preliminary treatment with vasopressor posterior lobe extract (I Chester Jones)

This is an impressive list of activities for a gland whose function was unknown sixty years ago Recent work suggests that the list is by no means complete

The whole symposium with the discussions is to be published as a book

Occasional Survey

EOSINOPHILS AND THE SPLEEN

SINCE Paul Ehrlich described the eosinophil leucocyte as a distinct structure, a great deal has been written about this mysterious cell. The literature on this subject shows a curious shift of emphasis earlier authors—for example, Ringoen [1]—were largely concerned with the phenomenon of eosinophilia , more recently, since the introduction of corticotrophin and the adrenocortical steroids, it has been eosinopenia which has attracted more attention But some of the crucial facts about eosinopenia came to light fairly early in the story of the eosinophil Ehrlich himself was already aware of the considerable decrease in the number of the blood eosinophils in "ordinary polynuclear leucocytosis," [2] an observation which led many European hæmatologists to regard the subsequent eosinophilia as the *Morgenröte* of impending recovery from an acute infection

As early as 1904, Opie [3] described eosinopenia in the guineapig under experimental conditions which today would be interpreted as "stress", and Schwarz,[4] in 1914, and Borchard,[5] in 1928, drew attention to the role of the suprarenal glands in the production of eosinopenia Yet it was easier to interpret eosinophilia in terms of a "positive chemotaxis" than to explain eosinopenia by "negative chemotaxis" [2], and later work on the rôle of the eosinophil in protein metabolism [6] offered a key to the understanding of eosinophilia, whereas the observations on eosinopenia remained largely unrelated Only when Dalton and Selye [7] noted eosinopenia in "non specific stress" could these isolated observations be drawn together, and this finally led to the introduction of the Thorn test [8] (the response of the blood eosinophil level to the administration of corticotrophin) The limitations and the usefulness of this test have recently would otherwise exist between the top of the fireplace and the top of the guard

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[1] Ringoen A R *In* Downey's Handbook of Hæmatology London 1938 vol 1, p 179

[2] Ehrlich P Lazarus A Histology of the Blood, Normal and Pathological London 1900 , p 144

[3] Opie E L *Amer J med Sci* 1904, 127 217, 988

[4] Schwarz E Quoted by Best et al (ref 9)

[5] Borchard W Quoted by Dustin and de Harven (ref 15)

[6] Biggart J H *J Path Bact* 1932, 35, 799

[7] Dalton A Selye, H *Folia Hæmatol* 1939, 62, 397

[8] Thorn G W , Forsham P H , Prunty, F T , Hills A G *J Amer med Ass* 1948, 137, 1005

As an alternative to drilling holes in the fireplace, the studs can be mounted on rubber suction discs The sucker shown in the accompanying inset figure was hardly good enough, but a better type which is used in a range of car accessories would give a very firm grip on a tiled fireplace Perhaps some manufacturer of fireguards would consider this idea

A BROCHURE FOR THE YOUNG PATIENT

Few attempts are made to write intelligently on medical matters for young people of 12–16 Perhaps this is because they are a between age group, neither child nor adult, for whom the English language does not even provide a generic name "girl" is acceptable but "boy" barely so, and the two together fail to convey the right impression, "teenager" is American and in this country is applied generally to the 15 or 16 plus We glance at them charily, and as subjects for medical literature pass them by with scarce a thought They are not often seriously ill, they are seldom grouped together in a ward, and they have little opportunity of asking for information Should we therefore ignore them? It has been the custom to do so, and custom is hard to change A brochure designed especially to appeal to them pulls us up with a jerk

The Brentwood Hospital Management Committee, with the help of the National Association for the Prevention of Tuberculosis, have produced such a brochure[1] for young patients who come to Highwood Hospital for treatment While the result is not beyond criticism, the intention is unreservedly commendable, the effort to win the young patient's cooperation is a compliment that he will appreciate The main objects of treatment are explained and the idea behind such treatment is conveyed—albeit rather haltingly There is a tendency to talk down ("Be a good patient and do what the doctors and nurses tell you") which may arouse resentment, too much is in the abstract (as in the differentiation between "negative distractions" and "positive distractions"), and there is rather too much of the phraseology applicable to adult tuberculous patients ("tearing your nerves to pieces with worry," "imposing a kind of self discipline," "you have to be a social and a human being") But the basic idea is fundamentally right

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University of London

Dr E M Glaser has been appointed to the readership in physiology at the London Hospital Medical College

Dr Glaser qualified from the University of Bratislava in 1939 and soon afterwards came to this country where he became a voluntary research assistant at the British Postgraduate Medical School During his service with the R A M C in the late war he received the M C In 1949 he took the PH D Camb and in 1951 the M R C P As a member of the Medical Research Council's scientific staff he worked in the department of experimental medicine at Cambridge Since he took up his present post as King Edward professor of physiology in the University of Malaya he has continued to serve on the M R C 's standing advisory committee on climatic physiology His published work includes papers on the prevention of motion sickness

Dr J C Sloper has been appointed to the readership in morbid anatomy at Charing Cross Hospital Medical School

Dr Sloper received his medical education at Cambridge and the London Hospital After qualifying in 19[illegible] he held house appointments at the London He took the M R C P in 1946 and the M D Camb in 1951 He is at present senior lecturer in morbid anatomy at the London He has published papers on Addison's disease mycotic infections, and idiopathic diffuse muscular hypertrophy of the œsophagus

The title of professor of genetics has been conferred on Dr Hans Gruneberg, F R S, in respect of his post at University College

National University of Ireland

The degree of M D has been awarded to Edward O'Sullivan

University of Dublin

On Thursday, May 10, at 5 P M, at Trinity College, Dr Moacyr E Alvaro, president of the Pan American Congress of Ophthalmology, will deliver the Montgomery lecture, when his subject will be the Ætiology and Pathogeny of Uveitis Prof A St G Huggett will give the John Mallet Purser lecture on Thursday, May 24, at 4 30 P M, when he will speak on Environment of the Fœtus and Postnatal Health

Royal Society of Medicine

The gold medal of this society has been awarded to Sir Gordon Gordon Taylor

Empire Rheumatism Council

On Tuesday, May 1, at 2 45 P M the annual general meeting of this council is to be held at St James's Palace, London, when the Duke of Gloucester will preside

Medical Association for the Prevention of War

This association is holding a conference at 90, Buckingham Palace Road, London, S W 1, on Saturday, May 5, at 2 30 P M, on the Development of the Child in the Cold War Era

International College of Surgeons

This college has awarded its scholarship ($3000) to Mr W F Walker, of Dundee, who is to spend a year with Professor Moore, of Boston, working on surgical metabolic problems

Navy Medical Compassionate Fund

A meeting of the subscribers of this fund will be held at 2 30 P M on May 4 at the Medical Department of the Navy, Queen Anne's Mansions, St James's Park, London S W 1, to elect six directors

Royal Appointment

Surgeon Captain E B Pollard, R N, has been appointed an honorary surgeon to the Queen in succession to Surgeon Captain J V Williams, R N

New Medical Director of Navy

As announced last October Surgeon Vice Admiral R C May is to succeed Surgeon Vice Admiral Sir Alexander Ingleby Mackenzie as medical director general of the Navy Sir Alexander retires on April 30

Central Council for the Care of Cripples

The annual general meeting of this council will be held on Thursday, May 3, at 3 P M, at County Hall, London, S E 1, when Mr Iain Macleod, the Minister of Labour and National Service, will speak

Medical Exhibition

The organisers of the London Medical Exhibition are holding their regional exhibition this year in Cardiff from May 7 to 11

Queen Charlotte's Maternity Hospital, London

On Thursday, May 3, at 2 15 P M, a meeting will be held at this hospital, Goldhawk Road, W 6, to commemorate the 25th anniversary of the opening of the Bernhard Baron memorial research laboratories and the isolation block Dr Leonard Colebrook, F R S, and Mr G F Gibberd will speak

Chiropody for Old People

The National Corporation for the Care of Old People announce in their annual report for 1955 that they have set aside £60,000 to be spent over three years in making grants to voluntary organisations providing chiropody at reduced rates for needy old people

Course on Personnel Administration

The Ministry of Health announces (H M [56]34) that the Royal College of Nursing has arranged a course on this subject from June 4 to 15 Hospital authorities, especially those concerned with the management of mental or mental deficiency hospitals where staffing problems are acute, are asked to consider giving their matron or chief male nurse facilities to attend The fee for the course (25 guineas) would, it is suggested, be "a suitable use for non exchequer funds" Applications for membership should be made to the college, Henrietta Place, London, W 1

Appeal for a Students' Summer School

The London region of the British Medical Students' Association is organising a national clinical summer school to be held in London from Sept 2 to 16 This school will be attended by 50 students from all over the British Isles, and by 15 Yugoslavian students as part of a British Yugoslavian exchange scheme The students will pay their fares and £14 towards their accommodation, but further outlay will have to be met in arranging visits to hospitals and other institutions The association also hopes to help the Yugoslavians with their heavy travelling expenses Contributions should be sent to the hon secretary of the association, B M A House, Tavistock Square, London, W C 1 hat “glucocorticoid” eosinopenia can be produced in plenectomised individuals has convinced many workers hat the spleen plays no part in the production of this henomenon[28]

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[1] How to Get Well Soon at Highwood Hospital Published by Brentwood Group Hospital Management Committee

That this conclusion may be an over simplification is hown by the observation of Kresbach and Sailer[29] who ioted that a significantly greater amount of corticorophin was required to give a positive Thorn test in plenectomised animals than in intact controls Similarly Sevitt, who compared the response in man of the blood eosinophils to corticotrophin before and 3–13 days after splenectomy, found that in some splenectomised patients an increase of the eosinophils preceded the corticosteroid eosinopenia, whereas in others the decrease in the eosinophils was greater than in normal controls Although, therefore, the spleen may not be essential for the production of eosinopenia—presumably other parts of the R E.S can compensate for its absence—it cannot at present be entirely excluded from the mechanism

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Public Health

ATTENDANCE AT CHILD-WELFARE CENTRES

H D CHALKE
OBE, TD, MA, MRCP, DPH
MEDICAL OFFICER OF HEALTH, CAMBERWELL, DIVISIONAL MEDICAL OFFICER, L C C

THERE has lately been considerable discussion as to the present need for child-welfare centres Not surprisingly, there has been some divergence of view, ranging from the belief that the day of these clinics is done, or at least that their scope should be severely restricted, to the conviction that the advent of the National Health Service has in no way diminished their importance

While much of what has been said is speculative, many interesting facts have come to light as a result of interrogation of mothers by health visitors and by social workers

Miller (1952) and others found that in Newcastle the artisan classes patronised the centres most, and that “poor” mothers, whose need for guidance was greatest, were less liable to attend than “good” mothers only 1 mother in 5 attended regularly during a whole year

Fisher (1953) believes that mothers prefer the clinic to the surgery because they dislike troubling the busy family doctor

The survey conducted by George et al (1953) in Birmingham and Cosely, Staffs, led them to conclude that one of the reasons for the attendance of 44% of mothers was the ability to purchase there proprietary foods cheaply , it was suggested that, while there was still a place for the local-authority clinic, the medical officer might well be replaced by a general practitioner

Reed and Reed (1954) have called attention to the value of these clinics as a means of assuring mothers of children who attend for routine examination that their children are healthy Their records of consultations with clinic medical officers show that advice (chiefly on feeding and skin conditions) was given in 63% of cases and reassurance in 27%

Attention has been drawn to the fact that a large number of children attend the child welfare centre once or twice only In the Newcastle investigation (Spence et al 1954) it was found that only 50% of the children attended more than three times during the first year, and there was a fairly regular fall in attendances after each visit , Spence et al suggested that if the reasons for this fall could be found out, a great deal would be learned about what mothers needed, and how these needs could best be met

Although in many places there is evidence that the number of mothers making use of child-welfare clinics has slowly decreased since 1948, there has been little to suggest that their popularity has really waned very much (*Lancet* 1954) , indeed the introduction of a free general medical service has hitherto not had the notable effect that many expected If group practice becomes more popular, however, maternity and child-welfare clinics will be held increasingly in practitioners’ surgeries, and the municipal centre attendances will be undoubtedly affected , but the extent to which this will happen is highly uncertain

The Report of the Ministry of Health (part II), 1953, emphasises the educational and preventive character of the maternity and child-welfare service, which is not an extension of the outpatient department for sick children , the need for these centres, with their emphasis on education, remains undiminished The report points out, however, that there is much variation in the standard and method of health education, and that undue emphasis is often laid on the weighing of babies

The value of child-welfare centres as part of a preventive mental health service has lately received increasing attention , many believe that there are great possibilities here, but it must not be forgotten that work in connection with problem families and maladjusted children has long formed an important part of the activities of clinic doctors and health visitors (L C C Study Group 1954)

Questioning the public on health and other matters has become increasingly popular, and perhaps the answers given today lack some of the spontaneity and sincerity of those obtained when the public opinion poll was first introduced It may be objected that the replies given to general practitioners, health visitors, and social workers do not necessarily represent the true point of view of those questioned, but careful planning of questionnaires should in some measure offset this

Plan of Inquiry

I describe here the results of an inquiry in two boroughs in South East London, where, in addition to municipal clinics, many are organised by voluntary committees The aim was to discover the views of mothers on the value of child-welfare centres, and their reasons for attendance or non attendance

The inquiry was conducted in three parts

(1) A simple questionnaire was given to all mothers or adult females in charge of children visiting the centres during one week Sealed ballot-boxes were used

(2) In order to try to find out the attitude of mothers who did not make use of the municipal and voluntary clinics, a sample survey was taken in three new housing estates The interviewers were preclinical medical students (Guy’s Hospital) “Lead in” questions on health topics were included

(3) Mothers who brought their children to the clinics on a few occasions only were asked to give their reasons for the poor attendance They were sent a form which they were asked to complete and return to the health office

Findings

REPLIES BY THOSE ATTENDING CLINICS

1361 persons replied to the questionnaire To the first question—“what is the main advantage of attending a child welfare clinic ? ”—the majority replied both “check on progress” and “for expert advice” , 37 said that they came for companionship, 128 to relieve anxiety (table I) Surprisingly, only about 16% gave the ability to buy foods cheaply as one of their reasons, but there were distinct differences in the replies from those who attended different types of clinics In the voluntary centres, in which proprietary foods were available on a lavish scale and a Ministry of Food clerk attended, this reason was given by 24% of mothers , the figure was 6 7% in the

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[28] Best W R, Muehrcke R C Kark R M *J clin Invest* 1951, 30, 629

[29] Kresbach E Sailer S *Klin Wschr* 1954 32 713

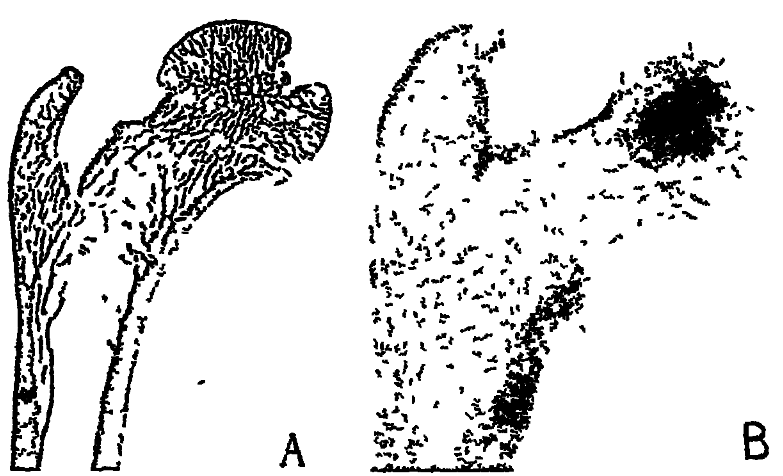

Fig 3—Radiographs of (A) section and (B) whole of femoral head of gorilla, showing *gravitational trabeculæ radiating towards whole surface of head*

degenerates earlier than that which is in current use during movement of the joint This view, which seems somewhat mechanical, is nevertheless essentially biological As a consequence of our more recent experiments we can suggest why the trabeculæ are shaped and reshaped and how they come to lie in the best position to carry the load of gravity and to bear other articular stresses

Organisation of Bone

In 1870 Julius Wolff described the ability of the spongiosa to orient its trabeculæ along the lines of force of mechanical tension and pressure That seems to have been the first expression of the relation between function and form in the living body His concept was confirmed by Roux (1885), and both Wolff and Roux established that pressure leads to the formation of bone This was contrary to the belief of von Volkmann (1862), who thought that pressure caused bone to atrophy Colmann (see von Meyer 1876), a mathematician, called medical attention to the similarity between the arrangement of the cancellous architecture of the femoral neck and that of a crane constructed on the principles of higher efficiency

However diverse the conclusions reached by many workers, there are some important points on which the majority agree, among them that the thickening of the cortical bone at the middle of the shaft corresponds to a region of danger, as happens in a bent beam at the point where the trajectories are closer to each other

Benninghoff (1927) found that osteone arrangement of the compact bone is a *continuation* of the trabeculæ of the cancellous bone A detailed study of the compact bone constituting the calcar femorale shows that this most dense of the cortical bones is formed by the pressing together of the great number of trabeculæ that come down from the head of the femur

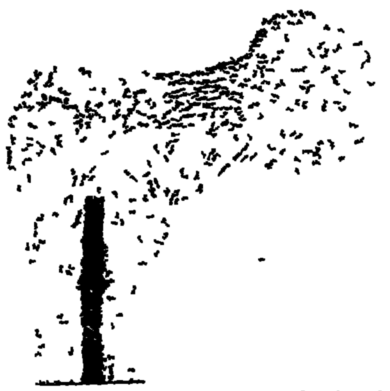

Fig 4—Radiograph of femoral head and neck of Neanderthal man (from O Walkhoff's "Studien über die Entwickelungsmechanik des Primatenskelettes," Wiesbaden 1904)

In 1920 Jores pointed out that the pressure is not always a stimulus but may be, on the contrary, often responsible for the reabsorption of bone He thought it was all a question of the amount and duration of pressure Scaglietti (1930) reported that an excess of pressure transmitted through the epiphyseal cartilage produces not a decrease in the thickening of the cartilage but an increase, together with a reduction in the growth rate No satisfactory reason had been given for the factors involved in this "inhibition"

It does not seem plausible to use in biology such terms as vulnerability, susceptability, inhibition, &c, all expressions that refer to, but do not explain, the real factors determining tissue behaviour In search of the explanation of this mysterious behaviour of bone and cartilage in transmitting the joint stresses, I made some experiments, at first with Mr J D Morgan and later with Dr A Trias, and the results are cited here

We already had evidence from cases of osteo arthritis that, when excessive pressure was transmitted through articular bone which was poorly protected, or totally unprotected, by cartilage, trabeculæ appeared with the central laminæ dead but surrounded by new living lamellæ We had suspected that, under the action of excessive pressure through the trabeculæ, the canalicular spaces by which the osteocytes are nourished were compressed and caused the death of the osteocytes even without requiring a miniature fracture of the trabeculæ The death of the trabeculæ seems to make an immediate appeal to the nearby vessels, which proliferate directly towards the dead laminæ and cover them by new lamellæ whose origin seems clearly vascular These findings seem to support Levander's (1938) hypothesis, which attributes to dead bone an osteogenetic action

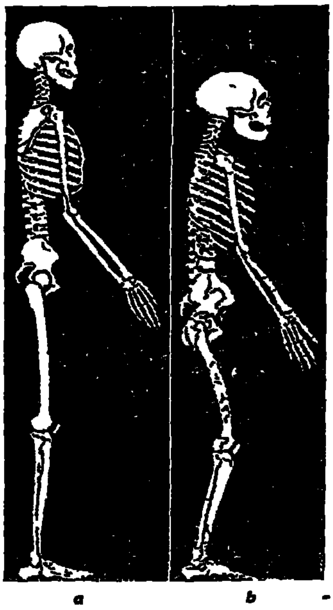

Fig 5—(*a*) Erect posture of modern man with hip and knee joints firmly locked in hyperextension, and (*b*) semiflexed position of both joints in primitive man

Changes Caused by Pressure

In our experiments on rabbits we used an apparatus based on Charnley's device for compression arthrodesis (fig 6) The knee of a growing rabbit was placed within the compressing frame, with one of its pins across the distal part of the femoral metaphysis and the other through the upper part of the tibial metaphysis As soon as it was noted that the animal tended to flex the knee to reduce the distance between the pins and thus the pressure across the knee a plaster slab or a complete plaster cast was added to prevent the leg from being moved In a few rabbits flexion took place at the joint either in spite of the splintage or because it had purposely

TABLE V—CRITICISMS BY 43 MOTHERS

Criticism	No
Risk of infection	16
Different views of people each week	4
Poor attention	4
Like to look after them myself	4
Long wait	3
Waste of time	3
Doctors rude	2
Never bothered	2
No faith in clinics	2
Interference	2
'Vague'	2
Do not agree with everything said	2
Not enough home visits	1
Prefer G P	1
Weighing only	1
'Too much messing about'	1
Did not get information required	1
Church hall too cold	1
No privacy	1
Ineffective	1
Put off by others	1
They want baby to grow up to their ideas	1
Some nurses better than others	1
Some nurses are poor advisers	1
Others	4

about frequency of attendance only 66% were prepared to say that the children had in fact been to the clinic

This is probably an underestimate of the true proportion since they were replying to a question to establish frequency of attendance, possibly a reply was withheld in some cases not because the children had never attended, but because the respondent was, in fact, uncertain of the frequency and did not care to say so

As might be expected, the frequency of stated attendance and the time since last attendance (asked only of those with children below school age) diverged, 20% said that they attend or attended weekly and, of those who gave a date for their last visit 14% said it was a regular visit made under a fortnight ago But whereas 67% said they attended monthly or more frequently, only 40% of those who gave a date for their last visit said it was a regular visit within the last six months It seems, therefore, that the stated frequencies of attendance must be regarded with some scepticism

TABLE VI—REASONS FOR DISCONTINUING ATTENDANCE

Reason	No
Too busy with other children	26
Child well, visit considered unnecessary	18
Attending own doctor	16
Indifference to child welfare	13
Mother ill	11
Mother at work grandparents looking after child	11
Distance to clinic too great	7
Too long a wait at clinic	5
Child ill	4
Satisfied with experience gained with older children	3
Unsatisfactory premises	3
Objection to advice given	2
Fear child might catch illness from other children	3
Child mentally retarded	1
Attends only to get help with child's clothing	1
Father a medical practitioner	1
Mother a nurse	1
Inconvenient day	1
Objection to referral to general practitioner	1
Fear and concern following death of first child	1
Did not want cheap foods	1
Difficult behaviour of older child at clinic	1

Criticisms, totalling 62, were made by 43 mothers out of a total of 306 questioned, 12 had never been to a clinic (table V)

REASONS FOR POOR ATTENDANCE

Scrutiny of the registers at eleven child welfare centres, selected at random, showed that in 1953 there were 2826 new attendances Of these 248 came on three occasions or less 145 (5%) once only and 103 (3 6%) came two or three times 58 had left the district 14 were attending other child-welfare centres, and 6 were in day nurseries

The remaining 170 children (6% of all first attenders) were followed up by writing to the mothers and asking them to state in confidence their reasons for not continuing to attend The replies (131) are classified in table VI In 72 cases the reason for ceasing to attend may have been unavoidable (inability of mother to attend, or child ill or under care of general practitioner) and in 59 cases the reason was avoidable (mother did not consider further visits necessary, 38 criticism of premises or advice 21)

The most significant point that emerges is the belief among a large number of mothers that, after the first baby, clinic attendance is not worth while unless the child is not making progress Evidently, also as the family increases in size, greater difficulty is experienced in finding time to visit It is surprising that there were so few valid criticisms of the clinic premises or the attention received Those who objected to the waiting-time were found on investigation to have grounds for complaint, but where the long distance to be travelled to the clinic was mentioned the complainants in no case lived more than a mile away The infrequency with which the general practitioner was mentioned was unexpected, in 1 case the reason given for ceasing attendance was an objection to the child being referred to the family doctor Needless to say the complaints made by mothers have all been followed up by the health visitors attached to the clinics concerned, and the complainants visited These visits have confirmed the view that the majority of the criticisms had little foundation, but they have demonstrated the need for keeping in touch with those who do not attend regularly or cease attendance

Conclusions

A large majority of mothers favour attendance at child-welfare clinics, because these provide a means of obtaining expert advice, checking progress, and relieving anxiety It is apparent, however that a large number do not think it necessary to visit if the child is making favourable progress, particularly in the case of subsequent children Many mothers feel that the knowledge gained (generally at the clinic) with the first child, equips them to deal adequately with those that follow Moreover the difficulties experienced in attending increase with the size of the family

Ability to purchase welfare foods was not as significant a reason for attendances as might have been expected It was found that at clinics where Ministry of Food preparations could be bought there had been very little increase in the number of clinic attendances Weighing was not mentioned to any great extent, and treatment (and this is gratifying) not at all The family doctor seldom figured in the replies, and preferences for the clinic or the surgery were fairly evenly balanced Risk of infection was mentioned only by respondents who were questioned at home, and nearly half of these had never attended

Those who frankly disbelieved in municipal clinics did not often give valid reasons in support of their objections, and criticisms even from unbelievers were few Those relating to the staff or premises were found on investigation to have foundation in some cases, and for this reason, if for no other, the inquiry had some value It also showed how essential it is for the health visitor to follow up all cases in which attendance ceases It is a matter for surprise—and conjecture—that criticisms of premises were so infrequent, for many of these are far from satisfactory Although most of the women claimed that they were regular attenders, there is a good deal of doubt as to whether this was a fact

The demand for child-welfare clinics is as great as ever, but their value in the promotion and maintenance of health is insufficiently appreciated For this the atmosphere of the clinic, if it has not changed with the trabeculæ leading to (*c*) a typical bone cyst under (*d*) degenerated disintegrating articular cartilage

Injected specimens show that no vessel of any importance penetrates the centre of the cyst (fig 10) If instead of killing the rabbit while the pressure was still being exerted, the pressure was removed and the rabbit was allowed to survive for a few days, regeneration of the ischæmic area by new vessels was immediate As supporting evidence we may add the sudden transformation of the hypertrophic growth cartilage in bone together with the invasion of the cyst by newly formed vessels (fig 11), showing the great tendency to heal of all these damaged tissues once the compression has been removed

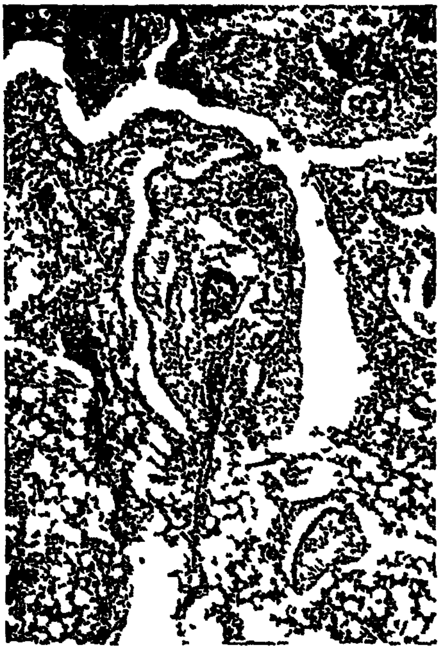

Fig 11—Four days after removal of sustained pressure revascularisation of "cyst" has already begun

The area of maximum pressure in the direction indicated by the changes of the articular and epiphyseal cartilages shows numerous trabeculæ whose central lamellæ are dead or dying, surrounded by new laminæ which in well injected preparations show intimate connection with vessels (fig 12) Some of the areas of bone condensation, such as those surrounding a bone cyst, exhibit this necrotic or dying core buried under the strata of new lamellar bone Thus experimentally the bone changes caused by ischæmia seem to stimulate the formation of bone through the mediation of vascular proliferation, this we had already suspected to be the case in human osteo arthritis Similarly, the consequence of interfering with the flow of fluid through an articular cartilage submitted to exercise and constant pressure will cause its final disintegration and, with it, the direct transmission to the underlying bone of all the evils of the crushing pressure

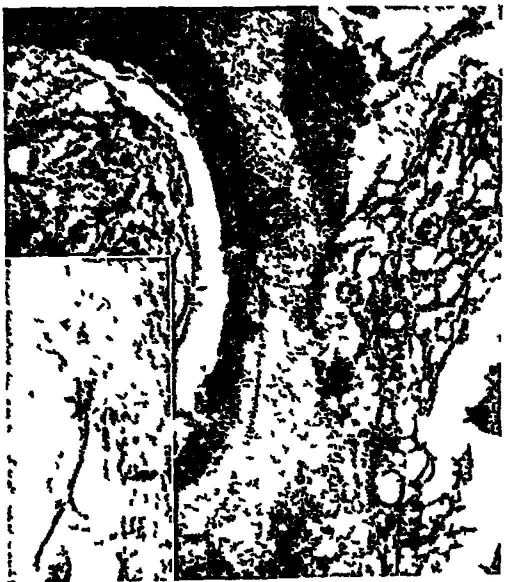

Fig 12—Dead or dying trabeculæ surrounded by new lamellæ of vascular origin Inset newly formed vessel adherent to old trabeculæ

Ischæmia as Cause of Reshaping of Trabeculæ

We tried to discover the mechanism by which the trabeculæ in the spongiosa and the osteones in the cortical bone are oriented, and our conclusion is that the whole process is guided by the intimate relationship between tissue pressures and the flow of blood and other fluids As long ago as 1905 Gerbhardt had the intuition that the architecture of bone is largely determined by the vascular system Later, in 1923, Weidenreich noticed that the lamellæ of cancellous bone are always placed round spaces containing vessels and follow their direction, he also believed in the importance of pressure in determining growth or atrophy of bone

In our research on osteo arthritis we repeatedly found suggestive evidence of the mechanism by which the trabeculæ most submitted to pressure—e g, those that carry the load of gravitation—become hypertrophied The increase in the load may be felt by the trabeculæ in three different ways (1) by increase in the weight borne by them, (2) by reduction of the area or space through which the weight is borne, and (3) by increased duration of the load The product of the weight and its duration, divided by the space $\frac{(W \times T)}{S}$ will indicate the amount of gravitational stress transmitted through the joint Other factors, well studied by Pauwels (1952), ought to be considered—e g, the distance of the great trochanter to the femoral head and to the mid pelvic line, the shorter the distance the greater being the stress To this I would add the crushing stress of locking the hip-joint in hyperextension this submits the femoral head to pressures similar to that exerted by a pair of pliers in cracking a nut

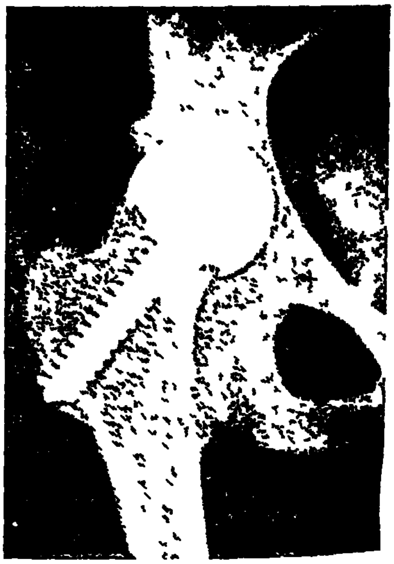

Fig 13—Hip arthroplasty aiming at better distribution of stresses between metallic prosthesis and surrounding bone

In the present experiments we studied not the earlier changes in the joint cartilage which we had found to be located in the non-weight bearing area but the results of excessive tissue pressure which, in man, is caused by the combined action of the gravitational and muscular stresses Degeneration of the articular cartilage causes the subchondral vascular proliferation which, penetrating the cartilage, abolishes its resilience by forming the osteophyte and causes pain Pain limits movement of the joint, thus a more reduced area of the head of the femur and the acetabulum now support the weight for much longer Muscular spasm joins with the other deleterious factors which end by destroying the joint

In England Now

A Running Commentary by Peripatetic Correspondents

In the book of elves and fairies beloved in my childhood, mental deficiency looked different from the problem which now I face.

The beautiful baby became a changeling—presumably through kernicterus or tuberculous meningitis—and lay brown, shrunken, and screaming in his cot till the goblins bore him back to fairyland. Nowadays the goblins' theft is often prevented by the cabbalistic rites of blood replacement or intrathecal antibiotics, and the changeling remains, failing to gain weight, demanding and angry, dancing with rage because Earth has denied it honeydew.

In the Irish myths the plump, slow, creamy girls, or lads, with the eastern eyes were once the "lucky ones" who had either been blessed by the saints or had strayed as two-year olds into the fairy ring, led by their slanting eyes and their "luck" into lonely adventures denied to others. They were laughed at, slow to learn, and loved music; they blundered but were tolerated. They too "joined the fairies" in childhood as did our own mongols before antibiotics were discovered.

Others, who had been left in a fairy ring by a careless sister or brother in infancy, were less lucky, for they could ermore escape its ceaseless dances. Charms were of no ul, nor even holy water, though sometimes a wise man ided their dance into useful ways, as we do with our astics.

The book of elves and fairies led me astray, or the aries have cursed the age of hydrogen. These are no onger the lucky ones. Today the changelings survive to rage and scream their way through the shrill echoing memories of their siblings. Mongols are no longer "blessed", their childhood is not guarded by a spell nor their musical gifts used. The wicked fairy Pædiatrica stands by the cradle, and removes the normal spell of motherhood. "You have borne a monster—a mongol—hide it from the sight of other children lest they be afraid." I wouldn't mind this so much if Pædiatrica would wave her wand until the long waiting-list for mental-deficiency institutions had vanished. Instead, like all wicked fairies, she disappears immediately in a puff of smoke, pocketing a domiciliary fee, or pontificating to the apprentices.

I wish you would go away, or stop your charms, Pædiatrica, and, pending more green hills for changelings, give the peculiar-looking baby a chance to turn out "lucky" at home.

* * *

A Cockaignshire local medical committee has been earing an interesting case. Dr X, a local practitioner, as asked why he had prescribed, on an E.C. 10, a stone of dog-biscuits.

Dr X explained that the patient, Mr Y, believed himself to be a dog, and was under the care of a Psychiatrist who insisted that he be humoured and prescribed certain tablets. The only way to get Mr Y to take the tablets was to conceal them inside small dog biscuits. Dr X contended that the dog-biscuits were therefore not a food, but an ancillary medicament or vehicle, the equivalent of a syrup or flavoured water. If the Chairman thought he could talk Mr Y out of his delusion (said Dr X), he was welcome to try; but so far Mr Y had proved unusually intransigent. Indeed, after his last session with Mr Y, the Psychiatrist had suddenly tied a small barrel under his chin and crawled out howling into a snowstorm.

Dr X claimed that his duty not only as a doctor but also as a citizen demanded that the patient be kept fit for work; for Mr Y was a key man. He made the tea for the men who made the tea at the Ministry of Incoördination in Ataxia House. He was irreplaceable also in that he was left handed, and nobody else could use his peculiar left handed teaspoons. The Committee would be aware from the Press (continued Dr X) that there was a crisis over the question of pay differentials between right and left handed tea stirrers, and he would ask the Chairman whether the national economy was to be endangered for the price of a stone of dog biscuits.

Dr X spoke for a further 45 minutes on the Englishman's love of animals, concluding by singing several verses of a ballad entitled, *My Four-legged Friend*, and inviting the Committee to join in the choruses. But the meeting had to adjourn, owing to the indisposition of the Chairman, who felt his nose becoming hot and dry.

* * *

The last patient at the clinic was a woman with neurodermatitis. The boss was evidently tired. He had reached the critical point at the end of the afternoon when his mind would accept nothing but the most relevant remark through its fatigue barrier.

"Now ma'am, you have had your skin trouble for how long?"

"For thirty years at least. I have seen most of the dermatologists in the country, and none have done me any good."

"And what makes you think we will succeed where they have failed?"

"I had heard you were supposed to be good at this sort of thing."

The boss closed his eyes and breathed deeply. Anyone who did not know him would think he had fallen asleep. I knew he was wrestling with his serpent.

"Tell me, ma'am, do you use nail varnish?"

"It seems rather a personal question, but if it is of any interest to you, I don't. My nails are naturally highly polished."

"Naturally. And do you scratch?"

"Never! Dr Smyth accused me of that. It simply isn't true. I want to scratch but I am able to control myself."

"Indeed. How long have you had your eczema?"

"Is that what it is! Then why do they call it dermatitis? every specialist that I come to has a different name for it. I do wish someone would explain to me in simple language what I have got and how to cure it."

The boss turned slowly on his swivel chair and addressed me as though we were alone together.

"Not so easy, Peter. How does one explain in simple language that this skin lesion is a localised area of unhappiness, a focus of frustration? It is a flag she is waving, but whether for help or in warning it is difficult to decide. This patch of eczema is a target on which she receives the slings and arrows of outrageous fortune; though, here again, if fortune is outrageous we are so often ourselves the cause of it being so. And she has, of course, scratched and scratched and scratched continuously for thirty years to sustain it."

"Do you mean to tell me that I have deliberately kept it going? It's ridiculous!"

" to sustain it for fear of losing it."

"Well, it is obvious that I am not going to get any help from you! It was a waste of time coming."

His voice lost its edge and I knew the physician had begun to rewind the serpent round its staff.

"Sit down, dear lady, and relax a little. I am sure we can help you. We will give you a paste and the rash will improve if you don't scratch. I shall also dispense for you some medicine."

"I have heard that before. Is it brown? I've had it! It never did me any good—only upset my stomach!"

"I shall dispense some bromide and nux vomica. This is *not* brown but red like claret."

The boss took my arm and led me out of the cubicle.

"Peter, I would like to see this patient again in six weeks, when I hope to prove to you that there are some skins that we have no right to cure if we have the comfort and happiness of our patients at heart."

I took a swift look to see if he was smiling. If he did smile it had already gone; but he did not look quite so tired.

* * *

News from School.—The music comp. was very good. The pianos were never together. Even the recorders were not together, let alone being in time with the pianos. Everybody was stifling their laughter.—House had cellos, violins, and viola, but people say it was not a match against last year's, as it was not nearly so out of tune.

TABLE I—SURVIVAL OF BACTERIA IN BROTH CONTAINING 16 µG CHLORAMPHENICOL PER ML

Species	Days of incubation					
	0	1	2	3	5	7
Strep. fæcalis	400	500	400	300	500	400
Strep. pyogenes	200	0	0			
Staph. pyogenes	400	250	100	35	3	0
S. typhi	500	200	65	3	0	
S. paratyphi B	1000	400	200	12	0	
Esch. coli	1000	100	9	0	0	

Note. The numbers show the number of colonies growing from a drop (c. 0.03 ml.) spread on agar.

indication of the course of events. When the broth appeared to be sterile, its sterility was often confirmed by centrifuging and resuspending a larger sample in fresh medium. The lag period in the subcultures was often prolonged in the later stages of a test, so that two or more days' incubation was needed. Subcultures on blood agar plates were found to be more reliable than those on nutrient agar, even with freely growing species.

4. The tests reported here were made with chloramphenicol which has the advantages of a wide spectrum, stability for more than two weeks in the incubator, and a reasonable level in the cerebrospinal fluid (a third to a half of that in the blood). Erythromycin seemed to be nearly as stable, but tetracycline was largely inactivated after five days. It has been assumed that blood levels of 16–32 µg chloramphenicol per ml. are readily obtained, corresponding to 5–10 µg in the cerebrospinal fluid, and that higher levels can be expected with heavy dosage. Most of the tests have therefore been made with concentrations of 16–25 µg., but the effect of 5 and 10 µg has also been observed with strains of meningococcus, pneumococcus, and *H. influenzæ* in view of their association with acute meningitis. In addition a few individual strains have been tested over a wider range of concentrations.

5. The majority of the strains were isolated from specimens sent to the London Hospital Clinical Laboratory. With some species (e.g., of salmonella and brucella) only laboratory cultures were available. It is realised that as many strains as possible should be tested, but it is hoped that enough has been done to show that species vary considerably in their ability to survive.

6. The inoculum used at first was such that the sample drop, spread as soon as the test was set up, yielded 1–500 colonies—a number which could be counted or estimated with reasonable accuracy. In later tests the inoculum has often been much increased with organisms which tend to die out rapidly.

Results

Table I is shown as an example of an experiment in which five strains of different species were exposed to a concentration of 16 µg chloramphenicol per ml. in broth. The first column shows the days on which subcultures were made, those on "Day 0" being taken as soon as the test was set up. The figures indicate, in round numbers, the number of colonies observed. It is possible that the variations with *Strep. fæcalis* are largely due to faulty estimation; but, even as shown, the ability of some strains of this species to persist under conditions of bacteriostasis is remarkable considering that none of the others survived for as long as a week, *Strep. pyogenes* failing in this case even to survive for a day.

Table II indicates the general results obtained with the various species, listed according to their tendency to die out rapidly. The susceptibility of the neisseria was to be expected from the clinical reports. The strains of *H. influenzæ* and pneumococcus were derived (except a pneumococcus type I) from routine cultures. All these strains were respiratory in origin with the exception of two *H. influenzæ* from the meninges, one type b and the other type f from an unusual case in an adult. The latter strain to some extent "spoiled" the figures for the species, being somewhat more persistent and less sensitive than most of the others. In general it seemed clear that in both species there were minor variations in susceptibility, and that a concentration of 10 µg chloramphenicol per ml. was necessary to ensure either sterilisation, or a near approach to it, within two days. The brief survival of the two laboratory strains of *Corynebacterium diphtheriæ* is interesting in the light of Forbes's (1954) report that erythromycin, a bacteriostatic drug, was more effective than the bactericidal penicillin in clearing up carriers.

Mention must be made here of an untoward finding observed once with the type-f hæmophilus in 5 µg chloramphenicol per ml. and once with a pneumococcus in 10 µg. Subcultures yielded a few colonies over a period of a week or more, the companion bottle in each case (and also two pneumococcal bottles with half the concentration of drug) becoming sterile much sooner. Examination of films suggested that the persistence was due to agglutination of the bacteria by antibody which chanced to be present in the blood.

Strep. pyogenes was not tested with the idea that penicillin might be supplanted by chloramphenicol in the treatment of acute streptococcal infection but in order to estimate the probable effect of a bacteriostatic drug on the carrier state, which often resists short courses of penicillin. The results suggest that this species would respond less rapidly than *C. diphtheriæ*, especially since in the carrier the presence of specific antibody would favour agglutination of the cocci.

The response of the staphylococcus, even in broth, is relatively slow; and, especially when the staphylococcus is clumped in blood broth, it is sometimes, though not always, indefinitely prolonged, positive subcultures sometimes persisting in the fourth week although frank multiplication is still controlled. These conditions may well reflect those in generalised staphylococcal infection, in which treatment, even with penicillin, against a sensitive strain must be prolonged in order to prevent recurrence derived from "persisters" in small abscesses.

Like the staphylococcus, the typhoid bacillus sometimes persisted in blood broth but sometimes died out in about a week. In the former case films once again suggested that agglutination of the bacilli into small clumps was responsible. In the human body, however, the bacillus probably multiplies to some extent within the host cells—a situation difficult to simulate in vitro. Similar results were observed in a few tests with *Salmonella paratyphi B* and *Escherichia coli*.

Although relapse is common in brucellosis after treatment with the bacteriostatic drugs, the use of blood

TABLE II—SURVIVAL OF BACTERIAL SPECIES IN PRESENCE OF CHLORAMPHENICOL

Species	Number of strains	Concentration of drug (µg per ml.)	Medium	Original number of colonies per drop (average)	Result	
					Days of incubation	% surviving
Gonococcus	1	8 or 4	B.B. (boiled)	89 × 100	1	0
Meningococcus	1	10 or 5 2.5	B.B.	50 × 10³ "	2 3	0 0
H. influenzæ	10 7 7	16–20 8–10 4–5	" " 	100 × 10³	1 2 2	0–<0.1 0–0.1 0–1.0
Pneumococcus	10 7 7	16 8–10 4–5	 "	100 × 10³	1 2 2	0–0.1 0–<0.1 Up to 10
C. diphtheriæ	2	16		20 × 10³	2	0
Strep. pyogenes	5	16		20 × 10³	5	0–<0.1
Staph. pyogenes	5 6	16–20 20–25	Broth B.B.	400 "	5–8 7–14	0* 0–>100
S. typhi	4 5	16–20 20–25	Broth B.B.	500	4–7 6–14	0 0–>100
Strep. fæcalis	3	16–30	Broth	200	7–11	100 ±

Notes. Size of drop: 0.02 ml. (approx.).
Colony count: 100 × 10³ = 100 colonies grow from spread of drop after 1:1000 dilution.
B.B. = 20% horse blood broth.
*Staphylococci occasionally persist longer.

still coronary disease is relatively uncommon in these populations Finally, there is no evidence that race is involved and a good deal of evidence that it is not, notably in comparisons between Negroes in Africa and in Chicago, in comparisons between people in the same region who differ in their economic circumstances (as found in our studies in Spain and in Italy), and in our current comparisons between Japanese in Hawaii and here in Kyushu But in all of these situations attention to the total fat in the diet seems to bring an orderly relationship into focus

Probably no such clear and simple relationship would be found if the dietary predilections of the world's populations for quantities and kinds of fats varied independently I should not expect to find the same serum cholesterol levels and frequencies of coronary heart disease in two populations both getting 40% of their calories from fats but the one deriving this from corn oil and sesame seed oil while the other got all their fats from coconut oil and lard But this does not happen to be the way people consume fats In a desperately poor land the people get very few fats of any kind As their lot improves economically they increase their total fat consumption, *and* the fats they eat tend to be more and more the more expensive kinds—the fats that, incidentally, are associated with the foods most highly prized for their nutritional as well as their gustatory value

To some of us, at least, it appears that this response to prosperity can go too far The problem has been complicated by the enterprise and ingenuity of food producers and technologists who provide a superabundance of all kinds of fats and then persuade us to eat them Are we now going to ask them, please, to put some more E F A in their wares ? Perhaps with a modest increase in cost ? This could be the shape of things to come Continue, or increase, your high fat consumption but be sure you get a lot of corn oil, sesame seed oil, fish oil, and the like and be careful to swallow it fresh and in the virgin liquid state !

Such considerations may seem inappropriate in a discussion of a problem that is basically chemical and pathological But the coronary problem has already reached dimensions that cannot be confined in the otherworldly atmosphere of some academic retreats In the meantime, it is clear that a great deal more research is needed on all aspects of the problem, including food economics and the psychology of food preferences While this is in course it may be well to ponder whether a diet containing 40% of its calories as fats is really essential for human happiness and, if not, how may it best be reduced

First Medical Clinic,
Kyushu University Medical School
Fukuoka shi Japan

ANCEL KEYS

VOMITING SICKNESS IN JAMAICA

SIR,—There are two important points which might be added to your leading article (April 14) As far as I know, chemical analysis has not yet been published to indicate in what part of the ackee fruit the toxins are found If they are only in the seed, then the population can continue to eat the arillus with impunity Children who eat the seed in play, or tragically driven by hunger, must be more carefully supervised The other point is quantitative not only which part, but how much of which part, of the fruit is likely to produce a toxic effect

The full report of the work done in 1952–53 (excepting the chemical section) was published by the Government Printers, Kingston, Jamaica, in 1954, as a monograph on Vomiting Sickness in Jamaica

London School of Hygiene and
Tropical Medicine W C 1

CICELY D WILLIAMS

REVISION OF THE CURRICULUM

SIR,—The only positive contribution in the proposals of the Royal College of Physicians anent revision of the medical curriculum is the suggestion that the G M C should cease to issue recommendations—in other words, abrogate its function as guide and supervisor of the training of medical students Otherwise the report (of which extracts appeared in your issue of April 14) consists in the usual ponderous, pontifical pronouncements that the aim of medical education should be to give "a broad cultural background," "the acquisition of a scientific attitude," "principles and outlines without the burden of fact," &c , &c We have heard most of it before in the perennial bellyache about the medical curriculum which is a perpetual item on the agenda of committees of medical schools and Royal colleges and corporations, in fact of every conceivable body except those best suited to advise—namely, the general practitioner No other training schemes—for lawyers, engineers, scientists, &c —are subjected to so much interminable "research ". Quite obviously the present training of the medical student is unsatisfactory, uneconomic, and much of it wholly irrelevant to the work subsequently undertaken by the great proportion of medical graduates

Medicine is not a philosophy nor is it a science It is a skill, much of it still empirical , and, like training for any other skilled job, the education of the medical student should include, from an early stage, a concurrent and remunerated apprenticeship The people want a doctor who knows his job—who can, for example, recognise scabies when he sees it and tell them how to treat it They are not particularly concerned whether he can discourse on Scabies in Mediæval Times or The Adaptive Mutations from which Evolved the Behaviour Pattern of *Acarus scabiei*

Would it be wrong to suspect that given freedom from G M C recommendations a "model" curriculum would emanate from the Royal College of Physicians, which might even be prepared to send its representatives to the various medical schools to initiate the new era ?

Department of Anatomy,
University of Glasgow

GEORGE M WYBURN

SIR,—The very interesting report by the Royal College of Physicians, prompts me to ventilate an idea which might possibly be applicable as an experiment at one, say, of our "red brick" universities

It is, in effect, the introduction of a tutorial system, whereby each of the younger clinicians attached to the medical school would act as tutor to some five or six students for the whole of their undergraduate life They would meet him perhaps for two one hour sessions each week, on one occasion to discuss an essay he had set, and on the other for a general round-table conference The value to the students would be obvious in bringing them from the first into personal contact with an active practitioner of their craft and would give them an initiation, particularly when they reached their clinical years, to the real as distinct from the textbook problems of medical work The value to the tutor would hardly be less, since it would necessarily keep him up to date not only with other branches besides his own specialty but with his anatomical, physiological, and psychological knowledge

One of the dangers of the age of specialism is that, while knowledge in a particular field may become ever more detailed and exact, the specialist is liable to fall behind even the newly qualified graduate where the rest of the subject is concerned , and my scheme would very effectively prevent this, since it would be useless to try and talk to a critical audience without an adequate familiarity with the matters under discussion

Darlington

JOSEPH V WALKER
Medical Officer of Health

one but significant from the clinical aspect, as the work of Cates, Christie, and Garrod (1951) has shown chlortetracycline and chloramphenicol were useless in the treatment of endocarditis due to infection with *Strep fæcalis*

It may also be argued that the action of a drug varies, being bacteriostatic for one bacterial species but bactericidal for another Biochemical studies on the effect of chloramphenicol on the assimilation of amino acids by bacteria, as reviewed by Gale (1953), were mainly concerned with the staphylococcus, in which the over all action is on protein synthesis, but they give no suggestion of an alternative effect likely to bring about the rapid death of, for example, the pneumococcus Further it should be noted that the species which seem to be most susceptible to the action of the drug are those which need frequent subculture, at least on simple media

Jawetz and Gunnison (1953) question the description of drugs as bacteriostatic or bactericidal Including penicillin in their argument, they state that, as the concentration of the drug rises, after a possible zone of stimulation, the growth of bacteria is inhibited before the lethal concentrations are reached Admittedly at one stage the number of survivors must remain constant for a time, but this does not imply inhibition in the true sense of the word The typical action of penicillin (see Florey et al 1949) is maximal when the bacteria, in the absence of the drug, would be multiplying freely Hence one may reasonably suppose that when the effect of penicillin is partial (because its concentration is low) its action on the individual bacterium is either bactericidal or ineffective—never being truly bacteriostatic It is true that at much higher concentrations—unattainable, or not normally attained, in systemic treatment—the actions of some of the antibiotics may perhaps be reversed, but for practical purposes the use of the two descriptive adjectives seems to be justified

Summary

Sensitive strains of various bacterial species have been tested for their ability to survive under conditions of bacteriostasis caused by adding chloramphenicol to the culture media This drug was chosen for technical reasons, but the effect of other bacteriostatic drugs on sensitive bacteria is probably similar

Tests were carried out both in simple media, such as nutrient or digest broth, and in 20% horse blood broth (The horse leucocytes appear to survive refrigeration for a week or more and incubation for a day or so) Subcultures from the blood broth tended to remain positive longer than those from simpler media—perhaps because the bacteria were preserved by agglutination or clumping

It seemed that, in relation to bacteriostasis, bacterial species might be regarded as

1 *Highly susceptible* —Gonococcus, meningococcus, *Hæmophilus influenzæ*, pneumococcus, *Corynebacterium diphtheriæ*
2 *Moderately susceptible* —*Streptococcus pyogenes*, *Staphylococcus pyogenes*, the coli typhoid group, *Hæmophilus pertussis*, and some strains of *Strep viridans* isolated from cases of endocarditis
3 *Insusceptible* (in practice) —*Strep fæcalis*

These findings are briefly discussed

My thanks are due to Prof C F Barwell, and other members of his staff, for advice, and to the staff of the Clinical Laboratory, under Dr H B May, for the supply of bacterial strains isolated during their routine work

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THROMBOTIC MICROANGIOPATHY

HISTOLOGICAL DIAGNOSIS DURING LIFE

W St C Symmers
M D Belf, Ph D Birm, M R C P
PROFESSOR OF MORBID ANATOMY IN THE UNIVERSITY OF LONDON AT CHARING CROSS HOSPITAL MEDICAL SCHOOL

Thrombotic microangiopathy (thrombotic thrombocytopenic purpura) is a well-established entity Including Moschcowitz's (1924, 1925) original case and the 3 described here, at least 85 indisputable cases have been recorded (*59 from the United States, 15 from Britain*, and others from Cuba, Czechoslovakia, Finland, Germany, Hungary, Italy, and Switzerland) In addition, I know of over 30 unpublished cases, most of which I have seen through the kindness of colleagues in Britain and oversea Only 35 of the 85 published cases had been reported by the end of 1951 of the 35 all but 3 British cases (Pagel 1949 [case 4—see Symmers 1952], Symmers and Barrowcliff 1951, Symmers and Gillett 1951) were from the United States, whereas 23 of the 50 more recent cases were reported from other countries Of these 50 cases 17 were diagnosed during life, in contrast with only 4 of the 35 earlier cases These figures reflect a greater awareness of the features of thrombotic microangiopathy, enabling it to be recognised oftener, both during life and post mortem

Clinical Diagnosis

The clinical diagnosis is usually suggested by the development of a characteristic tetrad acute febrile illness, hæmolytic anæmia, thrombocytopenic purpura, and neurological disturbances In most cases this syndrome develops fully only late in the comparatively short course of the illness, and the diagnosis is seldom made until very shortly before death If thrombotic microangiopathy is to be recognised early, the clinician must consider it in the differential diagnosis of every illness presenting with any of the components of the tetrad

Biopsy

At present, only biopsy offers any hope of providing irrefutable confirmatory evidence of the diagnosis, it has so far played only an insignificant part

Excluding the cases reported in this paper, biopsy was done in only 7 of the other 19 published cases which were diagnosed during life, and the result was positive in only 3 The lack of information from biopsies is due partly to the infrequency of the lesions in the vessels of the tissues which are usually chosen (skin and muscle), and partly to patients usually being too ill to undergo biopsy at the late stage when the diagnosis is ordinarily suspected

Altschule (1942) was the first to suggest that thrombotic microangiopathy could be recognised in life, and the possibility that biopsy might aid diagnosis was first mentioned by Bernheim (1943)

The first 4 cases to be correctly diagnosed clinically were reported by Engel et al 1947, Epstein et al 1948, Singer et al 1950, and Meacham et al 1951 Biopsy was first done following clinical diagnosis in a case reported by Blackman et al (1952), the first positive biopsy was recorded by Chediak et al (1952)

Several workers since Bernheim (1943) have advocated biopsy in the hope that early diagnosis might help investigation of the nature and treatment of thrombotic microangiopathy

Choice of Tissue

At necropsy, evidence of thrombotic microangiopathy has been sought in tissues accessible to biopsy, and these studies have shown considerable variation between cases for instance, there may be many lesions in skin and skeletal muscle, but oftener the vessels in these tissues are not involved

It is obvious, therefore, that both our results are in the sest possible accord and that together they supply nvincing evidence that the abnormality in myasthenia an alteration in the response of the motor end-plate acetylcholine

St Thomas's Hospital
London S E 1 — H C CHURCHILL-DAVIDSON

Royal Free Hospital
London, W C 1 — A T RICHARDSON

PARATYPHOID-C OSTEOMYELITIS

SIR,—In their article of April 7 Dr White and Dr eynell review the reported cases of osteomyelitis due to lmonella and indicate the rarity of this condition, rticularly in salmonella infections other than *Salmonella phi* and *Salm paratyphi B* The following recent case osteomyelitis of the parietal bone due to *Salm dublin* ay therefore be of interest

A woman, aged 72, was admitted to hospital, under the re of Dr C W Walker, with severe anæmia On examina on she was confused and had early heart failure and right asal pneumonia A swelling was present over the left parietal one A blood count showed Hb 37%, packed cell volume 0%, mean corpuscular hæmoglobin concentration 27 5%, nd white cells 10,000 per c mm, with a pronounced shift to ne left Radiographs of the skull suggested a vascular tumour n the parietal bone The presumptive diagnosis of secondary arcinomatosis from an unknown primary was made The atient's condition initially improved with blood transfusion nd penicillin Her condition then gradually deteriorated and he died on March 23 On retrospective inquiry it was iscovered that the patient had had mild diarrhœa in the ospital

At necropsy the parietal bone was found to be eroded and here was a collection of pus in the adjacent subaponeurotic nd epidural spaces, cultures of which yielded a profuse growth f *Escherichia coli*, *Clostridium welchii*, and *Salm dublin* *alm dublin* was also found in cultures from the intestine

On histological examination the parietal bone showed hronic granulomatous osteomyelitis with a predominance of mononuclear phagocytes, as in a typhoid lesion Similar ranulomatous lesions were present elsewhere in the body ections of the sternum, however, showed infiltration with arcinoma cells

On later inquiry it was learnt that the patient had ived on a smallholding where losses from calf diarrhœa—a condition frequently associated with *Salm dublin* nfection—had been a feature

It seems probable that the course of this patient's infection with *Salm dublin*—an organism which only rarely causes a systemic infection in man—was influenced by a lowered state of resistance due to the concurrent carcinoma

MARGARET E BARTON
D R CHRISTIE
County Hospital, Hereford — K VALTERIS

ANTENATAL DETECTION OF HEREDITARY DISORDERS

SIR,—The recent articles on a technique for determining the ABO blood group from epithelial cells[1] and confirmation[2] of the recognition of sex from epithelial cells from the amniotic fluid[3] have opened up the possibility of a new field of preventive medicine

It should eventually be possible for most prospective parents with inherited disorders transmitted by single genes to obtain a fairly precise estimate of the likelihood of their coming child being affected by the twelfth week of pregnancy,[3 4] when termination would be simple and would not impair subsequent fertility About half such pregnancies would be affected, and their interruption would probably not reduce the number of live births finally achieved by most parents At present such terminations would be illegal, except possibly in incipient erythroblastosis fœtalis

In sex-linked recessive disorders, such as hæmophilia, the interruption of girl-bearing pregnancies would eliminate transmission through known cases

The reduction in the transmission-rate of disorders determined by autosomal dominant genes requires knowledge of their linkage with genes determining the observable behaviour of the amniotic cells One such linkage with the ABO system has recently been described[5] The development of methods of recognising genetically determined attributes of such cells and an increased knowledge of linkage in man, should enable a great reduction to be achieved in the transmission of such diseases as Huntington's chorea, polyposis coli, arachnodactyly, and acholuric jaundice, without acting against the desires of the majority of afflicted persons

The prospect of such preventive measures, and of relevant legislation, is particularly important in that not only are environmental improvements allowing increased proportions of afflicted infants to mature, but the increasing exposure to X rays, atomic piles, and experimental war will inevitably increase the mutation-rate in man

London N 1 — J H EDWARDS

PERFORATED ACUTE AND CHRONIC PEPTIC ULCER

SIR,—I would like to support Mr Hermon Taylor and Mr Warren (April 14) in their opinion that not all perforated peptic ulcers should be treated in the same way, and agree with their treatment policy as far as it goes, having arrived at the same conclusions for other reasons[6]

I say "as far as it goes," for no less than 7 patients out of 93 were considered to be moribund on admission and their deaths inevitable, no details are given of these patients As I pointed out in my paper, patients who are gravely ill from the peritoneal effects of a perforated ulcer will all die if treated by aspiration, but some will recover if the peritoneum is cleared of free fluid at operation and vigorous resuscitation is applied, and reinforced by noradrenaline if there is no response to the usual methods

Exeter — H DENDY MOORE

RECURRENT DISLOCATION OF THE SHOULDER

SIR,—I might have overlooked the specious simplicity of your leader (April 14) had it not cast a reflection on the activities of that hard-worked branch of the profession—the orthopædic surgeon, imputing to him slackness in investigating an apparently simple problem

The fact to be decided is whether or not immobilisation after a recent dislocation of the shoulder is a contributory factor to the development of recurrent dislocation As you say, no protagonist of either side really knows, but to add "one of them must be wrong" is carrying logical positivism too far It is highly probable that one group of shoulder dislocations, possibly those associated with a deep depression on the head, always recur regardless of the treatment, and another group, without bone injury, show a reduced recurrence rate after adequate immobilisation In fact very considerable attention has been given to this problem, and the failure to solve it suggests that there must be some overlapping of the effects of immobilisation and non immobilisation, and is strong evidence that both sides might be right!

The leader goes on to state that "A definite answer could be given by a follow up study of a few hundred cases treated by each method" This is an over simplification The fact is, that we have not even got an accurate figure for the recurrence rate in a hundred cases treated

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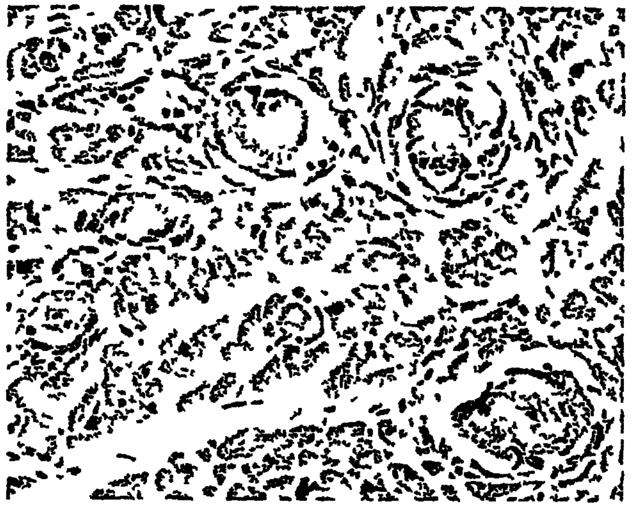

Fig 1—Thrombotic microangiopathy in dilated myocardial capillaries in case 1 (Hæmatoxylin and eosin × 250.)

Admission.—No treatment could be given at the time of biopsy because the patient was unwilling to remain under medical care; seven days later he was admitted to hospital because of sudden, painless hæmaturia. Temperature 99.4°F. He was very pale; clinical examination showed no other abnormalities, apart from the lymphadenopathy. Next day the patient was restless and confused, and had become slightly jaundiced; slight hæmaturia persisted, and blood oozed from his gums.

Investigations.—Empirical liver function tests normal. Serum bilirubin level 4.8 mg. per 100 ml.; serum albumin level 3.6 g. and serum globulin level 3.2 g. per 100 ml. Prothrombin, bleeding, and clotting times normal. Blood count: red cells 3,800,000 per c.mm.; Hb 11.0 g. per 100 ml.; white cells 13,000 per c.mm. (neutrophil polymorphs 9100, myelocytes 260, myeloblasts 65, eosinophils 260, lymphocytes 2665, monocytes 650); platelets scanty.

Treatment and course.—Blood transfusions had no effect on the clinical or hæmatological picture. Treatment with cortisone (300 mg. daily) was started on the patient's third day in hospital. Four days later he passed into a muttering delirium; his condition rapidly weakened, and he died in coma. No hæmorrhages were found in the skin at any time, and the tourniquet test was negative.

Investigations on day of death.—Blood-count: red cells 1,800,000 per c.mm. (12% reticulocytes); 6 normoblasts per 200 white cells; Hb 5.6 g. per 100 ml.; white cells 28,000 per c.mm. (neutrophil polymorphs 22,960, myelocytes 840, myeloblasts 140, eosinophils 280, lymphocytes 3080, monocytes 700); platelets 62,000 per c.mm. No red cell agglutination or hæmolysis in albuminous or saline media at 4°, 18°, or 37°C; Coombs test negative.

Necropsy.—Necropsy sixteen hours after death showed generalised, moderate enlargement of lymph nodes throughout the body, a few serosal and mucosal petechiæ, a spleniculus (weighing 35 g.) at site of splenectomy, and red marrow throughout the upper half of a femur and humerus.

Histological examination showed typical lesions of thrombotic microangiopathy, abundant in the myocardium (fig. 1), adrenals, lymph nodes, tonsils, pancreas, and bone marrow, and scantier in the hepatic portal tracts, cerebral grey matter, and spleniculus; *none* was found in the skin, skeletal muscle, or kidneys. Sections of marrow showed erythroid and myeloid hyperplasia; the megakaryocytes looked normal. There was no evidence of leukæmia or extramedullary hæmopoiesis.

Lymphadenopathy as the presenting manifestation of thrombotic microangiopathy has not been described before. Enlarged lymph-nodes, apart from septic lymphadenitis, were noted in only 6 cases (Engel et al. 1947, Fitzgerald et al. 1947, Clinicopathologic Conference 1951, Barondess 1952, Laszlo et al. 1955, Prokš and Tomší 1955a and b); in none of these was the lymphadenopathy as striking as in this case. Purpura is rarely absent, as it was here; hæmaturia has been noted often, and may be the presenting symptom. Leukæmoid blood pictures have often been described and may be present only transitorily; in Ritama's (1954) case the picture was that of acute myeloid leukæmia. An unusual feature of the case described above was the absence of clinical abnormalities of the nervous system other than confusion and terminal delirium, which may have been nonspecific accompaniments of a severe illness.

PRESENTING WITH CONVULSION AND MENORRHAGIA

Case 2.—A woman, aged 21, was admitted to hospital half an hour after a fit while sleeping in the sun. Her sister, a qualified nurse, said that they had sunbathed for four hours; she described the fit as a major epileptiform convulsion, and it was noted in hospital that the patient's sun suit was soaked with urine and that her tongue was bitten. There was no *previous history of epilepsy or of any untoward reaction to* exposure to the sun. She had previously had only trivial illnesses; since puberty she had been liable to boils, for which she occasionally took sulphonamides. Three weeks before the convulsion she had had a sore throat and pyrexia, treated with tablets containing sulphathiazole, sulphadiazine, and sulphamerazine; during this treatment a transient maculopapular rash developed.

On admission she was unconscious. Temperature 97.4°F. Pulse rate 42 per min. Urine normal. She was menstruating scantily. Heart normal; blood pressure 120/70 mm. Hg; electrocardiography showed sinus bradycardia. Pupils unequal in size, but reacted to light; tendon reflexes elicited with difficulty; abdominal reflexes absent; left plantar reflex extensor, right flexor.

Progress.—Two hours after admission the patient regained consciousness and complained of headache and thirst. Temperature 99.6°F; pulse rate 110 per min. Two hours later she had a rigor (temp. 106.8°F); she was pale and weak, her pulse rate was 148 per min.; and she had bled copiously per vaginam. (Her menstrual history was normal, except that the present period was a fortnight late.) 5 pints (2.8 litres) of blood were transfused within two hours; the bleeding stopped soon after transfusion began. Next morning, eighteen hours after the convulsion, she felt well but tired. There had been no further vaginal loss, and there were now no neurological abnormalities. Blood count: red cells 4,600,000 per c.mm.; Hb 12.0 g. per 100 ml.; white cells 7500 per c.mm. (normal differential count); platelets 310,000 per c.mm. That night uterine bleeding recurred; curettage was performed, and the bleeding stopped.

Histological examination of the curettings showed hæmorrhagic, menstruating endometrium; in addition, lesions typical of thrombotic microangiopathy were seen in the basal stratum of the endometrium and in the endocervix.

Repeated clinical examinations showed nothing abnormal apart from widespread sunburn (erythema without blistering) and slight evening fever. A patch test with sulphathiazole was positive.

Laboratory investigations were consistently negative, apart from erythroid hyperplasia in marrow films and a reticulocyte count of 5%. Red cell, white cell, and platelet counts,

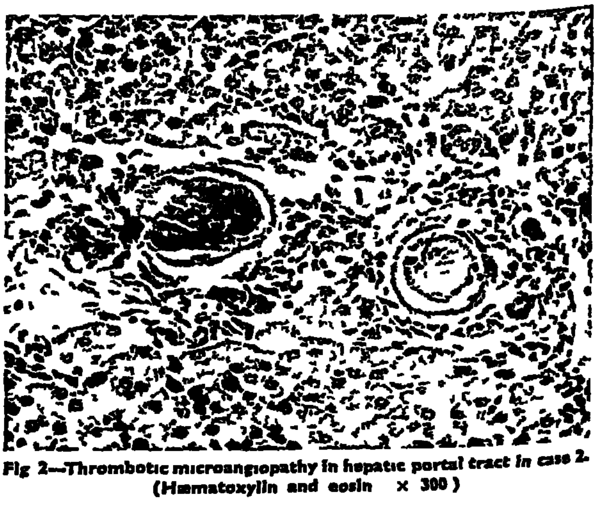

Fig 2—Thrombotic microangiopathy in hepatic portal tract in case 2. (Hæmatoxylin and eosin × 300.)

The sole purpose of the procedure is to help in the early selection of the case that must be treated by surgery The method is so simple and safe that I can see only two valid objections to its use one medical and one surgical. The dosage of adrenaline employed is unlikely to receive ready acceptance by one who has been trained to use it in carefully calibrated doses of up to as much as 1 ml or by the young surgeon who must depend on emergency operations for his quota of gastric surgery

"Men occasionally stumble over the truth but most of them pick themselves up and hurry off as if nothing had happened" (Sir Winston Churchill)

Carnwath
Lanarkhire

W J M BRANDON

PREVENTION OF RENAL LESIONS DUE TO ISCHÆMIA

SIR,—In view of the interest aroused by "artificial hibernation" we wish to draw attention to the effect of this procedure on ischæmic lesions of the kidney

Renal ischæmia constitutes a major problem in operations for partial nephrectomy and in shock

Partial nephrectomy necessitates temporary compression of renal vessels No untoward consequences result from this if the other kidney is normal, since function is restored within a few weeks, even after circulation has been arrested for a whole hour On the other hand if the patient has only one kidney and this must be operated on, ischæmia of ten minutes' duration may be tolerated, but the safety margin is dangerously narrow and the outcome depends mainly on the duration of ischæmia [1]

In *shock*, whether due to injury loss of blood, or any other factor, one of the chief complications is a renal lesion, which has caused the death of many a patient whose circulatory equilibrium had successfully been restored [2] The lesion, whether directly or indirectly, is always the consequence of ischæmia The tubular system is injured by anoxia simultaneously with the decrease of circulation there is a decrease in glomerular filtration, and, in consequence of anuria, in the tubules casts are formed and toxic effects manifest themselves [2, 3]

In animals, clamping the renal artery for four hours, three to four weeks after the other kidney has been removed, usually leads to death in uræmia Compression for two hours is usually survived, although complete restoration of renal function takes two to three weeks [4–6]

The pathogenesis of uræmia following renal ischæmia is identical with that associated with shock, and the morphological changes are also the same [5, 7] Considering that in both forms the basic problem is the disproportion between oxygen need and oxygen supply, it was assumed that by decreasing the tissues' oxygen demand it should be possible to prevent injury by ischæmia Experiments were therefore carried out to study the development of the lesions in hypothermia after administration of chlorpromazine

12 dogs which had had their right kidney removed three weeks before were used in the experiments They were divided into two groups In the control group of 6 animals, the renal artery was clamped for four hours at normal body-temperature In the "hibernated" group first 5 mg of chlorpromazine per kg body weight was administered in an intravenous infusion in two hours Then the animals were cooled to 24–25°C, and the renal artery was laid bare and compressed by means of a surgical clamp, with care to avoid crushing the accompanying nerves After four hours the clamp was released and the animals were re warmed Before arresting renal circulation, two normal clearance periods had been registered and also the non protein nitrogen level in the plasma After releasing the artery it was checked whether circulation had become normal in the kidney For fourteen days plasma non protein nitrogen values, and *p* amino hippurate and creatinine clearances, were determined every day in each animal The survivors were killed on the fourteenth day

Of the 6 animals in the control group, 5 died of uræmia within nine days Their plasma non protein nitrogen level ranged from 156 mg to 297 mg per 100 ml from the fourth day onwards Uræmia had also developed in the 6th dog, but this subsided by the fourteenth day In the hypothermic group all 6 animals survived In 5 animals the non protein-nitrogen level did not rise above the upper limit of normal (26–40 mg per 100 ml), in 1 there were high values for a few days

In the control group, grave cortical necrosis was present in every kidney, with calcium deposits in the tubules, extensive œdema, epithelial necrosis, and masses of casts, and in addition cellular infiltration from the renal pelvis In the hypothermic group, renal lesions were very slight, not exceeding some hydropic degeneration of a few tubules

In the control group, by the fourth day the clearance of *p* aminohippurate had decreased, on average, to 26% of the initial value, that of creatinine, to 16% (in agreement with the findings of others [8, 9]) In the hibernated group, *p* amino hippurate clearance remained normal in 4 dogs, while in the other 2 it decreased temporarily but regained the initial value before the fourteenth day Creatinine clearance did not change in 3 dogs, in 3 it decreased by 20–29%, and in 2 of these it was normal before the fourteenth day

We conclude from these observations that the lethal kidney lesion which develops as a result of ischæmia can practically be prevented by administration of chlorpromazine and subsequent cooling Since in previous experiments [10] it was found that the changes in renal function occurring in hypothermia do not persist after body-temperature has been raised to normal, on the basis of the present findings we feel justified in recommending administration of chlorpromazine and subsequent hypothermia preoperatively for operations in the course of which renal circulation is arrested Moreover, it seems probable that this procedure may help to prevent the renal lesions associated with shock

The findings described here are to appear in full in *Acta Physiologica Hungarica*

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P V VÉGHELYI
L HÁRSING
K LASZLÓ

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Appointments

BERESFORD C C M B Lond D P M physician superintendent The Retreat York

BLACK DAVID M B Belf D O M S part time asst ophthalmologist Walton Hospital Liverpool

CHURCHILL DAVIDSON I F J M B Camb D M R T physician radiotherapy department St Thomas s Hospital London

GARAI O F M R C P part time clinical asst cardiographic department Charing Cross Hospital London

JEFFERSON K E M B Camb M R C P F F R part time consultant radiologist Brompton Hospital London

NICOL C S M D Lond M R C P physician department of venereal diseases St Thomas s Hospital London

Births, Marriages, and Deaths

BIRTHS

OSTLERE—On April 19 at King s College Hospital, S E 5 to Mary (née Patten) and Gordon Ostlere—a son

DEATHS

MORRISH—On April 14 at Stafford, William John Morrish M D Lond M R C P, D P H late of Streatham Park London S W 16 spread but scanty serosal petechiæ Her appendix was removed

Histological examination of the appendix showed thrombotic microangiopathy in the mucosal and subserosal vessels, there was no other abnormality The significance of the vascular changes was missed at this time, and it was not until the pathologist saw sections from another case of thrombotic microangiopathy at a medical meeting some weeks later that he realised the nature of the lesions he had seen in the appendix He learned then that the patient had subsequently died elsewhere

Course —The patient had returned to school four weeks after the appendicectomy, seemingly well but a little pale and tired, due, it was thought, to the operation and epistaxis since then Two days after going back to school she complained of sudden headache, which rapidly became intolerable She had photophobia, neck rigidity, and a positive Kernig's sign, there was a macular rash on her trunk, with punctate hæmorrhage in some macules, and her temperature was 104°F She was admitted to hospital immediately as a probable case of meningococcal meningitis

On admission she was unconscious, shocked, and pulseless She was given 1 million units of penicillin and 50 mg of cortisone four hourly, as it was believed that she had developed the Waterhouse Friderichsen syndrome, the shock like state improved considerably, although she remained unconscious

Investigations —The C S F was uniformly bloodstained, no organisms were found in films or cultures Blood culture sterile Blood count red cells 2,600,000 per c.mm, Hb 6 3 g per 100 ml, white cells 8000 per c mm (neutrophils 6400, eosinophils 400, lymphocytes 1200), platelets 36,000 per c mm *When her coma lightened she was found to have* right sided hemiplegia, and cerebral hæmorrhage due to thrombocytopenia was then diagnosed She died on the day after admission

Necropsy —There were many petechiæ and ecchymoses in the skin and serosæ A very large hæmorrhage in the left cerebral hemisphere had burst into the lateral ventricle The other organs looked healthy

Histological examination showed thrombotic microangiopathy in the cerebral cortex, myocardium (fig 3), adrenals, and liver, no other tissues were sectioned

Abdominal pain has been reported in 15 cases of thrombotic microangiopathy (Altschule 1942, Engel et al 1947, Fitzgerald et al 1947, Muirhead et al 1948, Clinicopathologic Conference 1951, Symmers and Gillett 1951, Barondess 1952, Rackow et al 1952, Vassar and Spain 1953, Revill and Wilson 1954, Radnai et al 1954, Ritama 1954) It was a presenting symptom in 10 of these cases The patient whose case Gillett and I reported had polyarteritis nodosa, with an aneurysm in the pyloric region Of the cases reported by Vassar and Spain (1953) 1 had a chronic gastric ulcer and another had acute gastric ulcers, Ritama's (1954) patient had also had a chronic gastric ulcer In the rest of the cases there was no clear explanation of the pain

Laparotomy was done only in the present case, the finding of peritoneal petechiæ is noteworthy, especially as their significance was not then appreciated

Although the hæmolytic nature of the anæmia was not confirmed, this case was the only one of the 3 reported here in which the full tetrad of acute febrile illness, (hæmolytic) anæmia, thrombocytopenic purpura, and neurological disturbances developed The neurological manifestations were not of the classical changing and evanescent type observed in case 2

Massive intracerebral hæmorrhage has not been described in any published cases of thrombotic microangiopathy, but Adams et al (1948) mentioned an unpublished case in which a large hæmorrhage in the brain was the cause of death In most cases cerebral bleeding is petechial only, larger hæmorrhages (a centimetre or two in diameter) were described by Green and Rosenthal (1949), Pagel (1949), Meacham et al (1951), and March (1954)

Summary

The possible value of biopsy in the diagnosis of thrombotic microangiopathy is discussed

Biopsy, which so far has played little part in the study of this disease, should be considered as soon as the diagnosis is suspected, so that time may be gained for investigation of the disease and of possible lines of treatment

Combined rib, muscle, and skin biopsy may prove to be the method of choice

3 cases are described in which the diagnostic histological changes of thrombotic microangiopathy were found in surgical specimens (lymph-node, uterine curettings, and appendix) before the clinical syndrome developed

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Notes and News

FORWARDS IN MANCHESTER

"As a first step towards improving medical education in our University," Manchester are making some small but important adjustments in their curriculum[1] Revision had become demonstrably necessary because of the difficulty of arranging a time table classes clashed, students were doing clinical work in one subject while taking an examination in another, and no fewer than four examinations had to be taken in the last 18 months The object of the new arrangements is to remove these faults, to reduce the content of the course to free at least one long vacation, and to provide a period, at the end of the course for general revision

In the new curriculum the 2nd M B examination will be held 3 months earlier, and the introductory course preceding the clinical period will be discontinued in favour of a different type of instruction to students during their first medical and surgical appointments The time spent in the ear nose, and throat, eye, and skin departments will be reduced from 3 months to 6 weeks and the period at the skin hospital from a month to a fortnight The gynæcological appointment will be postponed to the final year and will include revision in obstetrics and pædiatrics Forensic medicine will have a terminal examination and social and preventive medicine will (very properly) come into all four subjects of the final (obstetrics and gynæcology, pædiatrics, medicine, and surgery) These and other changes will mean that no big examination is held between March of the fourth year and June of the sixth

Only those who have tried to alter a curriculum have a true conception of the difficulty of making even minor changes We congratulate the Manchester school on their improvements and trust that time will prove them right in describing these as "a beginning"

HOSPITAL ADMINISTRATIVE STAFF

LAST year in discussing the recruitment of hospital administrators[2] we mentioned a suggestion that King Edward's Hospital Fund should organise appropriate training for these men and women The need for such a plan was urged more lately in the Guillebaud report and by the Whitley Council for administrative and clerical staffs The King's Fund[3] has already announced its willingness to help and now the Government has launched a scheme that will make use of the Fund's offer

Trainees, who may be from inside or outside the hospital service, will be selected to fill training posts for a course of a maximum of three years They will be given practical experience of all branches of administration with different hospital authorities, along with courses of instruction at the Hospital Administrative Staff College of the Fund or the University of Manchester 16 posts are available for the first course, beginning in September The starting salary for trainees will be £540 (plus a small addition in the London area) with an increase of £20 in the second and third years Trainees already in the hospital service will retain their present salary if higher than this Fees and other expenses during training will be met Young people under 18 in the hospital service will be helped to continue their general education, and hospitals will be encouraged to institute on the job training schemes to give them experience of various types of work.

HEALTH IN INDUSTRY

THE London Transport Executive have published a detailed statistical analysis on sickness absence—"the absence from work accepted by the employer as attributable to sickness or injury"—among their employees[4] The book is the first analysis of its kind, and it will provide a standard for all concerned with the study of health in various branches of industry

Sickness absence statistics are not synonymous with morbidity statistics The records do not cover the episodes of sickness or injury which do not prevent the patient from following his employment chronic ill health which compels the patient to give up work altogether, or the sickness and injury of persons who are not employed and therefore do not come under an employer's observation They include, however, many short spells of absence which are not registered for National Insurance or friendly society purposes, because of the "waiting days" for benefit The problem is thus a specialised one, not covered in statistical tables hitherto available Its magnitude is reflected in a statement by the *Manchester Guardian*[5] "About seven million claims for sickness benefit are made each year, and the number of short absences from work because of sickness for which no claims are made is believed to be another six million"

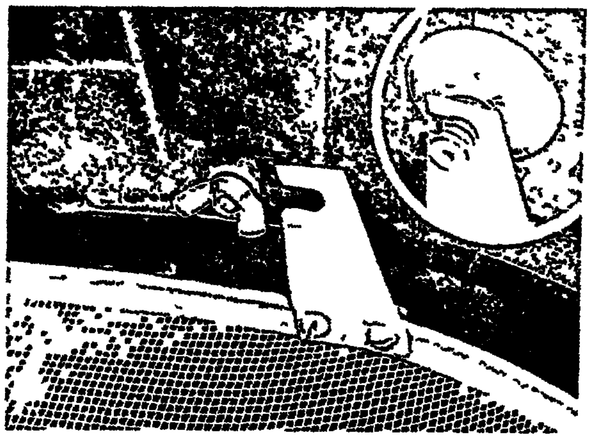
The data given in this book raise a number of questions of social and medical importance An interesting finding, for example, is that sickness which lasts more than four days tends to be measured in whole weeks Though this will need further elucidation, it seems that National Insurance regulations keep people away from work when they would otherwise be well enough to return On the other hand, we all know that a few days' convalescence after an acute illness may prove of benefit in the long run Another problem of great importance is the comparison between the periods of sickness absences of the under 45 and over-45 It would seem that, though long spells of absence, due to serious illness, are more common over the age of 45, short sickness absences are considerably commoner in the younger age group

SALARIES IN THE PUBLIC-HEALTH SERVICE

COMMITTEE C of the medical Whitley Council announces that agreement has been reached between the staff and management sides to recommend an increase in the salaries of doctors in the public health service as from April 1, 1956 The increase will be of $7^1/_2$% on the first £1250 of salary and of 5% on the excess of salary over £1250

IMPROVING A FIREGUARD

Dr G R Hervey writes Open fires still cause fatal accidents to children, in some instances even though a fire guard was in use The type of guard which seems to be most commonly used today is good in that it has a closely woven wire mesh, but less good in being so light that it can easily be moved by a one year old Fastening the guard to the fireplace overcomes this danger and greatly increases the safety given by the guard The accompanying figure shows one way in which this can be done, and the work required is well within the scope of any handyman' The lugs are made from small pieces of sheet metal The studs in the wall are $1^1/_2$ in × no 14 woodscrews with the heads cut off and the straight part of the shanks threaded with $^1/_4$ in Whitworth threads Fixing them is easier than it looks A hole is drilled through the tile and the cement beneath it with a no 14 'Durium' drill, a no 12 'Rawlplug' is inserted, and the stud is screwed in, held by two nuts temporarily screwed on to the shank and locked against each other These are subsequently replaced by the wing nuts and washers shown If loosening or tightening the wing nuts when the guard is moved is thought unduly burdensome, they can be replaced by domed washers backed by spring washers to give a friction grip A further modification made to this particular guard was the addition of a piece of expanded metal at the top to close a gap which



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[1] *Manchester University Medical School Gazette* January, 1956, p 11

[2] Lancet, 1955, ii 78

[3] Ibid p 1331

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there was no sensory change and little difference of power between the two sides

The aneurysm formed at the site of pressure of the axillary crutch on the arm and probably gave rise to an embolus, which lodged at the bifurcation of the brachial artery, producing the acute symptoms in March, 1954 It is uncertain whether the poor filling of the radial artery is a congenital abnormality or due to occlusion of the brachial bifurcation In view of this, and the possibility of further embolism, sympathectomy was done to maintain the collateral circulation and to prevent occlusion by spasm in the event of further embolism

Acute Thrombosis Due to a Blow

Case 5 —A man, aged 19, was, in May, 1954, standing on his bed cleaning his locker in an Army hut, when his friends pulled the bed from beneath him As he fell, the open door of the locker was between his left arm and his body, and its upper edge struck him a sharp blow on the arm just below the axilla Next morning his hand was cold, white, and powerless, and the hand and forearm were aching No pulse was palpable below the axilla Arteriography confirmed the diagnosis of thrombosis of the brachial artery

Operations —On June 18, 1954, at Queen Alexandra's Military Hospital, Millbank, the affected segment of artery was excised and an autogenous venous graft inserted Thrombosis developed in the graft, and on Sept 27, 1954, sympathetic ganglionectomy was done, removing the lower half of the stellate ganglion and the chain as far as the third thoracic ganglion A week later secondary hæmorrhage necessitated ligation of the second part of the subclavian artery

Follow up —When last seen in April, 1955, he had regained virtually normal use of his left arm, but found it a little weaker than his right There were no colour changes in the digits, but there was a delay of a few seconds in reactive hyperæmia There was still no palpable pulse in the arm

This case illustrates well the severe symptoms which may follow sudden occlusion of the main artery of a limb, and the good recovery which may ensue in the upper limb even after the loss of an extensive segment of the vessel

Case 6 —*A man, aged 45, slipped at work in 1953 and struck* the inner side of his right arm against the edge of a large wooden box Next day his hand was white and cold, and he had in the forearm an aching pain which was worse on raising his arm Severe ischæmic pain developed in the forearm muscles on attempting to use the limb When he was first seen by us in *October, 1955*, there had been *little* improvement The hand was still pale and cooler than its fellow, and he complained of pins and needles in his finger tips on raising his arm He found lathering his face difficult and could not satisfactorily strop his razor Using a hammer quickly produced ischæmic pain in the forearm

On examination the axillary pulse was normal, the brachial impalpable, and the radial much weaker on the affected than on the normal side Capillary blanching tests showed appreciable delay in the peripheral circulation in the fingers The diagnosis of thrombosis of the brachial artery was confirmed by arteriography, which showed local narrowing, amounting almost to occlusion, of a short segment of the artery in the middle third of the arm The vessels above and below appeared normal, and the films revealed no cause for the narrowing

Operation —Upper thoracic sympathetic ganglionectomy was done on Oct 24, 1955, and next day the hand was warm and of normal colour *The patient shaved without difficulty* and stropped his razor for the first time since his accident, there has been no further paræsthesia

Arterial Injury Associated with Skeletal Injury

Case 7 —A man, aged 22, was involved in a road accident at 11 P M on Oct 4, 1953, and admitted to hospital, where he was found to have an unstable fracture of the upper third of the right humerus, with no radial pulse on this side The hand was cold and blue, and there was no response to tolazoline or to papaverine He was admitted to St Mary's Hospital at 4 A M on Oct 5, 1953, in good general condition, with blood pressure 130/95 mm Hg There was considerable swelling of the upper arm and axilla, and the distal part of the limb was cold and blue as high as the upper third of the forearm No pulsation was detected below the axilla, and the capillary blanching test on the fingers showed a return of blood in 14 sec Despite these findings, power in the wrist and fingers was good, and there was no sensory disturbance The probable diagnosis was considered to be traumatic arterial spasm, and reflex heating was begun Four hours later the hand was warm and of normal colour, and the capillary blanching test was normal, but the arterial pulses were still absent

Operation —The fracture was therefore exposed and plated, and the main vessels were explored The posterior humeral circumflex artery had been torn from the axillary, and at this point there was a severe contusion of the main artery, with thrombosis for 8 mm Strong pulsation was present proximally The affected segment was excised and a freeze dried homograft inserted

Progress —Convalescence was normal, and in July, 1955, the patient reported his arm normal in all respects, and all pulses were present and equal on both sides

This case was explored despite the evidence of excellent collateral circulation, primarily to treat the unstable fracture, and the opportunity was taken to explore and repair the damaged artery

Case 8 was also of this type, rupture of the axillary artery being associated with anterior dislocation of the shoulder joint in an elderly patient This was treated by direct end to end anastomosis, with satisfactory restoration of the blood flow The arterial pulses were equal on the two sides when he was last seen three months after operation

Discussion

The group of patients who used an axillary crutch is of interest All the patients had used this type of crutch from childhood and for about fifty years before the onset of symptoms They had, in fact, used their arms as legs for most of their lives and entered the age group in which arteriosclerotic occlusions of the arteries to the lower limbs are becoming common During the three years in which these patients were seen only 1 was seen with spontaneous occlusion of an upper limb artery, compared with 225 patients who developed similar lesions in the arteries of the lower limbs It is therefore suggested that the stresses and strains normally borne by the lower limbs had been transmitted to the arms with comparable effects on the vessels

In none of these patients was there any evidence of damage to the axillary vein or to nerves, although the whole of the neurovascular bundle must be stretched over the head of the crutch and its components exposed to much the same pressure Nevertheless, all these lesions occurred at the site of pressure of the crutch on the limb, and clearly the trauma thus occasioned to the artery is a major factor in determining the onset of occlusion The diagnosis of occlusion of the axillary artery presents few difficulties, but in the management of occlusion several factors must be taken into consideration

(1) The prognosis is better than in similar lesions of the femoral artery, in that gangrene is less likely to supervene and, except in manual workers, any resultant ischæmic muscle pain is less of a disability in the arm than in the leg

(2) The site and extent of the block, by their effects on the collateral circulation, have an important bearing on the final disability

(3) The rate at which the artery becomes occluded largely determines the fate of the limb Gradual occlusion allows time for the collateral vessels to enlarge and to provide adequate channels when occlusion of the main vessel becomes complete, with the result that symptoms may occur only on exercising the limb A sudden occlusion, however, accompanied (as it may be) by spasm of a length of the artery and its collaterals, may leave the limb virtually bloodless and produce severe initial symptoms, with the danger of peripheral gangrene Gask (1913) quotes 2 cases of axillary thrombosis in which gangrene supervened

In cases of acute onset the aims of treatment are to prevent spread of the thrombosis and to dilate the

OSTEO-ARTHRITIS

AN APPROACH TO SURGICAL TREATMENT*

J Trueta

M A M D D Sc Oxfd F R C S F R F P S F R C S (C)

NUFFIELD PROFESSOR OF ORTHOPÆDIC SURGERY IN THE UNIVERSITY OF OXFORD

The findings reported here have been collected during the last four years or so and refer to the condition known in this country as osteo arthritis and in others as arthrosis This is, together with poliomyelitis, the most common of the severe disorders (other than the traumatic) *for whose treatment the orthopædic surgeon is responsible* One can foresee the day when paralytic poliomyelitis will rank with the other diseases—such as chronic osteo myelitis, skeletal tuberculosis, and rickets—which formerly constituted great orthopædic problems but are now becoming rare , but there has been nothing to raise our hopes of any early control of osteo-arthritis We are still in the unhappy situation of being forced to observe the progressive deterioration of the joint until, in many cases, it is sufficiently advanced to justify a major operation, for all lesser treatments so far attempted —lactic acid and other intra articular injections, cortisone, physiotherapy, hydrotherapy, and radiotherapy—have only too often failed to bring permanent relief

The present investigation was undertaken in the hope of learning something of the pathological changes in the early stages of the disease The main results of this work have already been published (Harrison et al 1953, Trueta 1953 1954), but since then I have gathered new facts from further experiments

Weight-bearing and Osteo-arthritis

The main conclusions already reported referred to the relationship between osteo arthritis and gravitation We found that the factor chiefly responsible for the initiation of the degenerative changes is the wrong distribution of intra articular pressures, which enabled us to explain why, in order of severity and frequency of occurrence, the spine, the hip, and the knee follow close to each other, with the ankle much less commonly affected Another finding was that the disorder begins always in the cartilage which, when it degenerates, is profusely invaded by vessels coming from the underlying areas of bone This vascular proliferation is responsible for changing the cartilage of the non-weight-bearing area into bone (osteophyte) and also for weakening the resistance of the bone in the weight bearing area Here the orientation of the trabeculæ permits an exact appreciation of the line of gravitation and thus of the exact position in which the femur is or was, held during life An explanation will be offered later of the mechanism underlying the reorientation of the trabeculæ which follow the lines of gravitation and increase the resistance of the bone

In the head of the femur the weight-bearing area which is submitted to increased direct pressure by the loss of the resilience and elastic protection of the cartilage begins to crumble away The bone thickens and acquires the radiological characteristics known as sclerosis or bone condensation The sclerosed area is cone shaped with the base of the cone on the surface of the bone and its vertex directed towards the centre (fig 1) It is an area of higher vascularisation and not of ischæmia as is commonly believed (fig 2) Nevertheless in the midst of this profuse vascularity and robust bone structure we find the so called bone cysts that contain fibrous, devitalised and sometimes even amorphous tissue

Orientation of Bone Trabeculæ

Both in the initial hypothesis and in the course of our work we suspected that the whole disorganisation of the joint including the vascular reaction leading to either bone atrophy or bone proliferation, was due to the inability of the cancellous bone to discharge its structural requirements once the hyaline cartilage had lost its resilience and elasticity

In higher animals and in both primitive and contemporary man evolution is evident in the type and direction of gravitational trabeculæ of the femoral head and neck In the gorilla the trabeculæ run, like the folds of an open fan towards all areas of the head (fig 3) , the same is found in a human child up to the age of 6 or 7 years In Neanderthal man we find the trabeculisation similar to that of a present-day boy aged 14 or 15 (fig 4) but in mature contemporary man the trabeculæ are concentrated towards the upper part of the head, the area which usually takes the weight in the standing position and also suffers the impact of the locking of the joint The ontogenic changes in man repeat here the phylogenic evolution We have acquired the ability of locking the hip joint in full extension—an ability which was not possessed by primitive man or by the apes (fig 5)

Apart from any contribution which endocrine or infectious disorders could make to early degeneration of the cartilage, osteo arthritis seems to be connected with the abnormal distribution of pressures within the joint The part of the cartilage which has not taken weight

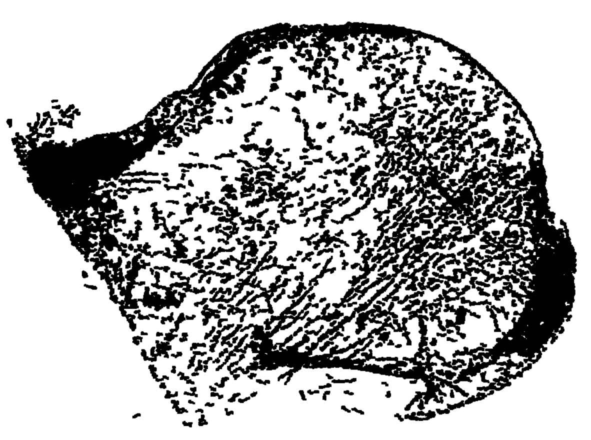

Fig 1—Section of osteo-arthritic femoral head showing triangular shape of area of sclerosed bone corresponding to weight bearing zone and osteophytes of non weight-bearing zone Sclerosis is conic in shape in unsectioned head

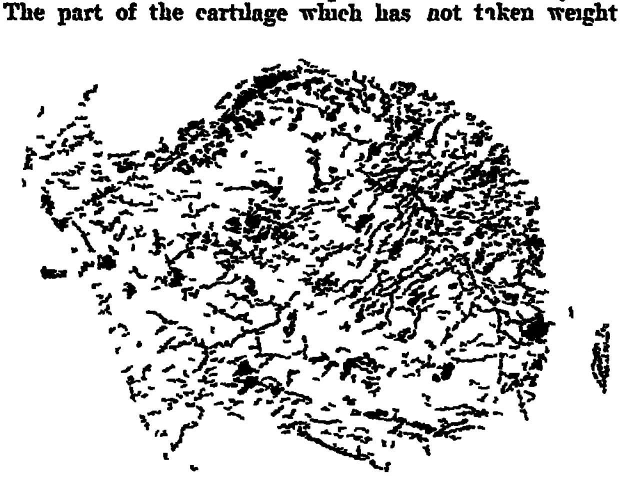

Fig 2—Highly vascular area almost exactly corresponding to zone of sclerosed bone

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* The Hugh Owen Thomas lecture 1955, delivered at the Liverpool Medical Institution on Oct 5 1955

TABLE I—MEAN HÆMOGLOBIN LEVELS RELATED TO PERIOD OF GESTATION

Period of gestation at first visit (wk)	No of patients	Mean Hb level (%)*	% of patients with Hb level below 10 15 g per 100 ml (70 %)	% of patients with Hb level below 8 7 g per 100 ml (60 %)
5–8	127	91 8	0 7	—
9–12	679	90 8	1 4	0 4
13–16	950	88 9	2 4	1 0
17–20	906	85 6	4 9	2 2
21–24	738	82 9	6 8	1 7
25–28	556	81 3	11 6	5 5
29–32	424	79 9	11 9	6 4
33–36	185	76 7	24 2	9 5
37 +	70	81 3	4 7	—

* 100 % = 14 5 g per 100 ml

possible Cases yielding more than one hæmolysed sample were omitted from the final analysis (see table II)

Hæmoglobin Levels During Pregnancy

In the City of Nottingham a sample of blood is taken from every expectant mother at her first visit to one of the ten antenatal centres of the local health authority The mean Hb levels of 4635 blood samples examined in 1951–52 are shown in table I

The mean Hb level is seen to be lower in patients whose pregnancy was more advanced, and the percentage of expectant mothers with a Hb level below the lower limit suggested by Adair et al (1936) is seen to be higher, the later they attend for their first visit

Benstead and Theobald (1952) showed that this "physiological anæmia" could be abolished by a dose of gr 18 of ferrous sulphate daily from the 24th to the 32nd week of pregnancy If this "physiological anæmia" can be abolished by a therapeutic dosage of iron from the 24th week, it should be possible to prevent its appearance by a smaller dosage of ferrous sulphate from an earlier stage, provided the mother is not already anæmic This was the principle underlying the present investigation

Material

In the first six months of 1953, 179 mothers whose Hb levels were not below 10 5 g per 100 ml volunteered to take part in the investigation They were divided into four groups according to the stage of pregnancy at which iron was introduced, as follows 16th week (30), 20th week (61), 24th week (45), and controls (43) Of these 179 women 65 (36 3%) yielded insufficient data to warrant their inclusion in the final analysis The reasons for their exclusion are shown in table II The remaining 114 mothers comprised 89 receiving iron and 25 controls

Hæmatological Findings

A detailed comparison of the findings in the control and 16th-week therapy groups is shown in table III and illustrated in the accompanying figure It was impossible to match these two groups exactly, but for the purposes of this study they are considered to be comparable in all relevant respects Thus, both groups were drawn from clinics in various parts of the city and received the same antenatal supervision The average age in the group receiving iron was 29 1 years and parity 2 5, compared with 28 1 years and parity 2 4 in the controls At the beginning of the investigation the Hb levels of both groups were similar

TABLE II—CAUSES OF EXCLUSION FROM INVESTIGATION

Group	Uncooperative or defaulted	Admitted to hospital	Premature delivery or abortion	Removed from area	Intolerance to iron	Hæmolysis of samples of blood	Hb fallen too low
Control	4	4	1	1	—	3	6
16th week	4	2	2	—	—	1	—
20th week	13	3	4	1	6	1	—
24th week	2	—	2	1	2	3	—
Total	23	9	9	3	8	7	6

In the control group there were the following findings

(1) A fall of 12% in the Hb level, maximal between the 32nd and the 36th weeks

(2) A fall of 13% in the red-cell count, maximal at 32 weeks

(3) A fall of 5% in the colour-index, maximal at 40 weeks

(4) A fall of 13% in the P C V, maximal between the 32nd and the 36th weeks

(5) A fall in the M C H C, maximal at 40 weeks

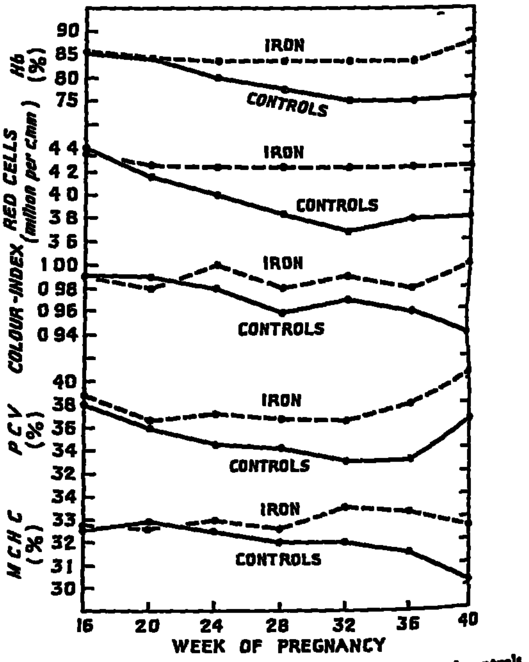
(6) An increase in the M C V, maximal at 40 weeks

All these findings, except the reduced colour index, are usually associated with the hydræmia of pregnancy

In the 16th-week therapy group all the estimations and indices were maintained within the limits of experimental error as defined by Whitby and Britton (1953), except the P C V which rose by 5 7%

To assess the value of the Hb level two further groups of mothers who received the same daily dose of ferrous sulphate were studied from the 20th and 24th weeks of pregnancy The findings are shown in table IV

In these two groups all the indices and the Hb levels were maintained The M C H C (the absolute index of iron deficiency) remained stationary, and the Hb levels, after a fall of 2–3%, reached at term a higher level than at the first examination



Hæmatological findings in 16th-week iron treated group and controls

In the three groups which received iron, therefore, the Hb levels and all the indices were maintained, whereas in the controls they all fell

Non-responders to Iron

Though it is true that the mean Hb levels were maintained throughout pregnancy in all three groups which received iron (tables III and V), there were some exceptions in each group Thus, of the 89 mothers who received iron there were 20 (22 4%) whose Hb levels were not maintained The hæmatological findings in these patients, comprising falls in Hb level, red cell count, P C V, colour index, and M C H C, were similar to those in the controls (The findings in these patients are included in the results given in tables III and IV) In all the cases been allowed to take place Some young rabbits, permitted to survive long enough, showed a progressive tendency to deformity of the knee caused by the early closure of part of one or other of the compressed epiphyseal cartilages In contrast to previous studies on the effect of pressure on the epiphyseal cartilage, we placed also the joint in the compressed area so that we could plot the joint changes against those of the epiphyseal cartilage

In a previous investigation (now in the course of publication) we had found that, if the blood supplying the metaphyseal side of the plate, or part of it, was interrupted, the layers of hypertrophic cartilaginous cells multiplied until often they were more than double the number of those of the normal cartilage (fig 7) The explanation is that blood is essential for the transformation of the cartilaginous columns of cells into bone, and in its absence these cells remain cartilaginous while new ones are added to the columns by the division of the basic layer at the epiphyseal end of the column When blood was allowed to penetrate the previously ischæmic area of the metaphysis, normal bone in its preliminary form appeared and the thickness of the cartilage was reduced to normal This tendency to recovery of the metaphyseal side of the growing cartilage was not paralleled by the cells of its epiphyseal side when submitted to an ischæmia of the same duration (fig 8) Then the ischæmic cartilage degenerated irreparably, and no further ossification took place when the blood was allowed to reach anew the ischæmic zone

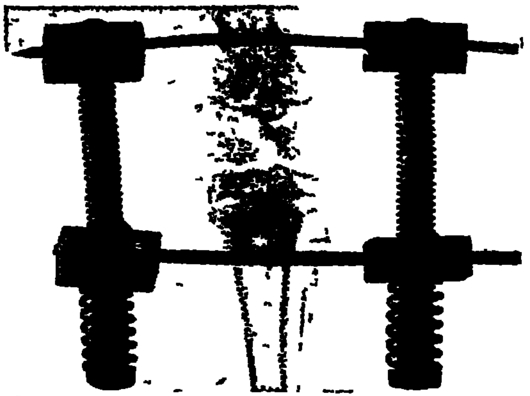


Fig 6—Apparatus used for compression of joint tissues, including epiphyseal plates, in growing rabbits

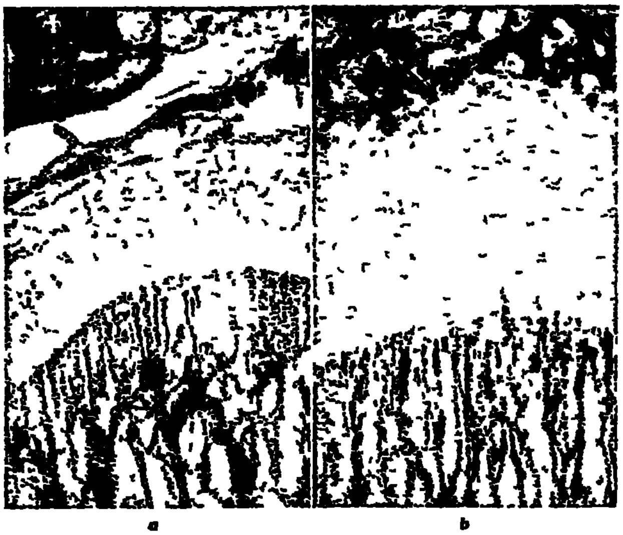

a b

Fig 7—(a) Normal epiphyseal plate with characteristic vascular loops , (b) metaphyseal blood flow has been substantially decreased by interposition of a polyethylene sheath

These experiments show that the behaviour of the epiphyseal cartilage depends largely on the rate of blood-flow near the two ends of its columns of cells Consequently the joint changes to be described here, obtained under the stress of persistent excessive pressure, if taking place together with the above-described alteration of the growing cartilage, can also be attributed to defective blood flow A few examples may suffice to show that this is so Following exactly the line of maximum pressure between the two transverse pins, we find in strict order advancing from the shaft towards the joint space (fig 9) (*a*) the increase in thickness of the growing cartilage , (*b*) above it some sclerotic thickened

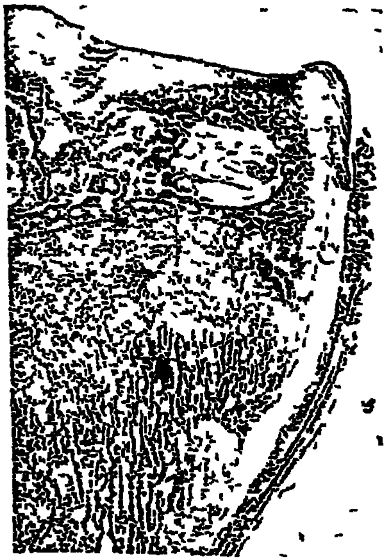


Fig 8

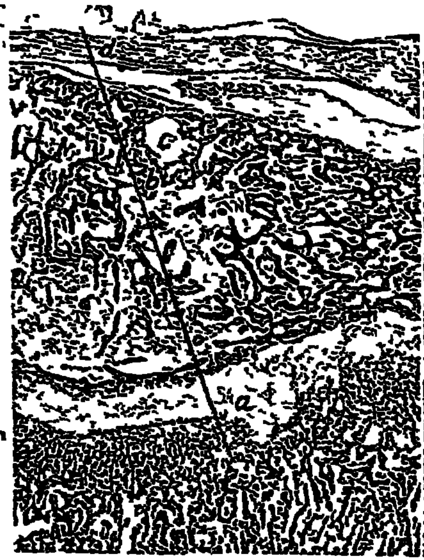


Fig 9

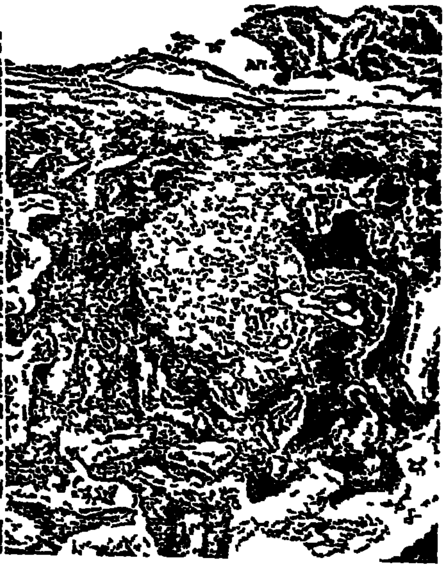


Fig 10

Fig 8—Blood supply to part of epiphyseal side of growth plate has been discontinued by interposition of polyethylene sheath Reproductive cartilaginous cells have degenerated but have continued growing without becoming incorporated into bone

Fig 9—Epiphyseal changes caused by persistent pressure : *a*, increased thickness of epiphyseal cartilage *b*, zone of sclerosis of bone , *c*, cyst ; *d*, degenerated articular cartilage.

Fig 10—" Cyst," filled by fibrous tissue without vascularisation, caused by pressure

investigation will be required only in a limited number of cases

We wish to thank Dr W Dodd, medical officer of health, City of Nottingham, for permission to make the investigation, and Mr F Hartley, F I M L T, for the technical work

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TUBERCULIN IN AQUEOUS AND OILY SOLUTIONS

SKIN-TEST REACTIONS IN NORMAL SUBJECTS AND IN PATIENTS WITH SARCOIDOSIS

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THE reaction to tuberculin in sensitised subjects depends on (1) the local persistence of the *tuberculin*, (2) the availability of sufficient antibody carrying cells, *and (3) the capacity of the tissues to react to inflammatory* stimuli resulting from the antigen antibody *reaction* The incorporation of tuberculin in an oily emulsion to form a "depot tuberculin" was found by Wassen (1936, 1939), Wassen and Swedin (1941), and Seeberg (1951*a*) to increase the local persistence of the tuberculin, leading to enhanced reactions of prolonged duration in sensitive subjects, and by Seeberg (1951b) to elicit positive reactions in patients with sarcoidosis, who had failed to react to *aqueous* tuberculin *solutions* The *conclusion* that the oily emulsion had prolonged the local persistence of the tuberculin is supported by the report of Talmage and Dixon (1953) that radioactivated proteins persist longer locally if mixed in a similar emulsion

We report here the results of comparing aqueous and "depot tuberculin" tests in

1 Normal Mantoux positive, normal Mantoux negative, and B C G vaccinated subjects
2 Patients suffering from sarcoidosis

Materials and Methods

Purified protein derivative of tuberculin (P P D, Weybridge) was used for testing in aqueous solution and in an emulsion consisting of 8 parts of light liquid paraffin *B P*, 1 part of anhydrous lanolin *B P* as the emulsifying agent, and 1 part of the appropriate concentration of the aqueous tubercul In the B C G -vaccinated subjects Old Tuberculin 1/100 w used throughout for the aqueous tuberculin testing Int dermal tests were made on the outer skin of the upper ar the volume of the injection being 0 1 ml of the aque tuberculin and 0 05 ml of the "depot tuberculin" and o the oily emulsion vehicle when this was used as a contr In preliminary *studies it was found that* P P D in a conce tration of 0 002 mg per ml *of the oily* emulsion gave a go reaction in sensitive persons, whereas higher concentratio *evoked too vigorous* reactions

Readings were made at forty eight hours and at interv *up to at least three* months Positive reactions to the "depot tuberculin" consisted of areas of erythema 20–40 *mm* i diameter with a central induration of 5–10 mm in diamete These reactions persisted long after any reactions to aqueo tuberculin had disappeared The possibility of non specifi irritation by the oily intradermal injection must be considered Seeberg (1951b) for example, *found that in tests made* on the thick skin of the thigh the vehicle excited erythemato reactions which could be readily distinguished from positive reactions to the "depot tuberculin" In this investigation the thinner, more elastic, skin of the upper arm was used, and there were no significant or enduring reactions at the sites where the vehicle alone was injected, or at the sites of the negative "depot tuberculin" tests These negative reactions to the oily material were marked by a barely palpable nodule in the skin

Results

Mantoux positive Normal Subjects

In 5 subjects giving positive reactions *to* 10 tuberculin units (T U) of aqueous tuberculin there were similar though more vigorous reactions to 5 T U of "depot tuberculin" at forty eight hours These reactions to both agents were 20–40 mm in diameter with central *induration 5–10 mm in diameter* The reactions to aqueous tuberculin subsided within the first seven to ten days, whereas the indurated erythematous reaction *to* the "depot tuberculin" persisted for two to three months, the erythema becoming duskier with time and showing superficial exfoliation

Mantoux-negative Subjects

18 normal subjects who failed to react *to* repeated intradermal injections of 100 T U *of* aqueous tuberculin also gave negative reactions to *5* T U of "depot tuberculin"

B C G -vaccinated Normal Subjects

9 healthy subjects who were negative to repeated *intradermal* tests with *100* T U of aqueous tuberculin (Old Tuberculin 1/100) were given intradermal injections of *the* "depot tuberculin," and *of* the vehicle, one month before the projected B C G vaccination Six weeks after the B C G vaccination, Mantoux tests were repeated with *100* T U of aqueous tuberculin on both arms for comparison with the earlier "depot tuberculin" tests The results were

Positive reactions to both aqueous and "depot" tests	[illegible]
Positive reactions to "depot" tests only	6
Positive reactions to aqueous tests only	3
Negative reactions to both aqueous and "depot" tests	

In 6 of the 9 subjects, reactions appeared at the sites of the previously negative "depot tuberculin" tests about ten days after the B C G vaccination They started insidiously with an area of erythema about 15 mm in diameter and became increasingly distinct during the ensuing week and remained unchanged for the next two months At this time the reactions became duskier and disappeared by the end of three months

5 persons failed to react to aqueous tuberculin after the B C G vaccination 4 of these had been vaccinated in the past and had either failed to convert or had converted transiently Of the 2 who reacted only to "depot tuberculin" and not to the aqueous tuberculin one was being vaccinated with B C G for the first time and the other was being revaccinated These 2 patients were studied *further by biopsy* examination of the B C G vaccinated sites, which showed active tuberculous

Causes of Failure of Arthroplasty

My own belief is that the biological, rather than the mechanical factors mentioned here are responsible for the failure of most current methods of arthroplasty The great contribution by Smith-Petersen had its benefits curtailed by the poor treatment that the metallic cup gave to the vessels of the femoral neck as much as by the great reduction in the area of the head bearing the gravitational stress The original method of the brothers Judet—a contribution which will be considered a landmark in progress towards a lasting solution—failed in numerous cases because the gravitational impact was too great for the vitality of the bone underlying and supporting the acrylic prosthesis New approaches by the Judets, Merle d'Aubigne Moore, Herbert, and others take into greater account the relatively frail nature of bone, and improvement in results must follow the use of methods that respect its vitality better I am trying a prosthesis which is mainly based on the experience of our previous failures, but also on the good features of both the Smith-Petersen and the Judet methods I prefer stainless steel and vitallium for their resistance and the absence of tissue reactions I use a large head whose contact with the newly moulded acetabulum resembles somewhat that of the Smith-Petersen cup—contact which was in general satisfactory (fig 13) Its shape is not far from that of the mushroom designed by the Judets the only essential difference is that it is connected to the neck not by the loose contact of the thick stem but by a screw with relatively large flanges and a narrow core

Preliminary results indicate that bone will remain alive between the flanges of the screw, as with previous types of screws The weight-bearing area—that of intimate contact between metal and bone—is very substantially augmented by the introduction of the large flanges The patient is kept off his feet for at least two months to allow sufficient time for the revascularisation of the central part of the neck in the spaces between the flanges So far the first part of the programme seems to be satisfactorily fulfilled The shortcomings, if any, of the method will probably appear before long

Conclusion

If, as I believe, osteo-arthritis is mainly a disease of the joint tissues and is caused by the wrong distribution of joint stresses, even in cases where an endocrine imbalance probably helps to weaken the resistance of the articular cartilage redistribution of pressures across the joint may bring lasting relief because the effects of excessive pressure are curable (Trueta 1954) It is this intrinsic curability of the osteo-arthritic process that makes me believe that, even in arthroplasty, lasting satisfactory results will be obtained when we learn to respect the laws of Nature, which work through the mediation of the blood-flow through the tissues Thus the explanation of Julius Wolff's law of the relation between function and form may be found in the stimulus that suffering or death has on life (in this study identified with the blood-vessels) in accordance with the dictum found in *Leviticus*, 17, 11 ' For the life of the flesh is in the blood "

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THE SURVIVAL OF BACTERIAL SPECIES UNDER BACTERIOSTASIS

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In 1946 Dubos reported that, in the presence of gramicidin, pneumococci died rapidly whereas *Streptococcus fæcalis* might survive for many days Since then much work has been done on the interaction of antibiotics, including the effect of bacteriostatic drugs on the action of bactericidal drugs Jawetz and his fellow workers (see review, Jawetz et al 1954) have taken a leading part in this and have emphasised the fact that bacteriostasis may gradually sterilise a culture But little seems to have been said about the varying ability of different bacterial species to survive under such conditions

Accordingly I decided to test the survival of some of the commoner pathogens, incubated in culture media containing bacteriostatic drugs in concentrations comparable to those attained in the body during treatment If considerable differences were found in the survival of different species this would I thought go some way to explain why bacteriostatic drugs will eradicate certain types of clinical infection but not others The results reported were all obtained with chloramphenicol, but additional tests leave little doubt that, with sensitive bacteria, the effects of the other predominantly bacteriostatic antibiotics—including the tetracyclines and erythromycin—would be similar

Bacteria undergoing bacteriostasis exist in very delicate balance between life and death, easily upset in any single test by minute changes in the environment. and an investigation of this kind. depending on in-vitro tests, is inevitably somewhat artificial. An attempt has been made to attain greater realism by using broth enriched with horse blood, and this has introduced an additional factor of variability into the experiments Variability is likewise to be expected, however, when one is treating different patients

Method

1 To prevent evaporation of the medium, screw-capped containers (usually of 5–6 ml capacity) have been used to hold the 2 ml. of suspension under test

2 Since bacteria undergoing bacteriostasis are presumably unduly susceptible to harmful agents, which may be present in an occasional bottle after cleaning, each test should be at least duplicated Misgivings on this score have led to many repetitions of the work.

3 The medium must permit free multiplication of the bacteria and for this purpose nutrient broth is often adequate —having the advantage that it allows a fairly accurate count of surviving organisms Using this broth however the test becomes highly artificial in the case of an organism like the staphylococcus which is mainly diplococcal in broth but forms clumps in serum and in pus Much use has therefore been made of 20% horse blood broth, first employed for delicate bacteria, such as *Hæmophilus influenzæ* and pneumococcus, but later for other species It was surprising to find that many leucocytes were still alive in horse blood which had been kept refrigerated for a week or more and that a considerable degree of phagocytosis took place But, although some of the bacteria may have been destroyed in this way, it appeared that the remainder, being aggregated in small clumps of dying leucocytes were better able to survive It seemed therefore that the conditions approximated to some extent to those in an abscess and that for certain purposes horse-blood broth gave more realistic results than ordinary broth

The numbers of bacteria surviving were estimated by spreading a standard drop (or, later a loopful) of broth on a sector of a blood-agar plate Aggregations of bacteria in the blood broth made accurate counting theoretically impossible but it was found that in practice the method gave a useful

BASAL HORIZONTAL LINES ON CHEST RADIOGRAPHS

SIGNIFICANCE IN HEART-DISEASE

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The value of radiology in the study of patients with mitral valvular disease is well established, and emphasis has recently been placed on the diagnosis of pulmonary hypertension from the chest radiograph Goodwin et al (1952) have described narrowing and tortuosity of the peripheral pulmonary vessels from angiocardiographic studies of patients with mitral stenosis and pulmonary hypertension Short horizontal lines at the periphery of the lower and mid zones of the lung fields were noted by Kerley (1951), and these too, have been regarded as a radiographic accompaniment of pulmonary hypertension in mitral stenosis (Goodwin et al 1952, Whitaker and Lodge 1953) Such lines may sometimes be a permanent feature of the patient's radiograph, in which case their pathological basis appears to be collagenous thickening with hæmosiderin deposition, occurring in the interalveolar septa (Parker and Weiss 1936, Fleischner and Reiner 1954) Transient lines, however, seem to be commoner, and these probably represent either dilated lymphatics (Kerley 1951) or the accumulation of tissue-fluid in the interalveolar septa (Gough 1955) In either case, the presence or absence of transient lines should depend on the magnitude of the pressure at the venous end of the pulmonary capillary, and Grainger and Hearn (1955) have described evidence in support of this A value approximating to this pressure can be obtained from calculations based on direct measurement of the left auricular pressure

The present study was undertaken to discover whether any relationship existed between the occurrence of these lines and either the left auricular or the pulmonary arterial pressure It was further hoped to reveal whether the magnitude of these pressures was a causal factor in the production of the lines

Materials and Methods

RADIOGRAPHIC METHOD

Standard postero-anterior radiographs were examined for basal horizontal lines, from 100 patients with mitral disease and 16 patients with pulmonary hypertension arising from other causes These films were then classified into three groups "lines absent," "lines poor to moderate," and "lines marked" All the assessments were made by an independent radiologist who was unaware of the left auricular and pulmonary arterial pressures Illustrative radiographs are not shown, owing to difficulty in reproducing fine lung detail

PRESSURE MEASUREMENTS

Left Auricular Pressure

Tracings of the left auricular pressure have been made from patients with mitral disease considered for valvotomy since 1952 as described by Allison and Linden (1953). From each of the last 100 of these curves a mean pressure was calculated (Wiggers 1950) The pressure curve throughout a heart cycle was considered, and both its length and the area under the curve were measured The mean pressure was then derived by dividing the area by the length This is illustrated on a typical tracing in fig 1, where the base of the rectangle equals the length of the heart-cycle and the height of the rectangle is the mean pressure To balance the respiratory variation of left auricular pressure, a heart-cycle in mid-inspiration or mid-expiration was selected for measurement This mean pressure probably approximates to the average pressure at the venous end of the pulmonary capillary

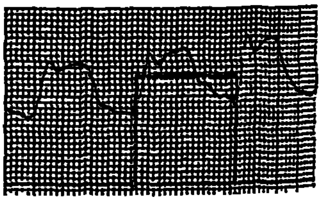

Fig 1—Tracing of left auricular pressure to illustrate method of deriving mean pressure

Pulmonary Arterial Pressure

Tracings of the pulmonary arterial pressure were obtained during the same bronchoscopy from 64 of the above 100 patients (Allison and Linden 1955) From each curve the mean pulmonary arterial pressure was calculated by adding a third of the pulse pressure to the diastolic level This value approximated closely to that obtained by integrating the pressure curve as in the determination of the mean left auricular pressure

The pulmonary arterial pressures of the 16 patients with pulmonary hypertension but without mitral disease were obtained during cardiac catheterisation, and mean pressures were again calculated from the tracings

The time interval between chest radiography and pressure recording was usually less than four weeks and never more than six months

RELATION OF LINES TO PRESSURES

The assessment of each radiograph was related to the pressures from that particular patient Thus, it was possible to relate lines to left auricular pressure in all of the 100 patients with mitral disease, and to pulmonary arterial pressure in 64 of them The association of each of these pressures was then compared with lines The 16 patients without mitral disease were included, in order to estimate the effect of pulmonary hypertension alone

The difference in pressures in the three radiographic groups of patients with mitral disease were compared statistically by Student's "t" test (Fisher 1930), conventional orders of significance being adopted Difference liable to occur less than 1 20 times by chance are described as barely significant, less than 1 100 times as moderately significant, and less than 1 1000 times as highly significant

Results

Relation between Horizontal Lines and Mean Left Auricular Pressure in 100 Patients with Mitral Disease

Lines were present on the radiographs of 63 of these patients No lines were found when the pressure was below 10 mm Hg, but they were invariably present at mean pressures exceeding 24 mm Hg The classification

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TABLE III—SURVIVAL OF SINGLE STRAINS IN VARYING CONCENTRATIONS OF CHLORAMPHENICOL

Species	Original no. of organisms per loopful	Overnight sensitivity (µg per ml.) (see text)	Chloramphenicol (µg per ml. in 20% blood broth)						
			64	32	16	8	4	2	1
H. influenzæ type 1	23×10^{5}	2			3/0	3/0	4/0	5–9/<10	1 – –
H. influenzæ (non-capsulated)	33×10^{5}	1			1/0	1/0	1/0	5/0	2 – –
Pneumococcus type 1	25×10^{5}	4–8			2/0	5/0	5/0	1 – –	
Strep. pyogenes	27×10^{5}	4	3/0	5/0	5/0	5/0	3/1000	1 – –	
H. pertussis (avirulent)	45×10^{5}	4–8		9/0	14/0	14/0	2 – –	1 – –	
Strep. viridans (endocarditis)	500×10^{3}	4–8		7/0	9/0	14/12	2 – –	1 – –	
*Staph. pyogenes**	71 × 10	8	7/0	14/500	14/1000	2 – –	1 – –	1 – –	
Strep. fæcalis	35 × 10	8	9/0	14/71	7 –	2 – –	1 – –	1 – –	

Notes: 1. Standard loopful estimated at 0·007 ml.
2. Symbol of results: 2/10 = loopful yielded 10 colonies after 2 days' incubation. – = moderate multiplication. – – = free growth. 5/0 = first sterile subculture on fifth day.

* Preliminary culture in serum broth with cocci in clumps.

broth allowed little more persistence of any of the brucellæ than was observed in broth—a period of about a week. These organisms, even more than the typhoid bacillus, live and multiply intracellularly and the methods described here are of little value in their study.

Strep. fæcalis has been singled out by Dubos and many others as an unusually persistent organism, and the present work has confirmed this. It was noticed, however, that not all strains of streptococci capable of growing on bile-salt medium—a simple preliminary test for the species—were of equal hardiness: even the three selected strains quoted in table II might vary in their performance. It is still remarkable that, when plain broth was the medium, subcultures over a period of two or three weeks sometimes continued to yield almost unvarying numbers of colonies.

Table III shows the results of titration of individual strains of various species in blood broth so as to show the course of events and the relation between the overnight sensitivity and the ultimate result. The overnight sensitivity was roughly estimated, after one night's incubation, from the discoloration of the blood when free multiplication was observed. With a large inoculum, however, some effect on the blood may be seen when multiplication has been largely controlled, as with the pneumococcal bottle containing 4 µg chloramphenicol per ml. The remarkable persistence in the 2 µg bottle of *H. influenzæ* I was shown clearly in films to be associated with agglutination, when on the twelfth day the colony count was slowly increasing after a fall to one colony on the seventh day; but the clumps were small and it was obvious that sterilisation had almost been achieved. Agglutination was also observed with the four organisms which persisted longest—*H. pertussis*, *Strep. viridans*, the staphylococcus, and *Strep. fæcalis*.

An avirulent strain of *H. pertussis* was used because in this form the organism grows more freely; in blood broth multiplication was rapid. It was thought that the ability to survive bacteriostasis was likely to be associated with the species rather than with virulence. The table shows that sterilisation of the cultures was slow, and it may be added that the colony count on the third day from the bottle with 32 µg chloramphenicol per ml. was estimated at about 1000. This result, considered in conjunction with those observed in treatment (Medical Research Council 1953), suggests that, as in scrub typhus, the ultimate extermination of the infection depends on the development of immunity, but that control of bacterial multiplication during the first week (when it is at its greatest) may modify the whole course of the disease, whose later symptoms may well be due to absorption of bacterial products during the earlier period.

Strains of *Strep. viridans* isolated from endocarditis may vary considerably, not least in their rate of growth. The organism referred to in table III multiplied slowly on blood-agar and it will be seen that sterilisation was rather slow, like that of *H. pertussis*. A similar result was obtained with another slowly growing strain from a case which failed to respond to penicillin even when combined with streptomycin, but was apparently cured when chlortetracycline (aureomycin) and penicillin were given together, the latter to prevent development of resistance. A third strain, a more rapid grower, died out in a few days in 10 µg chloramphenicol per ml. It is therefore suggested that although penicillin is the drug of choice in endocarditis other antibiotics should not be ignored if the bactericidal ones fail.

Discussion

As I have explained, chloramphenicol was used in these experiments because it was the most suitable of the bacteriostatic drugs for the particular purpose. I must emphasise that the indiscriminate clinical use of this antibiotic is to be condemned because its toxic effects, though rare, are so serious that they can be discounted only in face of very serious infection, such as enteric fever or certain forms of acute meningitis for which the drug is well suited if the heavy dosage can be maintained.

The results obtained are not surprising, but they may perhaps help towards a more rational use of bacteriostatic agents. On certain bacterial species these drugs have in fact a lethal effect, though their action is probably always somewhat slower than that seen with the bactericidal group. To other species however they will not be deadly unless backed by the full inflammatory reaction of the body, which is lacking in conditions such as acute meningitis and endocarditis.

The apparent correlation between the clumping or agglutination of bacteria and their longer survival may have significance in endocarditis—a condition in which the presence of antibody may cause both agglutination and possibly a slower rate of growth, thus making the extermination of the infection more difficult. The occasional appearance of the same phenomenon in susceptible species, *H. influenzæ* and the pneumococcus, was rather startling; but if, as seems possible, the persistence of a few organisms is promoted rather than prevented by the action of antibody, this can rarely have significance in meningitis, which is unlikely to occur in an immune individual. Nevertheless the frequent recurrence of infection of these two species in chronic bronchitis after antibiotic treatment (*Lancet* 1955) would be of interest in this connection if it could be shown that a true recurrence was usual, rather than a fresh infection.

It remains open to question whether, in a scientific sense, survival under conditions of complete bacteriostasis is possible even with such a species as *Strep. fæcalis*. As is shown in table III—and this was confirmed by further experiment—the strain used (N.C.T.C. 6782) died out in 64 µg chloramphenicol per ml., persisted with little change of numbers in 32 µg, and showed multiplication in 16 µg. When bacteria occur in clumps or chains it is impossible to be sure that certain individuals are not slowly reproducing themselves while others are dying. The margin in concentration of the drug is a small

TABLE II—FINDINGS IN 16 PATIENTS WITH PULMONARY HYPERTENSION ARISING FROM CAUSES OTHER THAN MITRAL DISEASE

Case No	Mean pulm art pressure (mm Hg)	Mean lt auricular pressure (mm Hg)	Lines	Diagnosis
1	88		–	Eisenmenger complex
2	104		–	" "
3	84		–	" "
4	60		–	" "
5	44	5*	–	Ventr septal defect
6	61		±	" " "
7	36	5*	–	" " "
8	77		–	" " "
9	103		–	Aur septal defect
10	56	2†	–	" " "
11	96		–	Pat ductus art
12	122	6*	–	" " "
13	68		–	Dextrocardia Single ventricle
14	29		–	Prim pulm Hypertension
15	68		±	" " "
16	78	2*	–	Emphysema Pulmonary hypertension

* Obtained by needle puncture during bronchoscopy
† Obtained by cardiac catheterisation

showed well marked basal horizontal lines She remained at home on medical treatment, awaiting operation, and on admission four months later a further radiograph of similar quality showed almost complete disappearance of the lines She was no longer orthopnoeic, though still dyspnoeic on exertion The left auricular pressure, measured two days before operation, showed a mean value of 17 mm Hg

This patient had a mean left auricular pressure of 17 mm Hg, associated with lines of "poor to moderate" quality If no radiograph had been taken at the time the pressure was recorded, the only available film would have been four months old and would have shown "marked" lines

Such a long time-interval was uncommon in this series, in most instances the interval was less than four weeks However, a period of medical treatment would always tend to lower the left auricular pressure, and patients in whom this occurred would have pressures lower than expected from the grade of lines shown on the radiograph taken before treatment was begun

2 Only on films of good quality can lines of "poor to moderate" degree be seen with certainty Under-penetration (accentuating the overlying soft-tissue shadows) or over-penetration (eliminating the fine detail) will each cause lines to be missed These radiographic factors may have applied to a few patients in this series These, in spite of being in the higher pressure range, would then appear in the "lines absent" group

3 The build of the individual patient sometimes caused difficulty, particularly in those female patients whose heavy breast shadows obscured the detail of the lower zones of the chest radiographs Here again, patients with left auricular pressures falling in the higher range would appear in the "lines absent" group

If the appearance of basal horizontal lines on the chest radiographs of patients with mitral disease depends on a critically raised left auricular pressure, such lines might be expected in other forms of heart disease in which pulmonary œdema occurs That they may appear in such patients is shown by the following case

A man, aged 38, was admitted to hospital in May, 1955, with a history of progressive dyspnœa on exertion for four months Chest radiographs showed basal lines of "poor to moderate" quality, and at this time the patient was orthopnoeic Myocardial infarction was diagnosed He improved slowly, and by June, 1955, he was no longer orthopnoeic, chest radiography now showed the lines to have disappeared He was discharged home, but was readmitted seventeen days later with pulmonary œdema from which he died Necropsy showed extensive myocardial and subendocardial fibrosis with one small area of recent infarction

This is one of several cases in which lines were first shown during a period of left ventricular failure such lines appear to be transient, and rarely fall in the "marked" category "Marked" lines would seem to require a high and relatively constant left auricular pressure—a state of affairs which must be unusual in disorders other than mitral disease

Finally, the relation of the lines to frank pulmonary œdema should be mentioned For pulmonary œdema to arise, the pulmonary capillary pressure must exceed the colloid osmotic pressure of the plasma protein (Hayward 1955) and tissue-fluid must pass through the alveolar walls into the alveoli themselves Parker and Weiss (1936) have shown that œdema of the interlobular septa can arise independently of alveolar transudation and that the thickness and texture of the alveolar wall plays an important part in determining whether or not alveolar transudation occurs It is reasonable to suppose that the recent appearance of lines in heart disease indicates a level of left auricular pressure not far below that necessary for production of pulmonary œdema Such recently occurring lines, therefore, are radiographic evidence of a dangerously high left auricular pressure and their appearance in a patient with mitral disease warrants early consideration of more intensive treatment including valvotomy

Summary

The chest radiographs of 100 patients with mitral disease have been examined for basal horizontal lines These were found in 63 patients, and the lines were correlated with both mean left auricular pressure and mean pulmonary arterial pressure A much closer relationship was found with the left auricular pressure than with the pulmonary artery pressure, the left auricular pressure has a dominant rôle in the production of lines

The chest radiographs of 16 patients with pulmonary hypertension arising from causes other than mitral disease were also examined 14 of these showed no lines, and the findings in this group support the view that pulmonary hypertension alone is not the cause of the lines

The recent appearance of basal horizontal lines on the chest radiographs of a patient with mitral disease indicates a dangerously high left auricular pressure, and warrants early consideration of more intensive treatment, including valvotomy

ADDENDUM

Since this paper was written Bruwer et al (1955) have presented evidence, based on determinations of pulmonary arterial and pulmonary capillary pressures recorded during cardiac catheterisation, that the pulmonary capillary pressure is the more important factor in production of lines Our conclusions accord with theirs

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The blood vessels in *lymph nodes* and *tonsils* may be heavily involved, but this seems to be quite unusual

Rackow et al (1952) suggested *gum biopsy*, in 5 of my cases multiple sections from many samples of gum and tongue at necropsy showed lesions deep in the tongue in 1 case and in the gums in none

The heavy involvement of vessels in the portal tracts prompted Rackow et al (1952) to suggest *liver biopsy* At about the same time, Chediak et al (1952) reported typical lesions in a piece of liver obtained during splenectomy (lesions were also present in the spleen) It is likely that the risk of hæmorrhage in thrombotic microangiopathy will contra-indicate liver biopsy except at laparotomy

Muscle biopsy has been uninformative in all 7 published cases in which it was recorded (Symmers and Barrowcliff 1951, Blackman et al 1952, Chediak et al 1952, Case Records of the Massachusetts General Hospital 1952, Adelson and Stefanini 1952, Adelson et al 1954, Fisher and Creed 1955), and in 6 unpublished cases known to me, in 1 of my cases muscle biopsy showed abundant typical lesions, although skin biopsy showed none

Skin biopsy, curiously enough, has rarely been done in thrombotic microangiopathy A positive result was obtained in 1 clinically typical case of mine in which, however, necropsy was not allowed (cited by Rackow et al 1952), the result was negative in 4 unpublished cases known to me, and in the case of Adelson and Stefanini (1952) Chediak et al (1952) did not give the result of their biopsy of a hæmorrhagic nodule in the forearm—presumably in the skin

Biopsy of *bone marrow* to demonstrate the vascular lesions was suggested by Fitzgerald et al (1947) Marrow biopsy for hæmatological investigation was described in 4 cases (Altschule 1942, Engel et al 1947, Epstein et al 1948, Goldenberg et al 1950) without mention of the blood-vessels it is not clear from the reports whether the term biopsy was used in these cases to describe films of marrow obtained by aspiration, or conventional histological examination of excised specimens Hæmatological examination of films of aspirated marrow has, of course, been recorded in many cases Cooper et al (1952) demonstrated thrombotic microangiopathy in paraffin sections of particles obtained by aspiration of bone-marrow in their 2 cases, the only other workers to adopt this procedure did not find vascular lesions in their case (Green and Green 1953) A high proportion of marrows examined post mortem in cases of thrombotic microangiopathy has shown the characteristic lesions, bone-marrow is probably second only to liver among tissues accessible to biopsy which are likely to contain diagnostic lesions Marrow biopsy may, therefore, prove of value, contrary to what is suggested by the few published observations

In contrast to the disappointing results of biopsy, there are 10 reports of finding the diagnostic lesions in *spleens* removed therapeutically

Splenectomy has been done during the course of the illness in 12 cases, in 2 the splenic vessels were not mentioned (Engel et al 1947, Ritama and Virkkunen 1953), but in all the others typical lesions of thrombotic microangiopathy were found (Baehr et al 1936, Muirhead et al 1948, Green and Rosenthal 1949, Gardner et al 1951 [case 2—see Singer 1954], Meacham et al 1951, Chediak et al 1952, Tacket and Jones 1952, Barondess 1952, Adelson et al 1954) In most of these cases the patient died shortly after operation

Careful histological study of every spleen removed in cases of hæmatological disorders may reveal unsuspected cases of thrombotic microangiopathy, the central arterioles and trabecular vessels are those likeliest to show the diagnostic lesions

The possible value of biopsy in the diagnosis of this disease requires further investigation *Rib biopsy* may prove to be the procedure of choice, and could be combined with biopsy of skin and muscle through the same incision

Rib biopsy demands particular care by the pathologist, when preparing the specimen, to reduce to the minimum the delay occasioned by decalcification, careful dissection is necessary because the thrombotic lesions are most numerous in the zone of the marrow cavity immediately beneath the cortex

The increasing accuracy of diagnosis in thrombotic microangiopathy has not so far had any material effect on the treatment of this mortal disease, nor has it added much to our knowledge of its nature This may be because diagnosis has usually been made at a late stage Biopsy done early in the course of any illness which presents unexplained hæmolytic anæmia, thrombocytopenia, or neurological disturbances offers the only means as yet known by which thrombotic microangiopathy can be recognised early enough to allow full investigation into its nature and treatment In 2 of the cases reported here diagnostic lesions were present for some time before the usual clinical manifestations developed Since not all cases run a fulminating course, even when the components of the tetrad begin to appear, there is some slight hope that biopsy immediately after the diagnosis is first suspected may give valuable time for investigation and treatment

Treatment

Until we understand the cause and nature of thrombotic microangiopathy, treatment can only be empirical Blood and platelet transfusions, splenectomy, sulphonamides, antibiotics, cortisone, corticotrophin, vitamins, and heparin have so far had no important influence on the course of the illness, except apparently in 2 cases, reported by Gardner et al (1951) (whose 2nd patient lived for nine months after splenectomy) and by Meacham et al (1951) (1 of whose patients had a remission lasting for over two years after splenectomy)

Case-reports

In the following 3 cases of thrombotic microangiopathy, the characteristic histological lesions were unexpectedly found before any clinical manifestations appeared The correct diagnosis was made at this stage in the first 2 cases, the lesions were not recognised until later in the 3rd case

PRESENTING WITH LYMPHADENOPATHY

Case 1 —A man aged 47, while living in England in 1953 began to show generalised enlargement of his superficial lymph nodes, without other symptoms His health had previously been good, apart from mild typhoid fever in 1942 He had been inoculated with typhoid paratyphoid vaccines several times while serving in the Afrika Korps A year before the typhoid infection his spleen was ruptured when a depth charge exploded nearby while he was swimming, his spleen was removed He had never had any chemotherapy or treatment with antibiotics

On examination three weeks after the nodes were first noticed the only abnormal findings were discrete, slightly tender nodes, up to 2 5 cm in diameter, in the neck, axillæ, and groins He had no fever

Investigations —Chest radiograph normal Urine normal Blood count red cells 5,100,000 per c mm, Hb 14 9 g per 100 ml, white cells 8600 per c mm (normal differential count), platelets in normal numbers in blood films Paul-Bunnell reaction negative Agglutination reactions (salmonellæ, shigellæ, brucellæ) were consistent with former T A B vaccination and typhoid fever, but otherwise negative Wassermann and Kahn tests negative Mantoux reaction positive (1 1000) Serum albumin level 3 4 g and serum-globulin level 3 3 g per 100 ml Erythrocyte sedimentation rate (E S R) 28 mm in first hour (Westergren)

Axillary lymph node biopsy —Sections showed simple reactive hyperplasia of the lymphoid follicles, many small arterioles and capillaries showed changes typical of thrombotic microangiopathy

TABLE I—MAIN DIFFERENCE BETWEEN LONG TERM AND SHORT TERM TREATED CASES

Treatment	Patients who have been in hospital last 30 days or more before delivery (%)	Average length of treatment in hospital just before delivery (days)
Long term	78	45
Short term	*10*	*15*

calculated term and treated in the hospital on average for the last 45 days before delivery, whereas the short-term group was admitted to hospital on the 35th day and treated for only the last 15 days The treatment, however, both medical and obstetrical, is the same in the two groups

Severity and Complications of Diabetes

Table II shows the severity and complications of diabetes and the number of primiparæ in the material of 1946–53 The diabetics are classified according to the system of White (1949) We have been forced to omit her group E because we have no information about the state of our patients' pelvic arteries About two thirds of the cases were severe (White's classes C–F), and our material, like White's, differs in this respect from most other material, which does not contain so high a proportion of severe cases

Short-term Group as Control

Table II shows that there is no major difference between the long-term and the short-term groups as regards severity and complications of diabetes, and, as already mentioned, all the patients are treated in the same way obstetrically and medically Only one factor varies—the duration of treatment So our material is well suited for research into the significance of the strict medical treatment in a hospital for a long time compared with a short time during the later part of pregnancy (table I)

Fœtal Mortality

The fœtal mortality (stillbirths and neonatal deaths within 10 days after delivery) of babies weighing 1000 g (2 lb 3 oz) or more is shown in tables III–V We have only a very few early abortions, spontaneous as well as induced, because such cases are admitted to other hospitals On the other hand, our puerperæ with their infants are routinely transferred to their homes (or other hospitals) on the 10th day after delivery

TABLE II—SEVERITY AND COMPLICATIONS OF DIABETES AND FREQUENCY OF PRIMIPARÆ IN LONG TERM AND SHORT TERM TREATED DIABETICS (1946–53)

—	No of cases (%)	Long term treated (%)	Short term treated (%)
White's classes			
C D, and F	64	65	62
D and F	32	33	32
Diabetic retinitis	23	26	21
Diabetic nephropathy (pyelonephritis)	24	28	22
Calcified arteries	5	8	4
Primiparæ	44	37	49

In 1926–45, before the introduction of the strict treatment, the over all fœtal mortality was 38% (table III) Since then this mortality has decreased to 27% (1946–52) and 15% (1953–55) The first decline from 38% to 27% was due to the introduction of the long-term group, in which the mortality was only 12%, whereas the fœtal mortality in the short term group (36%) remained unaltered The further drop in the total fœtal loss to 15% was mainly due to the fact that an increasing proportion of cases were long term and to small decreases in the fœtal mortalities—in the long term group to 8% and in the short term group to 27% The fœtal mortality in the long term group was about a third of that in the short-term group in both 1946–52 and 1953–55 Table IV shows that the difference of the mortalities, with a ratio about 1 3, holds good in several subdivisions of the material

The mortality in the short term group was due partly to pre coma or to other forms of gross neglect relatively early in pregnancy, further to death in utero or to early delivery for conditions—e g, malformations—which could not have been cured even by the most strict supervision and treatment Table V shows that such conditions are not the main cause of the difference in mortalities In the babies weighing at birth 1600 g ($3^1/_2$ lb) or more and alive at the onset of labour there was still a difference of 1 3 in the mortalities (6% in the long-term treated cases and 17% in the short term treated cases) In the total material of 122 infants born alive to long-term treated diabetics the neonatal mortality was 5 (4%), such a baby very seldom dies *in the neonatal period*

TABLE III—FŒTAL MORTALITY * FROM 1926 TO SEPT 30, 1955, CLASSIFIED BY TREATMENT IN 422 BABIES

Period	Treatment					
	Long term		Short term		Total	
	No of babies	Fœtal loss	No of babies	Fœtal loss	No of babies	Fœtal loss
1926–45	—	—	—	—	157	59 (*38%*)
1946–52	58	7 (*12%*)	94	34 (*36%*)	152	41 (*27%*)
1953–55	72	6 (*8%*)	41	11 (*27%*)	113	17 (*15%*)

* Stillbirths and deaths in first 10 neonatal days of babies weighing at least 1000 g (2 lb 3 oz) at birth

2 mothers died, but none in the last eighteen years

How much can we hope to reduce this fœtal mortality? In our total series major congenital malformations leading to the baby's death before the 11th postnatal day amounted to about 3% Moreover the perinatal mortality in Copenhagen is about 3% (Kærn 1955) (Perinatal deaths comprise stillbirths and deaths in the first week after birth of infants weighing at least *1000 g*) So perhaps a fœtal mortality of about 6% in pregnancy in diabetics might not be far from the mark

Classification of Risk to Fœtus

To estimate the risk to the fœtus we use the well known classification of White (1949) In our 1946–55 *material of 265 cases 13 belong to class A* with no fœtal mortality and 10 to class F with a fœtal mortality of 50% Although the number of cases is small, this fits perfectly with White's classification But table VI shows no pattern in mortalities of classes B, C, and D either in the long term group (this might be due to our treatment) or in the short term group We feel that White's classification is a good one although not entirely satisfactory—Oakley (1953) thinks the same—but we have not yet succeeded in devising a better one

Comparison with Other Treatments

It is appropriate to compare the results of our treatment with those of White (1949) and White et al (1953) from the Joslin Clinic in Boston, those of Peel and Oakley (1949), Oakley (1953), and Peel (1954) in London, and the report to the Medical Research Council (1955)

As is well known, White and her colleagues are the pioneers in this field and have reported the largest personal series (White et al 1953) and lowest fœtal mortality so far (10%) White's treatment consists in (1) treatment of diabetes to achieve the best possible blood cell morphology, osmotic and mechanical erythrocyte fragility tests, hæmoglobin level, and E.S.R. were all repeatedly within normal limits No hæmolysins or erythrocyte or platelet agglutinins were demonstrated. Wassermann and Kahn tests were negative Cerebrospinal fluid (C.S.F.) normal. Serum chemistry, kidney and liver function tests and urine normal, radiographs of chest and air encephalographs normal, electro encephalographs normal.

Two weeks after admission the patient went home, against medical advice

Second admission —Three days after discharge the patient was readmitted in a hypomanic state (There was no history of previous mental disturbance) After sedation she was found to have left hemiparesis, right facial twitching and choreo-athetoid movements of the right arm Next day the mental symptoms had disappeared, and the only neurological abnormalities were a left abducens palsy and some incoordination of fine limb movements There was a slightly puffy erythema of the forehead nose and cheeks Symmetrical, linear ecchymoses had formed in the skin below the breasts and across the scapulæ where her bust-bodice was tight and a few petechiæ developed under the sphygmomanometer cuff when her blood-pressure (120/70 mm. Hg) was measured No other clinical abnormalities were found and her temperature was normal Two days later she felt and looked ill, and her condition began to deteriorate Fever developed, and continued until she died, with a daily temperature range of 100–102 4°F On some days the tip of the spleen was felt Neurological abnormalities disappeared, except for persistent exaggeration of the left patellar and ankle reflexes, and a left extensor plantar response

Further investigations and course—The red-cell count and hæmoglobin level fell from 3,800,000 per c.mm. and 10 4 g per 100 ml. on readmission to 2,000,000 per c mm. and 5 0 g per 100 ml two weeks later, after which the anæmia remained stationary The white-cell counts remained about 9000 per c.mm, with about 6000 neutrophils No immature red or white cells were seen in the peripheral blood, reticulocyte-counts were between 10 and 18% Platelet-counts ranged between 20,000 and 250,000 per c.mm., with rapid variation throughout the illness, although the count was often below the "critical level" (40,000 per c mm.) there was no purpura or further bruising, and no more petechiæ were found when the blood-pressure was taken. L.E. cells repeatedly sought without success Blood-cultures sterile Agglutination reactions (salmonellæ, shigellæ, brucellæ, leptospiræ) negative Jaundice appeared on the fourth day and increased with the anæmia Urine trace of protein, excess urobilinogen but no bilirubin, a few red cells. Cortisone (300 mg daily) and aureomycin were given from the day of readmission, without effect Repeated transfusions of fresh blood through silicone-treated apparatus did not influence the anæmia or the platelet-count the variations in which were independent of the treatment A fortnight after readmission the patient began to have hallucinations and went into a withdrawn, schizoid state Choreiform movements and other transitory neurological abnormalities recurred, and her general condition deteriorated rapidly Cortisone was administered in diminishing doses over four days, and was then discontinued The patient began to have severe headaches, the retinæ and C.S.F. were normal. There was frank hæmaturia once The blood-urea level rose to 108 mg per 100 ml. and urinary output fell The blood-pressure remained normal Seven weeks after the initial fit she collapsed with sudden abdominal pain and rapidly deepening shock, and she died an hour later while being prepared for laparotomy

Necropsy—Many hæmorrhagic ulcers in the jejunum and ileum, one ulcer had perforated, flooding the abdominal cavity with intestinal contents and blood Scattered serosal petechiæ. Pale, tough vegetations, up to 0 4 cm. in diameter, on mitral cusps cultures of these were sterile Spleen (weight 200 g) and all other organs appeared healthy

Histological examination showed thrombotic microangiopathy in most organs, particularly the myocardium, adrenals, liver (fig 2), brain, bone-marrow and myometrium, the lesions were scanty in ovaries, uterine tubes, stomach, colon, and kidneys, and were not found in skin, skeletal muscle, or lymph nodes The mitral vegetations had the histological appearances of verrucose endocardiopathy (Libman-Sacks disease)

This patient's history included 3 features of possible ætiological significance (1) sensitisation to sulphonamides, (2) throat infection three weeks before the acute illness and (3) onset of symptoms while sunbathing

Sensitisation has been noted in other cases of thrombotic microangiopathy—to sulphonamides (Engel et al 1947, Fitzgerald et al 1947) penicillin (Gendel et al 1952), oxophenarsine (Symmers 1956), formaldehyde (Clinicopathologic Conference 1951), and adhesive tape (Bernheim 1943) The significance of such sensitisation is not clear

A recent *acute infection*, usually of the upper respiratory tract, has been noted in several cases

Laszlo et al (1955) described a case in which the illness developed after some weeks of *sunbathing*, the clinical manifestations suggested disseminated lupus erythematosus, and L.E. cells were found.

L.E. cells were sought unsuccessfully in 9 cases including the present one (Gendel et al 1952 Case Records of the Massachusetts General Hospital 1952 Barondess 1952 Cooper et al 1952 Green and Green 1953, Vannucchi and Doni 1953, 1954 Clinicopathologic Conference 1955) Skin changes resembling lupus erythematosus were observed by Gendel et al (1952) as in this case Abnormalities of porphyrin metabolism were present in 1 case (Clinicopathologic Conference 1951) and were absent in the present one Verrucose endocardiopathy was reported in 10 previous cases (Baehr et al 1936, Engel et al 1947, Meacham et al 1951, Gendel et al 1952, Barondess 1952, Vassar and Spain 1953) this is interesting because it supports the possibility of a relation between thrombotic microangiopathy and disseminated lupus erythematosus and other "collagen diseases" (Symmers 1953, Laszlo et al 1955) Menorrhagia has been noted in 4 other cases (Fitzgerald et al 1947, Blackman et al 1952, Radnai et al. 1954) and metrorrhagia in 5 (Muirhead et al 1948, Epstein et al 1948, Green and Rosenthal 1949, Ellison and Lloyd 1954, Stuart and MacGregor-Robertson 1956) The absence of purpura in this case is particularly striking in view of the repeated finding of platelet-counts well below the "critical level" Intestinal perforation, the immediate cause of death in this case has not been described before in thrombotic microangiopathy

PRESENTING WITH ABDOMINAL PAIN

Case 3 —A previously healthy girl, aged 15 while at school, had a sudden sharp pain in the right iliac fossa and vomited The pain lasted for a few seconds only, and was followed by a persistent dull ache in the hypogastrium. Her doctor saw her a few hours later Because her periods had occurred regularly every thirty days since their onset two years earlier, and she was at mid-cycle, he considered that the pain was caused by the bursting of an ovarian follicle, however, there was tenderness in the right iliac fossa, and he sent her to hospital

On admission his diagnosis was confirmed by the finding of a hæmatoma in the right ovary, with a blood-clot protruding from it and blood in the pelvis, examination of the rest of the abdominal cavity showed no abnormality except wide-

Fig 3—Thrombotic microangiopathy in myocardium in case 3. (Hæmatoxylin and eosin × 250)

Effect of Long-term Treatment

We are convinced that the decrease in total fœtal mortality in our series through years is due to our long-term treatment Although expert obstetrical management is a *conditio sine qua non*, the main credit goes to the treatment during pregnancy, because the long term and the short term cases have had the same obstetrical care during delivery

The main factors in our treatment are treatment by one physician, confinement to hospital for several weeks, and keeping down the blood-sugar level The "one physician close supervision" during the last months of pregnancy seems to be necessary to get a low fœtal mortality As regards confinement to hospital we have to admit that, although treatment in hospital for a long period has been shown here to be superior to treatment for a short time, we have not tried to prove that such a period of treatment in hospital is superior to very close personal supervision of an ambulant patient (cf White 1949)

Clearly, methods including close supervision of the pregnant will decrease the number of cases with precoma, lead to early treatment of toxæmia and other complications, and thus lower the fœtal mortality In addition our long-term treatment has a strong effect on the baby the long term treated baby has a higher blood sugar level (Pedersen 1952, Pedersen et al 1954) and is smaller (Pedersen 1954b), the amount of amniotic fluid is smaller (Pedersen and Jørgensen 1954), and the long term treated baby withstands labour better than does the short-term treated baby On all points so far examined the long-term treated babies are more like normal babies In contrast to this, the number of complications during delivery and the number of obstetrical procedures has not decreased in the long-term treated mothers compared with the short-term treated mothers (unpublished) The effect on the baby seems to be due either to the lowering of the mother's blood sugar level for a long time or to unknown factors favourably influenced by this strict control of the diabetes—a control which can hardly be achieved outside a hospital

We must conclude that the long-term treatment is a prophylactic procedure whose effect is to make the babies more like normal babies in different ways At present we cannot tell exactly which mechanisms are involved, except that the metabolism of the fœtus must be more normal (Pedersen 1952)

Summary

The long term treatment of pregnant diabetics is described

By applying this treatment to 130 cases in 1946–55 the fœtal mortality was reduced to 10%, whereas in 135 short term controls it was 33%, compared with 38% in 157 cases in 1926–45

The total fœtal mortality in 265 cases in 1946–55 is steadily decreasing but varies according to the proportion of long term to short term treated cases

At present, in the material of 1953–55, the total fœtal mortality is 15% in 113 cases, 64% of the cases belong to the long-term treated group and have a fœtal mortality of 8% In these last 113 cases 17 cæsarean sections were done (15%)

Theoretically the lowest fœtal mortality achievable is at present about 6%

To get a low fœtal mortality it is necessary to give intense medical treatment by one or a few doctors during pregnancy and to have access to one or a few expert obstetricians It is unnecessary to give sex hormones or to do many cæsarean sections

Our treatment is prophylactic, making the babies more like normal babies in different ways, especially as regards neonatal blood sugar level, weight and length, volume of liquor amnii, and fœtal mortality

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VITAMIN-A LEVELS IN IDIOPATHIC HYPERCALCÆMIA

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The ætiology of the syndrome described by Lightwood (1952) as "idiopathic hypercalcæmia in infants with failure to thrive" is unknown, but it has been suggested that intolerance of vitamin D is the cause (Hutchison 1955) In view of the close association of vitamin A with vitamin D in nature, the plasma vitamin A levels in this syndrome were studied as part of an investigation into vitamin-A metabolism in infancy

Material and Methods

The plasma vitamin A levels of 7 healthy children, 5 marasmic infants, and 8 infants with idiopathic hypercalcæmia were estimated before (fasting levels) and four hours after a large oral dose of vitamin A 2 of the infants with idiopathic hypercalcæmia (cases 11 and 13) also had renal acidosis The preparation of vitamin A used was synthetic vitamin-A palmitate in arachis oil ('Avoleum,' B D H) The dose administered was 12,500 international units (I U) per kg of body weight up to a maximum of 250,000 I U One infant with idiopathic hypercalcæmia (case 12), however, was given 20,000 I U per kg of body-weight In a further 10 healthy children only the fasting plasma vitamin A levels were estimated The patients received their ordinary diets, but no patient was given vitamin A concentrates for at least forty-eight hours before the date on which the estimations were made The term "fasting" has been applied to the plasma vitamin A

TABLE I—PLASMA VITAMIN-A LEVELS IN HEALTHY CHILDREN

Child no	Age	Weight (kg)	Plasma vitamin A (I U per 100 ml) Fasting (duplicates)		4 hours after the standard oral dose of vitamin A (duplicates) *	
1	3 mos	4 9	160	—	605	605
2	4 mos	7 3	130	—	805	—
3	15 mos	14 6	120	120	195	180
4	3 yr	15 3	200	—	500	530
5	4 yr	15 0	70	120	1250	1260
6	5 yr	20 0	125	—	195	—
7	8 yr	—	160	—	470	—
8	3 yr	—	195	180	—	—
9	4 yr	—	175	—	—	—
10	4 yr	—	150	180	—	—
11	6 yr	—	125	160	—	—
12	7 yr	—	205	—	—	—
13	8 yr	—	165	—	—	—
14	8 yr	—	115	175	—	—
15	8 yr	—	70	100	—	—
16	9 yr	—	135	—	—	—
17	10 yr	—	100	110	—	—

* The standard oral dose of vitamin A was 12 500 I U of vitamin A palmitate in arachis oil per kg of body weight up to a maximum of 250 000 I U of vitamin A

CLOSED TRAUMATIC LESIONS OF THE AXILLARY AND BRACHIAL ARTERIES

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IN three years we have seen 8 patients in whom closed injuries led to serious lesions of the axillary brachial artery. Since few such cases have been published, we report them here.

Injury by Axillary Crutch

This group comprises 3 cases of thrombosis and 1 of aneurysm of the axillary artery. 6 cases of thrombosis from this cause have previously been published.

Platt (1930) described 2 examples, in men aged 38 and 46, both of whom had used axillary crutches from early childhood and eventually recovered full function of the limb without active treatment on changing to an elbow crutch.

The patient of Leriche and Stricker (1929) lost two fingers from gangrene before Leriche did an arteriectomy, removing 10 cm. of the artery; two years later the patient was free from pain and vasomotor symptoms.

In the cases described by Ryle (1922) and by Souques and Terris (1924) the outcome was not stated.

The present cases illustrate the symptoms and varying course of the condition.

Case 1.—A man, aged 56, who had used a left axillary crutch since an above knee amputation of the left leg in 1907, was admitted on Dec. 11, 1954, complaining of numbness of the left hand and pain in the left forearm. Nine days previously he had wakened at 1 A.M. with tingling, numbness, and loss of power of the left hand, which had been normal the previous evening, though earlier in the day he had knocked it against the door of a railway coach. He noticed in the left forearm a dull aching pain which subsequently he found to be aggravated by use and relieved partially by rest with the limb dependent.

On examination his left hand was cold and pale, with no œdema and no distension of the superficial veins. He was barely able to flex or extend the fingers or wrist against gravity, though the power of elbow movements was little less than normal. Sensation to light touch and to pinprick was reduced over the whole limb below the elbow. The left axillary pulse was easily palpable as far as the posterior fold of the axilla, below which the artery could be felt as a pulseless thickened cord. The radial and ulnar arteries were impalpable. The pulse-rate was 80, blood-pressure 160/90 mm. Hg, and the heart clinically normal. All pulses in the right limbs and the left femoral pulse were normal and the vessel walls not thickened. The Wassermann reaction and Harris tests were negative. The diagnosis of axillary artery thrombosis was confirmed by arteriography, which showed 4½ inches of artery to be occluded.

Operation.—On Dec. 20, 1954, left sympathetic ganglionectomy was done, the lower half of the stellate ganglion and the chain to below the 3rd thoracic ganglion being removed.

Postoperatively the left hand became warm and of normal colour. The patient was provided with an elbow crutch and warned against using the axillary one. Nevertheless, in view of the difficulty of using an elbow crutch with a weakened hand, he had continued to do so. On Jan. 28, 1955, pulsation was first detected in the brachial and radial arteries, though he complained still of numbness and weakness of the hand and hypoæsthesia persisted below the wrist. In August he reported the return of normal sensation and no colour changes, but still some weakness of his hand.

Case 2.—A man, aged 54, had used a right axillary crutch for as long as he could remember after poliomyelitis in early childhood. He consulted his doctor for an attack of sudden pain in the right forearm and hand, associated with coldness, numbness, and loss of power of the limb.

On examination no arterial pulse was felt below the axilla, and the limb showed the appearance of threatened gangrene.

Operation.—Upper thoracic sympathetic ganglionectomy was done, and gradual recovery ensued. The patient is now symptom-free and following his normal occupation of book-binding.

These two patients illustrate sudden complete occlusion of the axillary artery after the use of an axillary crutch. In neither was there overt evidence of generalised arterial disease or any evidence of embolism.

Case 3.—A man, aged 57, with bilateral flaccid paralysis of the lower limbs since the age of 6 months, had used axillary crutches from early childhood. In January, 1953, he noticed in his right hand tingling and numbness, which became gradually worse. In February he developed pain in the right forearm and noticed that his fingers went white on raising his arm to the horizontal, and that the radial pulse was absent, with thickening along the course of the vessel. He was seen by a physician, who confirmed the diagnosis of thrombosis of the radial artery; above this the pulsation was normal. He was given tolazoline and nicotinic acid. By early May the thrombosis had extended upwards to the brachial artery, and he complained of pain at rest in his finger-tips. Anticoagulant therapy was started, and he was transferred to St. Mary's Hospital.

On admission he said that he could not sleep for pain unless his arm was hanging down. His right hand was pale and cold, and severe ischæmic muscle pains developed in his forearm on the slightest exercise of his fingers. His right axillary pulse was strong, but the brachial pulse ceased abruptly in the middle of the arm, below which the artery was palpable as a thickened cord. The pulses on the left side were normal, but the arterial walls were thickened though not tortuous. The reactive hyperæmic flush reached the level of the metacarpophalangeal joint 22 sec., and the finger-tips 46 sec., after release of the occluding cuff, compared with 3 and 5 sec. respectively on the normal side.

Operation.—Sympathetic ganglionectomy, removing the stellate ganglion and the chain to below the second thoracic ganglion, was done on May 19, 1953. This relieved the rest pain at once, and the hand became much warmer, but there was little improvement in the ischæmic muscle pain. On May 30, 1953, the thrombosis had extended up to the third part of the axillary artery, and when shaving he was compelled by ischæmic pain to stop every minute to lower his arm to his side.

Follow-up.—He was seen in September, 1955, when he was symptom-free at rest and could write, type, and play the piano without pain but developed ischæmic muscle pain if he shook a bottle vigorously (he is a dispenser). Pulsation has not returned at the elbow or the wrist.

The sequence of events in this patient is thought to be damage to the axillary artery by his crutch leading to partial occlusion of the vessel; subsequent breaking free of an embolus, which lodged in the radial artery and caused the initial symptoms; followed by ascending thrombosis, which eventually reached the site of the original abnormality in the axillary artery.

Case 4.—A woman, aged 58, with congenital hypoplasia of the right leg, had used since the age of 3 years a single unpadded axillary crutch made by her father and renewed as required. In January, 1954, she noticed in her right axilla a small swelling which her doctor considered to be of no significance. On March 8, 1955, she developed a sudden severe pain in her right arm from the shoulder downwards, and her hand and fingers became numb, cold, white, and powerless. She had no treatment other than rest, and a month later the pain had passed off, she could do her housework, and her hand was no longer white but was still so cold that she used to warm it on the teapot.

On examination in May, 1955, arteriography showed a fusiform aneurysm of the lower axillary artery and recanalisation of an occlusion of the brachial artery at the elbow. The ulnar artery was carrying most of the forearm circulation, and the radial artery filled poorly.

On admission on June 7, 1955, she said she was symptom-free. All the pulses were present in the right upper limb, though the radial was weaker than its fellow. The aneurysm was easily palpable, and she said that this was the lump she had noticed in 1954. Her hands were of normal colour, and show that vitamin-A metabolism is abnormal in idiopathic hypercalcæmia

I wish to thank Prof Stanley Graham and Dr J H Hutchison for much helpful advice and criticism and for permission to study patients treated in their wards, Mr W M Dennison for permission to study patients treated in his wards, Dr Ellis C Wilson, in whose laboratory this work was done, for his interest and helpful advice, and Dr R A Robb, of the mathematics department of the University of Glasgow, for the statistical calculations

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POTASSIUM-CHLORATE POISONING WITH OLIGURIA

TREATED BY THE BULL RÉGIME

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IN 1882 Riess noticed unusual globules and granules in the erythrocytes of a patient who died of renal failure after swallowing about 30 g of potassium chlorate Similar bodies were described by Heinz (1890) in animals poisoned with acetylphenylhydrazine

Potassium chlorate is still used medicinally as a local antiseptic, either as a solution or as lozenges for sore throats and oral ulcers Poisoning is rare nowadays but may follow a single large dose or repeated small doses

Witthaus (1911) collected 143 examples, of which 116 were fatal He noted that poisoning was usually accidental, but he recorded 15 examples of suicide, of which 2 may have been accidental, and 3 of homicide

Cochrane and Smith (1940) reported a patient with nephritis who died of renal failure following ingestion over three days of 30–35 g of potassium chlorate dispensed in error for potassium chloride

Gordon and Brown (1947) described yet another example in which death was due to renal failure

A R Cushny (Grollman and Slaughter 1947) noted that death in subacute poisoning resulted from renal failure

The following example illustrates the toxic effects of potassium chlorate and the value of the Bull régime in the treatment of the associated oliguria

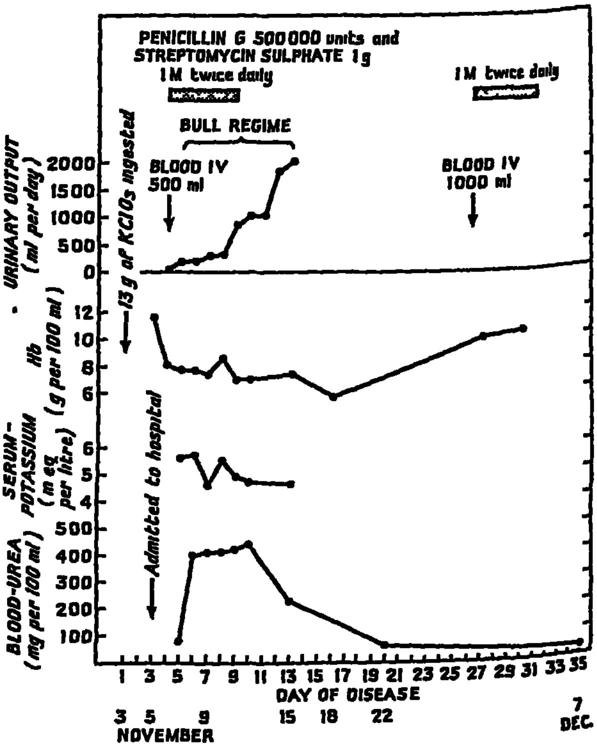
Case-report

A caretaker, aged 54, with a past history of chronic bronchitis, was admitted to hospital on Nov 5, 1954 Two days previously a frænal ulcer had developed to which he had applied during an hour or so about 13 g of potassium chlorate This he had obtained from his chemist He had not followed the pharmacist's instructions to wash out his mouth and had swallowed the crystals The same night anorexia, nausea, and a burning retrosternal pain developed He noticed that he was blue and that his urine and stools were dark There was no past history of jaundice, but he had been a moderately heavy drinker of spirits and beer

On admission he was ill, with signs of acute bronchitis and pyrexia (99°F) There was no trace of the frænal ulcer, but there was gross pyorrhœa He was jaundiced but not cyanosed, and his liver was enlarged to the umbilicus and tender His spleen was impalpable, and there was no purpura Clinically the cardiovascular and nervous systems appeared to be normal (blood pressure 130/85 mm Hg)

Laboratory Investigations—Examination of his blood showed Hb 11 5 g per 100 ml and leucocytes 30,000 per c mm (neutrophils 92%) Abnormal leucocytes were not seen The erythrocytes showed bizarre fragmentation, considerable polychromasia, and numerous Heinz bodies in wet preparations Spectroscopy of the serum showed an absorption band at 624 mμ typical of methæmalbumin, and Schumm's test showed the formation of a hæmochromogen with an absorption band at 558 mμ The serum bilirubin level was 5 mg per 100 ml The urine contained a moderate amount of protein, scanty red and white cells, numerous granular and cellular casts, and traces of hæm pigments, bilirubin, and urobilin These various features pointed to a Heinz body hæmolytic anæmia due to potassium chlorate

Treatment and Progress—The severe coincident bronchitis responded satisfactorily to a five day course of penicillin G 500,000 units daily and streptomycin sulphate 1 g given intramuscularly twice daily Twenty four hours after admission oliguria developed, which was treated with the protein free high calorie diet of Borst (1948) and Bull and Joekes (1949) Through an intragastric tube an emulsion of 100 ml of arachis oil in a litre of 40% glucose with gum acacia q s was given daily Fluid equivalent to the previous day's output of urine and vomit was added Intravenous therapy was not attempted, and neither alkalis nor potassium salts were given by mouth Vitamin B complex was given as 'Becosyn' 2 ml intramuscularly daily, and special attention paid to oral hygiene For the next few days the patient remained very ill with persisting oliguria and jaundice (see table and figure) Intravascular hæmolysis continued, and his Hb decreased from 11 5 g to 7 9 g per 100 ml in the first twenty four hours following admission Next day he was therefore given a transfusion of 1 pint of stored blood from which the plasma (and in it much of the red cell potassium) had been removed An electrocardiogram on the following day did not show any evidence of hyperkalæmia For several days his condition remained critical He continued to vomit, and his blood urea level rose to over 400 mg per 100 ml, but his electrolyte balance remained satisfactory, and his jaundice began to fade about the seventh day of the illness The urinary output rose steadily, and on the thirteenth day the intragastric drip was discontinued By then the jaundice had gone and liver function tests were normal On the sixteenth day the liver edge was no longer palpable and urinalysis was



Blood analysis and urinary output.

collateral vessels as quickly and as much as possible They can be achieved by a course of anticoagulants, by the reflex dilatation of the vessels by heating the body and unaffected limbs; and by prescribing vasodilators of which we believe that alcohol is the best Meanwhile the affected limb is kept cool and at rest (not raised) to reduce its oxygen requirements

Should the patient not be seen until several days or weeks have elapsed, further thrombosis is unlikely, and we believe that sympathetic ganglionectomy is the best treatment at this stage, for, though gangrene is unlikely and useful recovery will usually take place in time, releasing the collateral vessels from vasomotor tone appears to hasten the process

There remains the place of a direct attack on the occlusion Gask (1913) attempted the operation of thrombo endarterectomy of an occluded axillary artery of thirty seven hours' duration He succeeded in re-establishing the blood-flow, but the operation failed because clot re formed almost immediately on the arterial suture line More recent experience has shown that this operation is likely to be successful only in larger vessels

If operation is required for some complicating condition (as in case 7), or if the patient is a young manual worker, an attempt can be made to restore the normal channel by excision of the affected segment, followed by either end to-end anastomosis or the insertion of a blood-vessel graft

Summary

8 cases of occlusion of the main upper limb artery due to closed trauma are described

The natural history of the condition is shown, and the aims and methods of treatment are outlined

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ADMINISTRATION OF IRON IN ANTENATAL CLINICS

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PREGNANCY is a physiological state and should have no pathological effect on the hæmopoietic system of a normal healthy woman receiving an adequate diet Nevertheless, to meet the requirements of the growing fœtus, adjustments in the hæmopoietic system are necessary, and of these the most important is an increase in the blood volume (Dieckmann and Wegner 1934, Roscoe and Donaldson 1946, Berlin et al 1953) This increase is not uniform whereas the plasma is increased by about 25%, the red cells and hæmoglobin are increased by only 12–13% (Roscoe and Donaldson 1946, McLennan and Thoun 1948) The disproportionate increase in plasma often causes the Hb level to fall progressively as pregnancy advances between the 26th and 36th weeks of pregnancy the Hb level and red-cell count may be diminished by as much as 15% (Whitby and Britton 1953)

These changes, often called the hydræmia of pregnancy, have long been regarded as physiological, without any general agreement upon the definition of normal limits Various workers have defined different minimal normal values A red-cell count as low as 3,360,000 per c mm, a Hb level of 10 g per 100 ml and a packed cell volume of 33% have been suggested by Adair et al (1936)

These blood changes are associated not only with an increase in blood volume but also with a deficient intake of iron (Young et al 1946, Cartwright and Wintrobe 1949, Scott and Govan 1949, Ventura and Klopper 1951, Benstead and Theobald 1952, Davis and Jennison 1954, Fisher and Biggs 1955)

The iron requirements in pregnancy are known to be considerable McCance and Widdowson (1946) found that the daily amount of iron needed by the pregnant woman was 16–20 mg, and Neuweiler (1938) estimated that the growing fœtus requires some 375 mg of iron These requirements may not always be fully met from the ordinary diet, which has been shown by Bransby and Magee (1947) to be close to iron starvation

Present Investigation

The aims of the investigation were to determine the following facts in routine antenatal clinic practice

(1) How far the blood changes associated with the hydræmia of pregnancy can be prevented by the daily administration of a small dose of iron

(2) The effect on the Hb level of a small daily dose of iron introduced at different stages of gestation The stages chosen were the 16th, 20th, and 24th weeks The lower limit of the 16th week was selected because few mothers ordinarily make their first attendance at the clinic before that date, and the upper limit of the 24th week because beyond that date the blood changes associated with hydræmia have in many cases already taken place

(3) The value of the Hb level as an index of iron deficiency during pregnancy

Choice of Iron Preparation

For administrative reasons iron in tablet form was preferred, and, despite its disadvantages, no suitable alternative to tabellæ ferri sulphatis compositæ (*N.F*) was found When the investigation was planned, ferrous gluconate was unobtainable, and enteric coated tablets, although likely to overcome the nausea associated with tab ferr sulph co, were rejected because iron is absorbed mainly from the stomach and the upper part of the small intestine (Endicott et al 1949) Between 30% and 40% of pregnant women find it difficult or impossible to tolerate tab ferr sulph co (Benstead and Theobald 1952), but this intolerance may be partly psychological (Girdwood 1952) Accordingly we used, instead of the familiar green tablets usually issued at the antenatal clinics, white sugar coated tab ferr sulph co containing gr 3 of ferrous sulphate

Hæmatological Investigations

The values determined were Hb level, red cell count, colour index, packed-cell volume (P C V), mean corpuscular Hb concentration (M C H C), and mean corpuscular volume (M C V)

Specimens of blood were taken from patients every four weeks into bijou bottles containing Wintrobe's oxalate mixture Hb values were determined photo-electrically as oxyhæmoglobin in a single cell 'Biochem' absorptiometer (100% Hb = 14 5 g per 100 ml), P C V by Wintrobe's method, and red cell counts with a standard improved Neubauer hæmocytometer

Administrative considerations prevented the making of fresh films, but the use of oxalate films did not cause any difficulties All the films were stained with Leishman's stain and examined by one and the same observer

The colour-index was calculated in addition to the standard absolute values, to facilitate comparison with previous series

In some specimens the hæmatocrit revealed a degree of hæmolysis sufficient to invalidate blood count values These specimens were excluded from the investigation, and immediate repeat samples were obtained when

Reviews of Books

Sigmund Freud Life and Work

Vol II *Years of Maturity 1901–1919* ERNEST JONES, F R C P London Hogarth Press 1955 Pp 534 30s

WHEREAS a bad biographer adds a new terror to death, a good one assists towards immortality Much of Freud's published work and some one-sided recollections had created in people's minds a figure remote from the attractive, reserved, complex man of genius whom Dr Ernest Jones is now portraying for us with great skill and fullness The present volume describes the steadier yet troubled years in which Freud felt sure of his way, despite the painful schisms which gradually separated him from Jung, Adler, and Stekel These defections led to the formation of a committee of stalwarts, a secret council of trustworthy defenders of the citadel, to each of whom Freud gave an intaglio ring Dr Jones was the founder of this committee and in many other ways was at the centre of the psycho-analytic movement His contact with Freud was always close and unmarred by the doubts and rifts which were so distressing a feature of many of the personal relationships he describes with penetrating candour His portrait therefore has the authenticity derived from intimate acquaintance and access to much correspondence, as well as from the imaginative and intellectual sympathy of a devoted pupil and helper

The present volume is in three sections The first is a straightforward narrative of what happened to Freud and psycho analysis from 1901 until the end of the first world war The second is an organised survey of the voluminous writings in which Freud carried further his clinical and theoretical conceptions and applied them in diverse fields such as anthropology and literature The third section describes his mode of life and his character Inevitably it repeats much that has already appeared in the two volumes, but the full-length sketch of Freud as a man rounds out the total picture

Dr Jones has a great subject and ample materials, in his dignified, restrained account it is easy to see with what admiration and devotion he has approached his task

Land and People in Nigeria

K M BUCHANAN, B A, professor of geography, Victoria University College, Wellington, New Zealand, J C PUGH, M A, lecturer in geography, University College, Ibadan London University of London Press 1955 Pp 252 35s

THE subtitle of this book is the Human Geography of Nigeria and its Environmental Background, and the book has been written round 172 maps, mostly drawn by Professor Buchanan and Mr Pugh, which clearly illustrate the physical features of the country, the pattern of the population, agriculture, forests, mining and industry, transport, and the public and social services The information has been derived from published and unpublished material (largely from government sources) and from field observations made by the authors The direct medical interest lies in 19 pages on the prevalent diseases, and 2 pages on the medical services They could have been expanded to the advantage of the general reader

For instance, though it is stated that the epidemics of cerebrospinal fever are related to cold, dryness, wind, and dust, the mode of transmission—which make these factors important—is not described Similarly no account is given of the mode of spread of leprosy, relapsing fever, undulant fever, schistosomiasis, and onchocerciasis Guineaworm is related to water, but not in a manner which would be instructive to a water-engineer

The rest of the book is a detailed account of geography, in its wide sense, and because in most countries—and especially in Africa—the physical characters of the country, and the resulting economic and cultural background, strongly affect its diseases, this lucid account, rather than the short medical section, should prove invaluable to medical administrators and research-workers who adopt the biological and ecological approach to the study of disease advocated by Sir Macfarlane Burnet and others

One of the most important functions of a doctor is to make sure that changes in environment which may seem advantageous from the economic point of view are not carried out at the expense of health, another is to stimulate the proper people to change an environment when it is deleterious to health This book will help doctors to discharge both these responsibilities, and they will not find the information so attractively set out elsewhere

Modern Trends in Obstetrics and Gynæcology

2nd series Editor KENNETH BOWES, M D, F R C O G, obstetric physician, St Thomas's Hospital, London London Butterworth 1955 Pp 394 60s

THIS is in no sense a second edition Of the 26 chapters, nearly all are on subjects different from those covered in the first series It does not, therefore, attempt to be comprehensive, but in each chapter the busy specialist will find, in a well-condensed form, the important recent contributions to knowledge which should influence modern clinical practice The fact that ten of the chapters are by authors who are not themselves obstetricians or gynæcologists is a good indication not only of the scope of the book but also of the increasing importance to each specialty of work in related fields We hope that further series will be published from time to time because this volume, like its predecessor, correlates in a very helpful way the more academic and fundamental researches with the practical applications which arise from them

Problèmes de structures, d'ultrastructures, et de fonctions cellulaires

Published under the direction of J ANDRÉ THOMAS, professeur de biologie cellulaire a la Sorbonne Paris Masson 1955 Pp 358 Fr 3300

THE articles in this volume are amplifications of ten lectures given at the Sorbonne during the spring of 1954 They deal with the applications of the physical and biological sciences to the problems of cellular biology They are perhaps too specialised for the general reader but they will be of value to those who can read them critically

J Barraud briefly summarises the information to be obtained from classical and X ray crystallography and goes on to consider crystal growth, the biosynthesis of proteins, and the theories concerning the rôle of desoxyribonucleic acid in this latter process R Wurmser describes the elucidation of the active groups on enzyme molecules and the nature of the forces which attract the substrate molecules to it He also discusses the application of thermodynamics to this study and the process of electron transfer in the cytochrome complex L R Rey, in his paper on the structure of the desoxyribonucleic acid molecule, gives prominence to the recent work of the X-ray crystallographers but does not neglect the earlier work on the anomalous viscosity, birefringence, diffusion, electrophoretic mobility, sedimentation, and other physical properties

D G Dervichian reviews some of the theoretical structures of cell membranes and describes the kinetics of active and passive penetration Ch Devillers discusses cellular adhesion and morphogenesis He describes investigations on the nature of the adhesive substances, the changes brought about by simple molecules and ions, and their relation to morphogenesis René Couteaux, in his article on inter tissue junctions, describes the structure and function of nerve sheaths and various motor and sensory nerve end organs

A Fessard's description of the ultrastructures and functions of the neurone is mainly concerned with the evidence obtained with the electron microscope Tracings obtained with intracellular electrodes are rather elegantly displayed alongside photomicrographs showing the electrodes in position The paper of Ch Oberling and W Bernhard is devoted exclusively to the electron micrography of cancer cells C Thibault describes recent work done on the survival of spermatozoa and the conservation of their fertility He deals with the protective effect of egg yolk, milk, and other diluters, and the rôles of oxygen, temperature, and antibacterial drugs in conserving fertility Finally, R Coujard describes the pioneer work of Reilly and his own interesting experiments on "sympathetic" lesions

TABLE III—MEAN HÆMATOLOGICAL FINDINGS IN 16TH-WEEK THERAPY GROUP AND CONTROLS

Period of gestation (wk.)	Hb (%)*	Red cells (million per c mm.)	Colour-index	P C V (%)	M C H C (%)	M C V (c μ)
16th week group (21 cases)						
16	85.3	4.35	0.99	38.4	32.7	85.6
20	83.8	4.25	0.98	37.0	32.6	88.0
24	83.3	4.20	1.00	37.4	32.9	88.8
28	83.3	4.24	0.98	36.8	32.5	87.0
32	83.4	4.24	0.99	36.7	33.6	85.0
36	82.6	4.25	0.98	38.0	33.2	88.9
40	87.5	4.25	1.00	40.6	32.6	90.0
Controls (25 cases)						
16	86.5	4.39	0.99	37.8	32.6	86.1
20	84.0	4.15	0.99	36.2	32.9	86.0
24	80.1	4.02	0.98	34.4	32.6	86.0
28	77.4	3.85	0.96	34.2	31.8	86.3
32	74.6	3.70	0.97	33.0	32.0	88.0
36	74.6	3.80	0.96	33.0	31.5	90.0
40	76.6	3.80	0.94	36.3	30.2	91.5

*100% = 14.5 g per 100 ml

showing a significant fall in the M C H C or a fall in this index below 32% there was also a fall in the Hb level.

Discussion

The administration of iron during pregnancy presents certain difficulties. It has been estimated that 30–40% of expectant mothers will not take ferrous sulphate tablets routinely prescribed (Benstead and Theobald 1952). It has also been stated that iron administered during pregnancy does not maintain the Hb level (Hahn et al. 1951).

In this series the controls showed the changes associated with the hydræmia of pregnancy: the M C H C fell from a normal 32.6% at 16 weeks to 30.2% at full term—a level indicating iron deficiency not amounting to anæmia (Discombe 1954).

In the three groups treated with iron, however, the hæmatological values were maintained within normal limits throughout pregnancy in 69 out of 89 cases (77.6%) by the administration of a small daily dose (gr. 9) of ferrous sulphate.

Because of the relatively small number of expectant mothers included in the investigation the findings cannot be regarded as conclusive, but they do suggest that normal hæmopoiesis is only possible in the presence of an adequate intake of iron. These findings are therefore in keeping with those of Young et al. (1946), Cartwright and Wintrobe (1949), Scott and Govan (1949), Ventura and Klopper (1951), Benstead and Theobald (1952), Davis and Jennison (1954), and Fisher and Biggs (1955). The findings also indicate that the Hb level can be maintained by smaller doses of ferrous sulphate than those generally used. This is in keeping with the findings of O'Sullivan et al. (1955).

Only 8 women (5.4%) were excluded from the investigation because of intolerance to iron, and only 1 of the remainder who received iron complained of nausea of sufficient severity to interfere with her taking the tablets.

TABLE IV—MEAN HÆMATOLOGICAL FINDINGS IN 20TH-WEEK AND 24TH WEEK GROUPS

Period of gestation (wk.)	20th week group (33 cases)				24th week group (35 cases)			
	Hb (%)	P C V (%)	M C H C (%)	M C V (c μ)	Hb (%)	P C V (%)	M C H C (%)	M C V (c μ)
20	83.6	36.8	32.8	88.3	—	—	—	—
24	80.2	36.1	32.6	89.5	83.4	37.7	32.5	88.2
28	80.0	36.0	32.3	89.0	82.8	36.4	32.7	88.3
32	80.6	35.0	33.0	89.4	81.6	36.6	32.6	88.0
36	81.2	36.0	32.3	89.3	84.4	37.2	32.4	87.3
40	84.0	38.1	32.8	91.5	85.5	37.2	32.6	89.1

Although the mean Hb levels were maintained in the three groups taking iron, the Hb levels of 20 of 89 mothers in these groups were not maintained.

Since none of these patients had an anæmia not associated with iron deficiency, or suffered any blood-loss, the fall in Hb level can only be attributed to the following causes:

(1) The mothers did not take the tablets (this was not established).

(2) The iron was not absorbed.

Non-absorption of administered iron has been reported by Scott and Govan (1949), Fisher and Biggs (1955) and O'Sullivan et al. (1955).

The Hb level is related both to the P C V and the M C H C, and a fall in the Hb level may be associated with a fall in either or both of these indices. A fall in the P C V is associated with hydræmia, and a fall in the M C H C with a decrease in the iron content of the red cells. The Hb level during pregnancy therefore cannot by itself be taken as an accurate index of iron deficiency unless the P C V remains stationary. This does not, however, lessen the usefulness of the Hb level in antenatal clinics.

Full hæmatological examination cannot be applied to even one sample of blood from every expectant mother attending an antenatal clinic, because this would place an impossible burden on laboratory services, and it is unnecessary.

In the absence of evidence of anæmia the following routine is suggested:

(1) The Hb level should be estimated at the first visit of every expectant mother to an antenatal clinic irrespective of her period of gestation.

(2) Every expectant mother should receive iron as a routine.

(3) The Hb level should be estimated again between the 32nd and the 36th weeks to determine whether it is being maintained.

If the Hb level is not maintained, a full hæmatological examination should be undertaken to determine the reason for the fall.

The Hb level used in this way can be a simple and reliable guide for routine purposes. Table I shows that the later an expectant mother attends for her first antenatal examination the more likely is she to have a low Hb level, and that in most cases this indicates a deficient intake of iron. Every expectant mother should therefore be encouraged to attend for antenatal care as early in pregnancy as possible.

Summary and Conclusions

A tendency to iron deficiency was revealed in expectant mothers by a progressive fall in Hb level, red-cell count, colour-index, P C V and M C H C. In a comparable group this tendency was prevented, and the hæmatological values maintained within normal limits, by the administration of a small daily dose of iron in the form of ferrous sulphate (gr. 9 corresponding to 315 mg. of elemental iron). Only 8 women (5.4%) were excluded from the investigation because of intolerance to iron, and failure to respond was observed in 20 of 89 cases (22.4%). Possible reasons for this failure are discussed.

The use of ferrous-sulphate tablets as a routine measure was effective in maintaining the Hb level and other hæmatological indices throughout pregnancy in 77.6% of 89 cases.

For the purposes of antenatal care routine estimation of the Hb level is a useful guide to the behaviour of the more accurate hæmatological indices and of determining the response to oral iron.

The Hb level should be estimated at the first visit and again at 32–36 weeks. Further hæmatological of local anæsthesia The greater part of the book is concerned with the indications for operation and the management of its complications The common clinical conditions are well described, but the illustrations are indifferent

Recent Advances in Neurology and Psychiatry (6th ed London J & A Churchill 1955 Pp 311 30*s*)—In the ten years that have elapsed since the previous edition neurology has made many advances Under the editorship of Sir Russell Brain and Dr E B Strauss this book has been entirely rewritten, and three extensive chapters included on electro encephalography by Denis Hill, neuroradiology by David Sutton, and intracranial tumours by Douglas Northfield The references at the end of each section are numerous and recent, and the authors have shown good judgment in selecting the papers that deserve special notice The exposition is concise and to the point As the preface rightly states, the common ground between neurology and psychiatry increases in importance This is well illustrated in the chapter on consciousness and unconsciousness, and that dealing with the parietal lobe Unfortunately another relevant chapter, on the mental aspects of the frontal lobe, falls below the standard maintained in the rest of the book

Biographical Memoirs of Fellows of the Royal Society (Vol 1 London The Royal Society 1955 Pp 263)—The Royal Society has started a new series in continuation of the *Obituary Notices of Fellows of the Royal Society* which covered the years 1932–54 in nine volumes This first group contains 19 biographies of varying length, including those of Sir Stafford Cripps and Albert Einstein, all written by distinguished colleagues Each is accompanied by a photograph and a bibliography of published works Some of the portraits show the remarkable artistry of Karsh of Ottawa The biographies are of so high a class that they could be bettered only by a full scale book about each fellow Three are of particular interest to the medical reader Frederic Wood Jones and Arthur Keith by Sir Wilfrid Le Gros Clark and Edward Mellanby by Sir Henry Dale They reawaken admiration for the accomplishments of each of these men in such wide fields

New Inventions

A BED CRANE

The crane illustrated here was made for a patient who had severe paralytic poliomyelitis in 1949 and was left with flaccid paralysis of both legs and weakness of the muscles of her trunk and right upper arm For six years she could not lift herself out of bed into her wheel-chair or on to a bedpan without help

Mr James Genet, senior orthopædic technician at Wellington Hospital, designed the crane to give the patient much greater independence, particularly when getting to and from her bed and wheel-chair He has successfully achieved this and considerably improved her morale

The apparatus consists of a frame clamped on to the end of the bed and incorporates an ordinary motor-car hydraulic jack, which the patient works with the handle, jacking herself up off the bed or the wheel-chair She then very easily moves herself over to the wheel-chair or the bed and lowers herself by turning the handle which decompresses the jack

The crane can also be used by nurses to lift patients off beds and on to wheel-chairs and, if the sanitary type of chair is used, for taking them to the lavatory or to a shower where they can be washed, thus obviating the difficulties of bathing, particularly in the case of heavy elderly patients

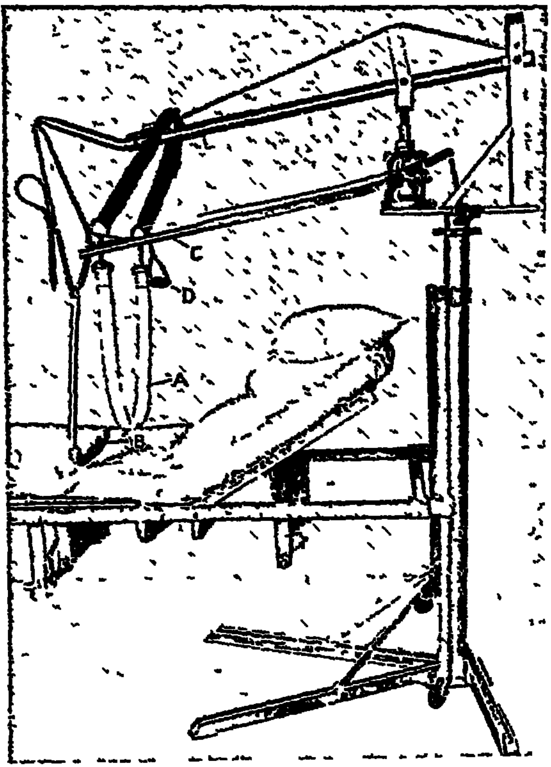


Fig 1—The crane in position A, sling to pass under arms and around patient's back, B, sponge-rubber and leather-covered hook to pass under patient's knees, C, operating handle of jack D, hand grip which is control for raising or lowering the patient and is working handle for C in certain positions To lift patient, handle is pushed fully in towards jack by giving hand grip a quarter-turn and pumping To lower, hand grip is turned until handle is pulled about $^1/_2$ inch out of jack, handle is then pressed down as far as possible Slinging is so arranged that front strap runs over roller on spreader, this action transfers patient from partly prone position on bed to sitting position on wheel-chair A stop prevents patient from swinging too far

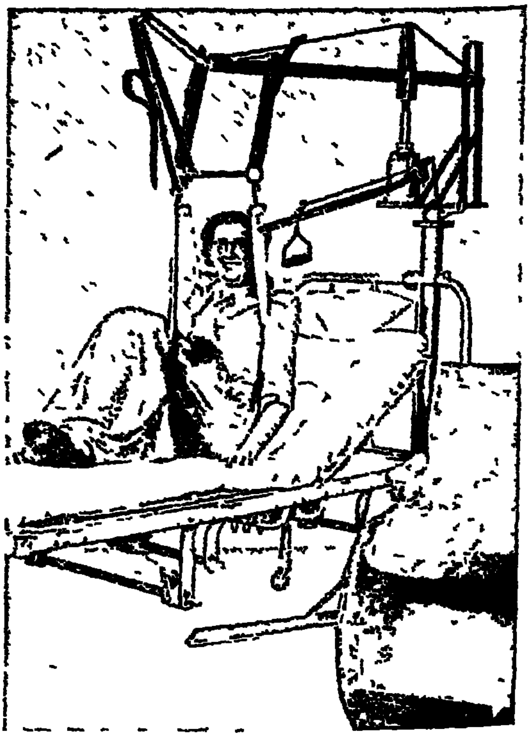


Fig 2—Patient in sling

This apparatus cost about £23 to make The price compares very favourably with that of other apparatus on the market The apparatus can be made mobile by being fitted with castors, future models will be so fitted

Mr Genet feels that it is wrong to patent apparatus of this kind and it is therefore available for any hospital to copy

Wellington Hospital,
New Zealand

I A M PRIOR
M D N Z, M R C P, M.R.A C P

issue indicating that the B C G had taken successfully Of the remaining 3 persons who failed to react to either "depot" or aqueous tuberculin, 2 had failed to convert after previous B C G vaccination, and 1 had converted transiently after vole bacillus vaccination

Patients with Sarcoidosis

The responses to 100 T U of aqueous tuberculin and 5 T U of "depot tuberculin" were compared in 23 proven cases of sarcoidosis of various degrees of activity The results were

Positive reactions to both the aqueous and "depot" tests	4
Negative reactions to both the aqueous and "depot" tests	6
Positive reactions to the "depot" test only	13
Positive reaction to the aqueous test only	0

	Negative	*Positive*
Aqueous tuberculin	19	4
"Depot tuberculin"	6	17

The "depot tuberculin" produced a brisk erythematous reaction about 35 mm in diameter with central induration of 5–10 mm within two days, except in 2 persons in whom an erythematous reaction appeared after seven days in one and nine days in the other

Discussion

We know little of the fate of tuberculin in the tissues except that it starts to become fixed early, and that this is completed within one to two hours with a moderate skin-test dose (Pepys 1955a) The proportion of injected tuberculin retained locally by this "fixation" is unknown, but factors which influence its local persistence can modify reactions considerably Increased lymphatic absorption of the tuberculin decreases reactions, whereas increased local retention increases reactions (Seeberg 1947, 1951a, Pepys 1953, 1955a) The long persistence of the tuberculin—e g, with a "depot tuberculin"—favours a higher concentration for a longer period and leads to prolonged reactions in Mantoux-positive people Such an enhancement could be expected to reveal lower degrees of sensitivity not elicited by aqueous tuberculin

The interval of about ten days between the B C G vaccination and the appearance of reactions at previously negative "depot tuberculin" tests corresponds to the time required for the development of hypersensitivity due to the infection These reactions correspond to Wassen's (Wassen and Swedin 1941) findings in rabbits He injected "depot tuberculin" into their skins and then infected them with tubercle bacilli The "depot" tests reacted sixteen days after the infection, at which time aqueous Mantoux tests were also positive These observations resemble the "revivescence" reaction in man, in whom previously negative tuberculin skin tests become positive on the appearance of active tuberculous infection, even months later, thus indicating the persistence of some of the tuberculin locally

The "depot" tests were used as a deliberate "revivescence" test in the B C G vaccinated subjects In the 2 patients who failed to react to aqueous tuberculin but gave positive reactions to the "depot tuberculin," the presence of tuberculous tissue at the B C G vaccination sites was evidence of a successful take In these patients the "depot" material may have revealed a degree of sensitivity too low to be elicited by the aqueous tuberculin In the ordinary way these patients would have been regarded as candidates for repeated B C G vaccination on the assumption that a failure to react to 100 T U of aqueous tuberculin meant that they had not converted There are reports of Mantoux-negative B C G -vaccinated people in whom enhanced reactions to revaccination with B C G showed that they were hypersensitive to the product of these organisms (Saye 1948) The positive reactions to the "depot" tests in these 2 patients were evidence of conversion to tuberculin hypersensitivity

The positive "depot" tests in patients with sarcoidosis may be due to a similar demonstration of a low degree of sensitivity which escapes aqueous tuberculin testing Seeberg (1951a) obtained positive "depot" reactions in 6 of 8 Mantoux-negative patients with sarcoidosis He claims that histological examination of the sites of these negative Mantoux tests in patients with sarcoidosis shows evidence of a tuberculin-type reaction, and he regards this as evidence of "latent" tuberculin sensitivity (Schaumann and Seeberg 1948) He suggests that the reaction to the "depot tuberculin" in patients with sarcoidosis is due to the prolonged retention of the tuberculin, which enables sufficient antibody carrying cells to arrive and to react with the tuberculin There is general agreement that the proportion of patients with sarcoidosis who fail to react to 100 T U of aqueous tuberculin is higher than in the general population That these patients with sarcoidosis may nevertheless be basically tuberculin-sensitive is shown (1) by the reactions elicited with "depot tuberculin" by Seeberg (1951b) in 6 of 8 patients and by us in 13 of 19 patients who failed to react to aqueous tuberculin, and (2) by the report of Pyke and Scadding (1952) that Mantoux-negative patients with sarcoidosis could give positive tuberculin reactions when tested while under cortisone treatment

Recent reports indicate that the sources of antibody responsible for the tuberculin type of hypersensitive response are cells of reticulo endothelial origin, and that circulating lymphoid cells appear to be responsible for the initiation of the reaction (Pepys 1955b) The results of "depot tuberculin" tests in patients with sarcoidosis suggest that these cells are a poor source of reacting antibody in this disorder This may explain the decreased sensitivity of such patients to a variety of delayed-type hypersensitive antigens (Sones and Israel 1954) The deficiency of delayed-type hypersensitive antibody is in contrast to the ready production of circulating antibodies in patients with sarcoidosis (Sands et al 1955) Circulating antibodies are concerned in hypersensitive reactions of the immediate type, and there are many reports of undiminished reactivity to immediate-type tests in patients with sarcoidosis

The remaining 6 patients with sarcoidosis who gave negative reactions to both aqueous and "depot" tests may be considered to be either insensitive to tuberculin or less sensitive than those patients who reacted to the "depot tuberculin" Some of the completely negative patients were among the more active cases, as judged by the more recent onset, florid skin changes, raised erythrocyte sedimentation rate, and positive Kveim test As regards the response to inflammation, there does not appear to be any obvious impairment in patients with sarcoidosis, since they reacted vigorously to the "depot tuberculin"

Summary

The reactions to intradermal injections of tuberculin in aqueous solution and in an oily emulsion ("depot tuberculin") were compared

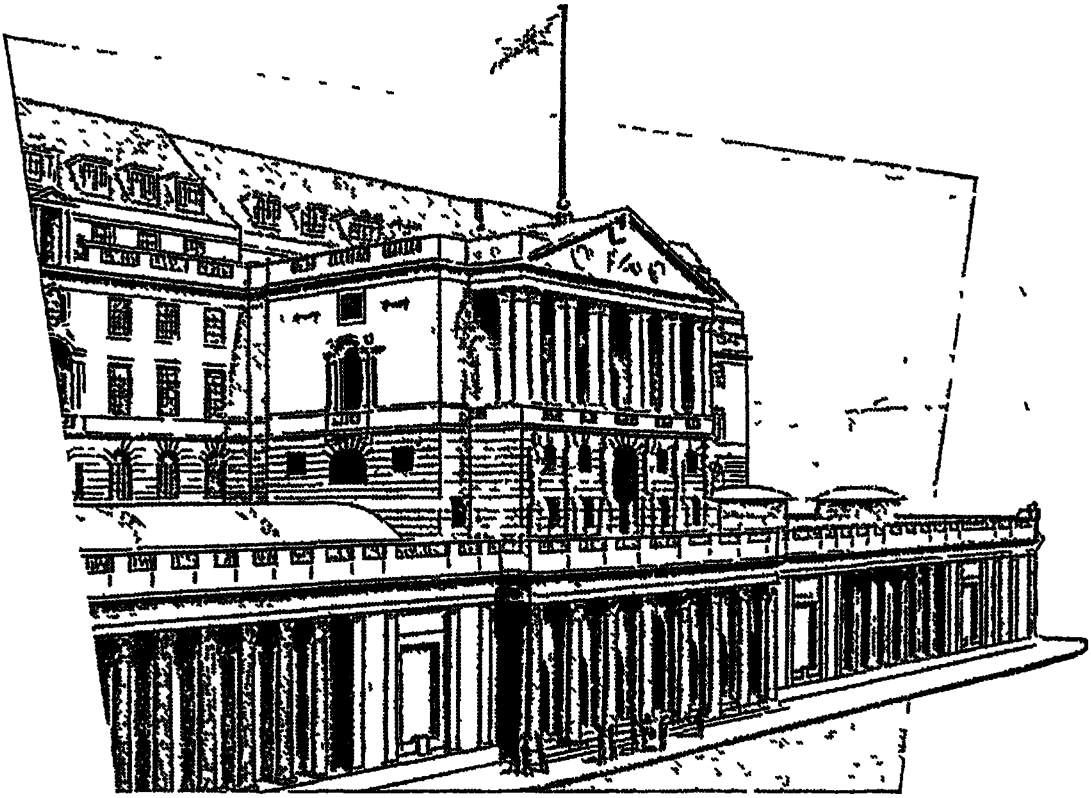
In 5 Mantoux positive subjects, the oily tuberculin excited reactions which persisted for three months No reactions were produced in Mantoux-negative subjects.

In 6 of 9 Mantoux negative subjects vaccinated with B C G, positive reactions appeared within ten days of vaccination, at the sites of previously negative "depot tuberculin" tests made four weeks before the B C G. vaccination

4 patients with sarcoidosis gave positive reactions to both the aqueous and "depot" tuberculin Positive reactions were elicited by the "depot tuberculin" in 13 of the remaining 19 patients with sarcoidosis who did not react to aqueous tuberculin

The long local persistence of the tuberculin in the oily emulsion probably made it possible to demonstrate degrees of sensitivity too low to be revealed by aqueous tuberculin tests

References overleaf



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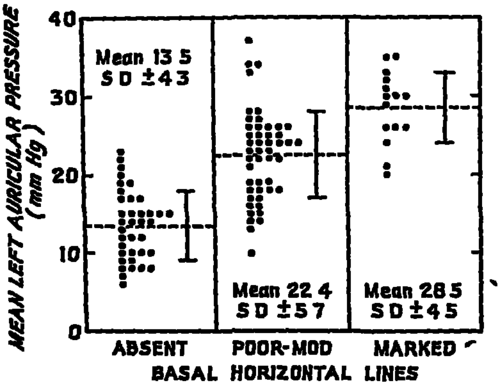

Fig 2—Relation of lines to mean left auricular pressure

patients into the three radiographic groups is shown fig 2, which also indicates the range of pressures in ch group In the "lines absent" group, the individual ressures are scattered about a mean value of 13 5 mm g, and in the "poor to moderate" and "marked" oups the means are 22 4 mm Hg and 28 5 mm Hg spectively These means show clearly the higher ressures found in the groups with lines Thus, the resence of lines on the chest radiograph of a patient th mitral disease seems to be direct evidence of a nsiderably raised left auricular pressure at the time e film was taken

elation between Horizontal Lines and Mean Pulmonary rterial Pressure in 64 Patients with Mitral Disease

No lines were found below a mean pressure of 4 mm Hg, but they were consistently present above 1 mm Hg The classification into groups and the istribution of the pressures are shown in fig 3 In each group the range of pressures is much greater than in fig 2, as indicated by the standard deviations shown for comparison in figs 2 and 3

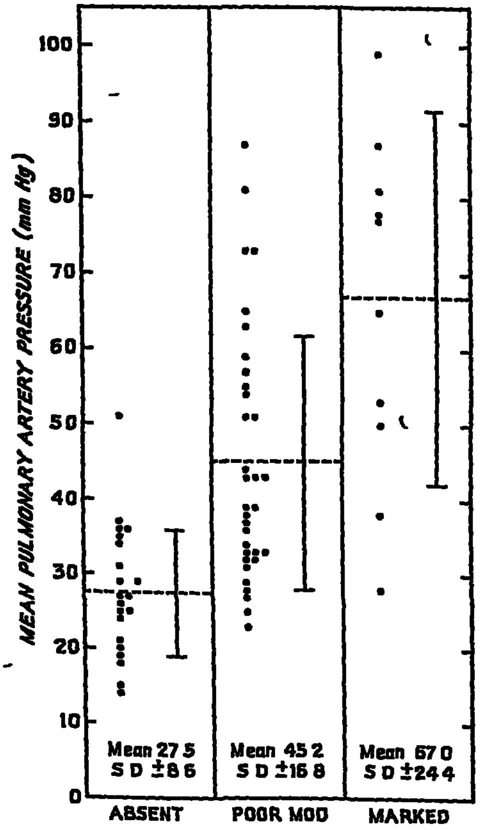

Fig 3—Relation of lines to mean pulmonary arterial pressure.

Statistical comparison of the three radiographic groups in the association of left auricular pressures with lines (fig 2), shows the difference between the means of any two groups to be highly significant When pulmonary arterial pressures are considered (fig 3), although the difference between the means of the "absent" and "poor to moderate" groups is highly significant, that between "poor to moderate" and "marked" is only moderately significant The statistical data are summarised in table I

Relation between Lines and Mean Pulmonary Arterial Pressure in 16 Patients with Pulmonary Hypertension from Causes other than Mitral Disease 4

Although the mean pressure for the whole group was 73 mm Hg, only 2 showed doubtful lines, and no lines were seen in the remaining 14 patients For 5 of the patients, measurements of left auricular pressure were available, 4 made during bronchoscopy, and 1 during cardiac catheterisation through an auricular septal defect All these left auricular pressures were normal Table II summarises the data from these 16 patients These findings suggest that whereas patients with mitral disease and severe pulmonary hypertension almost invariably have lines, pulmonary hypertension alone is not the cause

TABLE I—CLASSIFICATION OF RADIOGRAPHS IN PATIENTS WITH MITRAL DISEASE

—	Group 1 (lines absent)	Group 2 (lines poor to mod)	Group 3 (lines marked)
Mean lt auricular pressure (mm Hg)	13 50 ±4 312*	22 44 ±5 709*	28 53 ±4 514*
Mean pulm art pressure (mm Hg)	27 50 ±8 609†	45 24 ±16 76†	67 00 ±24 45†

* Comparison 1 and 2 $t = 4.383$ $n = 52$, $p < 0.001$
, 2 and 3 $t = 3.693$ $n = 61$, $p < 0.001$
, 1 and 3 $t = 10.91$ $n = 50$, $p < 0.001$
† Comparison 1 and 2 $t = 4.383$ $n = 52$, $p < 0.001$
, 2 and 3 $t = 3.095$ $n = 41$, $p < 0.01$
,, 1 and 3 $t = 6.404$, $n = 29$, $p < 0.001$

Discussion

From the results presented above, three important facts emerge

1 Basal horizontal lines on the chest radiographs of patients with mitral valvular disease are accompanied by a raised left auricular pressure

2 Lines invariably appear when the mean left auricular pressure exceeds 24 mm Hg

3 Elevation of the pulmonary arterial pressure alone appears to play little part in the production of lines

The first two of these facts suggest that the factor responsible for radiographic evidence of lines is a rise in pulmonary capillary venous pressure to a level exceeding the colloid osmotic pressure of the plasma proteins This is indirect evidence for the now widely accepted view that the anatomical basis of the lines is an increase in the bulk of the interalveolar septa Distension of these with tissue-fluid leads to the production of distinct and characteristic shadows on the chest radiograph

From fig 2 it seems that the scatter of the individual pressures about the means is larger than might have been expected Some overlap of the pressures in the three groups is apparent, and the following reasons may account for this

1 The time-interval between taking the chest radiograph and recording the pressures is important, this is illustrated by the following case-record

A woman, aged 41, with mitral stenosis was orthopnœic when first seen in May, 1955, and her chest radiograph then may develop after a surgical portacaval anastomosis if hepatic function is impaired , but shunting of portal blood into the systemic circulation in the presence of a healthy liver does not produce the syndrome Neurological and mental changes may also appear as the result of the severe liver damage which occasionally follows virus hepatitis Clearly hepatic function must be depressed before this condition can arise, and its onset is precipitated by the development of communications between the portal and systemic veins Moreover, the neurological disorders can be induced by raising the intake of nitrogenous substances, such as dietary protein, ammonium salts, and urea Methionine, which has in the past been used in the treatment of liver disease, may have a similar effect,[4–7] and **SHERLOCK** and her associates have investigated the mechanism of this action [8] Methionine given by mouth produced neurological deterioration in 7 out of 9 patients who had previously had episodes of impending hepatic coma It was without effect in other patients with hepatic cirrhosis who had never had neurological complications The rise in the blood-methionine level was the same in the two groups Intravenous methionine had no effect in 3 patients who had previously relapsed after oral administration and in 1 it produced only a delayed exacerbation No significant change in blood ammonium, pH, or bilirubin level accompanied the neurological deterioration produced by methionine When chlortetracycline (aureomycin) was given at the same time as methionine, no toxic disturbances developed in patients who had previously reacted, despite the fact that higher blood-methionine levels were reached when the antibiotic and amino-acid were given together These observations suggested that the toxicity was not due directly to methionine but to some substance derived from methionine by the action of intestinal bacteria sensitive to chlortetracycline Bacteriological studies showed that the fæcal flora of patients with liver disease and neurological disturbances was no different from that of healthy people and of patients with uncomplicated cirrhosis Methionine by itself did not alter the bacterial composition of the fæces Chlortetracycline produced similar changes in all three groups—namely, a rise in proteus with elimination of bacteroides and an inconstant fall in *Escherichia coli* The streptococcal types changed and lactobacilli increased

The breakdown product of methionine responsible for the neurological changes has not so far been identified Clearly, however, methionine is potentially toxic if given by mouth to patients with hepatic cirrhosis In the past methionine has been recommended on rather slender grounds as a treatment of liver disease, but there is no definite evidence that it does any good, and its use should certainly be abandoned Chlortetracycline has already been given with apparent success in the treatment of hepatic coma [9] The neurological disturbances that may appear spontaneously in cirrhosis of the liver vary greatly in severity, and the effect of treatment is difficult to assess accurately , but **SHERLOCK** et al 's clinical impression is that chlortetracycline therapy is of benefit in spontaneous hepatic coma Other measures must of course be used—in particular, curtailment of the intake of protein and other nitrogenous substances during the acute phase of the disturbance

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Hypoglycæmia in Diabetics

WHENEVER hypoglycæmia in a diabetic cannot be attributed to one of its usual causes—failure to eat, over-exertion, or too much insulin—other possibilities must be considered The blood-glucose comes from the alimentary tract or from the liver by glycogenolysis or gluconeogenesis Poor absorption may cause hypoglycæmia in myxœdema [1] and sprue,[2] and glycogenolysis is deficient in some types of hepatic failure, even without other obvious signs of liver disease [3] The liver may fail because it contains too little glycogen or because it is unable to mobilise stored glycogen as in von Gierke's disease, and possibly in the type of brittle diabetes with hepatomegaly recently described by **EVANS** and his colleagues [4] Gluconeogenesis is largely dependent on the adequate function of the adrenal cortex and thus indirectly of the anterior pituitary The association of diabetes with Addison's disease and Simmonds's disease is admittedly uncommon [5 6] , but early recognition of adrenal insufficiency in a diabetic is particularly important, for these patients become extremely sensitive to insulin, in the same way as the Long cat [7] or the Houssay dog,[8] and hypoglycæmia may well be fatal before the true state of affairs is appreciated [9] Such a diabetic, previously needing much insulin, may be able to do without any at all, although an intravenous glucose tolerance test will still show a diabetic curve After infarction of the anterior pituitary for example, there is characteristically a severe headache followed in a day or two by hypoglycæmic reactions to the usual doses of insulin [10] If the patient survives, and insulin treatment is either drastically curtailed or stopped, signs of hypofunction of the gonads and thyroid gradually appear, but they respond well to replacement treatment Diabetic intercapillary glomerulosclerosis (Kimmelstiel-Wilson syndrome) may sometimes be associated with decreasing insulin needs,[11] but no satisfactory explanation has been suggested **RUNYAN** et al [12] concluded that the renal lesions were not related to any change in insulin needs

The importance of hypoglycæmic episodes in prognosis lies in the susceptibility of the brain to what may be irreversible damage [13] The risk is greatest after long-continued severe hypoglycæmia and in

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[6] Balfour W M , Sprague R G *Amer J Med* 1949 7, 596
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FŒTAL MORTALITY IN PREGNANT DIABETICS

STRICT CONTROL OF DIABETES WITH CONSERVATIVE OBSTETRIC MANAGEMENT

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Pregnancy in diabetics has not been studied long, and not until the 1940s was it generally known that the fœtal mortality was still very high (about 40%) and not much different from the mortality in the pre-insulin era, in contrast to the prognosis of the mothers, which became good after the advent of insulin.

It seemed to us that, before introducing any additional therapy, we should determine the basic fœtal mortality after intensive classical treatment. Accordingly in January, 1946, we started in this department a clinical trial of strict control of the diabetes and conservative obstetrical management by a few doctors.

This trial has now lasted nearly ten years, so we outline our treatment and report the fœtal mortality observed during that time. The material comprises 265 cases from January 1946 to Sept. 30, 1955. In addition we use for comparison our old Rigshospital material of 1926–45, comprising 157 cases—a grand total of 422 cases.

Control and Treatment

The mother is examined as an outpatient every three weeks during the first four months of pregnancy and then weekly. About eight weeks before the expected term she is admitted to hospital and remains there until delivery, which is induced about three weeks before term.

The main feature of our new programme is the control and treatment of the diabetic in hospital during the last months of pregnancy. Our aim is to obtain the best possible chemical control of diabetes by giving a measured diet and plenty of insulin. The diet contains about 1900 calories, 80–90 g. of protein, 175–200 g. of carbohydrate, and about 80 g. of fat, and in addition a supplement of vitamins, calcium, and iron is given. The blood-sugar level is controlled by altering the insulin dosage and by distributing the diet over five or six meals, according to individual requirements. We nearly always use protamine-insulin retard (N.P.H. insulin) combined with ordinary insulin twice a day, the average daily dose being 70 I.U. Capillary blood-sugar determinations, of which three are postprandial, are made four times daily by the Hagedorn-Jensen method (total reduction), and we try to keep the blood-sugar at the physiological level. The extent to which this aim is attained is exemplified by the fact that in the first 18 long-term treated cases (see below) the level of the blood-sugar (average of the four daily determinations during the last continuous stay in hospital, which averaged 52 days for the 18 patients) ranged from 108 to 167 mg. per 100 ml., the over-all average being 133 mg. per 100 ml. In the later years we have calculated the average level for one day now and then and found averages of 133, 135, and 130 mg. per 100 ml.

To combat toxæmia, hydramnios, and œdema, table salt is restricted. Phenobarbitone has been administered in some cases, and abdominal amniotomy tried in a few, but no hormones, mercurial preparations, ammonium chloride, rutin, or similar substances are used.

Pregnancy is usually terminated at the beginning the 38th week, on average 20 days before the calculate term. Nearly all deliveries are induced with dru and/or by rupture of the membranes. Up to now onl 29 cæsarean sections (11%) have been done on obstetric indications, whereas low forceps deliveries are commo In about 20% of the cases labour started spontaneousl

As a routine the newborn babies are placed incubators and given oxygen, warmth, and humidit for the first twenty-four hours. During this period th babies are fasted (Pedersen 1952, Pedersen et al. 1954 A pædiatrician is called when needed.

The treatment of long-term treated patients (se below) during the ambulatory period and the dail treatment of all inpatients are given by one physicia (J. P.). The delivery too is managed by only a fe doctors under the supervision of one of us (E. B.).

Long-term and Short-term Treatment

Knowledge of the control and treatment of diabete in Denmark is essential for an understanding of wha follows. The control is decentralised, and apart fro two private hospitals for diabetics (Steno Memori Hospital and Hvidöre Hospital) we have no diabet clinics or units; the treatment is given by gener practitioners and to some extent by medical outpatien departments, specialised physicians, and the two abov mentioned clinics. The antenatal care too is decentra ised, and we have only a few obstetrical outpatien departments in Denmark.

Our department receives emergency cases and a kinds of obstetrical complications without selection, an from 1946, all pregnant diabetics wanting or needin admission to the Rigshospital. We have pleaded wit diabetics to get in touch with this department not late than about the 30th week of pregnancy.

Thus the diabetics attend our department at ver different stages of pregnancy, a few from the earlie months and others not until they are in labour. But mos of them are seen toward the end of pregnancy. Thus w have not been able to follow our recommended schedul for all the patients, and they have not had the sam amount of control and treatment. We have to divid the material according to the amount of treatmen received, but this must be done by dividing according t the stage of pregnancy at which the patient first applies t the clinic, because this determines how long the patien might be treated. Those who are seen at least 53 day before the calculated term are classified as long-ter treated, and those who are not seen until later as short term treated. (These phrases should not be confused— as has been done—with long-term and short-ter diabetes.) The patient is always designated short-ter if she is in pre-coma or in labour or has already bee delivered when first seen. Likewise short-term applie if delivery takes place, or the baby dies, within 8 day after the patient's first application for admission.

This classification is objective and unbiased and i made 9 days after the patient's first application. Th reason for choosing 53 days before term is historical an is explained by Pedersen (1954a). The criterion fo long-term treatment makes the results in this grou seem worse than they are because the deaths of babie whose mothers applied to the hospital in due time ar allotted to the long-term group after only 8 days treatment, whether the mothers have been outpatient or inpatients during this short period.

The most important difference between the long term and short-term groups is the length of treatmen in department B (table I): 78% of long-term but only 10% of short-term patients stayed continuously i hospital for 30 days or longer immediately before delivery In other words, the long-term group was admitted to hospital on an average on the 65th day before the there is a risk that the claims for what can be accomplished, mentally and physically, for the spastic have been too optimistic There has been a tendency to regard the solution too much in terms of finance, of bricks and mortar rather than plodding and dispassionate scientific study Money is, of course, of immense importance in this unusually difficult and costly programme, and it may well be that the British Council for the Care of Spastics, with its more professional membership, has failed to appreciate the sense of urgency, enthusiasm, and passionate vigour of the National Spastics Society

At any rate, surely the time has come for an effective working compromise—for the union of the cautious, objective, professional approach of the council with the lively strength of the "parents" movement To have a permanent division means duplication and overlapping —for example, in having separate medical advisory committees, and this must lead to rivalry and a competitive spirit at the expense of the real welfare of spastics This view was taken by the Archbishop of Canterbury, and it has been supported by the director-general of the National Society, Lieut-Commander Ian Henderson, apparently to his own discomfiture The main principle at issue is the question of where ultimate control should lie The articles of association of the National Spastics Society hold the provision that not less than two thirds of the members of the executive committee must be spastics or parents of spastics The British Council has always had parents on its committee, but it is mainly representative of medical, educational, and other professional bodies which are deeply interested in the subject National interests should take precedence over local demands, and there is a very real need for balance and judgment

FORM OF CONSENT

IN law, a patient must not be examined or treated unless consent has been given The question is seldom raised in the law courts, for consent is usually taken for granted, but the principle is obviously a sound one, and its neglect can be dangerous Except in an emergency, when prompt action is essential, consent is always obtained before operation or the giving of an anæsthetic, but specific permission is less regularly sought before investigations which the doctor is apt to regard as routine An intradermal tuberculin test on a child is an example of a minor procedure which it is unwise to undertake without the agreement of parents, indeed tests of this nature, and prophylactic injections, are seldom done by local authority doctors without it Clearly, the need for permission is greater where the patient is a child, but adults, too, are entitled to a careful explanation of the investigation or treatment proposed Consent by word of mouth, in the presence of a witness, is acceptable in law, but a written declaration is, of course, legally safer On the other hand, an "omnibus" form of consent, couched in general terms, may be open to strong objection, for the purpose of getting consent is to be sure of the patient's approval of something he has genuinely understood

This subject was discussed recently by a hospital management committee[1] whose medical advisory committee recommended the introduction of a special consent form The form had particular reference to investigations and tests which adult and child patients might require, and we understand that the immediate reason for the request was the (highly commendable) proposal to Mantoux-test all children on admission The management committee, however, were reluctant to grant powers of examination and investigation on so wide a scale, and decided to defer decision until at least they had seen suggested forms of consent drawn up by the medical committee after consultation with an appropriate medicolegal organisation The publicity given to their discussion of this important issue may stimulate other management committees to review their own arrangements, in collaboration with their medical committees The safeguarding of doctors against unreasonable litigation can be important, but even more important is the safeguarding of patients against investigation or treatment they do not desire The good relationship of patient and doctor, in hospital or elsewhere, depends on confidence, which should be founded as firmly as possible

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[1] *Crystal Palace Advertiser* March 1, 1956

EXIT PLOMBAGE ?

BEFORE chemotherapy tilted the balance of opinion in favour of resection, thoracoplasty was regarded as the best major operation for the treatment of pulmonary tuberculosis The results indeed were good, and the gross demolition of the upper thorax that was necessary to secure them was viewed tolerantly by clinicians though less so by patients Chemotherapy has radically changed all this, and past standards have slipped into the discard so rapidly that many stoutly held principles have had to be revised and established methods subjected to searching review

Apical plombage was *not* an established method before the introduction of chemotherapy, but it had been tried with some success in America by Wilson[1] The initial idea was that the introduction of an inert plastic substance into the extrapleural space would overcome the disadvantages inherent in extrapleural pneumothorax, and at the same time leave the patient with an intact chest wall Complications, however, as reported by Trent et al[2] and Walkup and Murphy,[3] were far too many and serious, particularly as regards pressure phenomena, to warrant the continued use of the operation, and the plomb was then placed extraperiosteally where it could do less damage to the lung and great vessels, the periosteum, after separation from the ribs, formed with the attached intercostal muscles a protective barrier between the plomb and these vital structures, and results became more encouraging Soon it appeared that, except when the apex of the lung was grossly adherent, apical plombage would constitute a serious rival to thoracoplasty and even bid fair to replace it as the main surgical measure Early results were good,[4–6] particularly as new and more suitable plastic materials were forthcoming, surgeons and patients alike were pleased with the one stage no deformity operation which had so few postoperative complications, and chemotherapy at first seemed to confirm these impressions by rendering the disease less active at the time of operation, thus further diminishing the risk of complications But the well known hazards of the permanent retention of a foreign body in the tissues were not to be so easily overcome Infection sometimes revealed itself early, when it was usually staphylococcal, more often it appeared late, and it was then commonly due to the tubercle bacillus[7] Ruefully, the infected plombs were removed and thoracoplasty performed to close the space The main cause for concern is that infections continue to become manifest some years after *operation and* it is this factor which completely undermines confidence Meantime, resection in the increasingly favourable conditions produced by more thorough preoperative chemotherapy has rapidly

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[1] Wilson D A *J thorac Surg* 1948, 17, 111
[2] Trent J C, Moody, J D, Hiatt, J S, McCann N C *Ibid*, 1949, 18 173
[3] Walkup, H E, Murphy, J D *Dis Chest*, 1949, 16, 118, 456
[4] Bing, J *Acta chir scand* 1950 100 293
[5] Morriston Davies, H, Temple L S Stathatos, C *Thorax*, 1951, 6 209
[6] Laird R, Stephens, T W *Tubercle* 1953 34 68
[7] Desforges, G, Gibbons, G, Strieder, J W *J thorac Surg* 1954 28 636

TABLE IV—FŒTAL MORTALITY * FROM 1946 TO SEPT 30, 1955, CLASSIFIED BY BIRTH-WEIGHT AND ACCORDING TO WHITE (1949) IN 265 BABIES

Classification	Treatment			
	Long term		Short term	
	No of babies	Fœtal loss	No of babies	Fœtal loss
Birth-weight				
1000 g (2 lb 3 oz) or more	130	13 (*10%*)	135	45 (*33%*)
2500 g (5½ lb) or more	117	9 (*8%*)	110	26 (*24%*)
White's classes				
A, B and C	74	5 (*7%*)	94	26 (*28%*)
D and F	56	8 (*14%*)	41	19 (*46%*)

* See footnote to table III

chemical control, (2) measures to prevent or correct œdema and hydramnios, (3) sex-hormone therapy, intramuscular stilbœstrol and progesterone given daily in increasing doses throughout pregnancy, (4) early induction of labour, with cæsarean section in 70% of cases; and (5) special care of the infant

White claims that her good results are due mainly to the prophylactic sex-hormone therapy In one of their recent series (Nelson et al 1953), consisting of 128 babies, weighing at birth 960 g (2 lb 1½ oz) or more, observed in 1950–52, the mothers were seen once or twice a week during the latter half of pregnancy, most often simultaneously by the physician and the obstetrician All the patients were admitted to hospital at the end of the 34th week (about 40 days before the calculated term) and remained in hospital until delivery Patients with complications were admitted earlier Class-A patients did not have hormone therapy and were allowed to go to term It was the intention to deliver all the other patients by the end of the 37th week, but 25% had to be delivered at the end of the 35th week or earlier

TABLE V—FŒTAL MORTALITY * FROM 1946 TO SEPT. 30, 1955, CLASSIFIED BY BIRTH WEIGHT AND RELATION OF DEATH TO LABOUR

Treatment	*Death before labour or of infants with birth weight 1000–1550 g (2 lb 3 oz – 3 lb 6 oz)*		*Birth weight 1600 g (3 lb 8 oz) or more and baby alive at onset of labour*		Total	
	No of babies	Fœtal loss	No of babies	Fœtal loss	No of babies	Fœtal loss
Long term	130	6 (*5%*)	124	7 (*6%*)	130	13 (*10%*)
Short-term	135	26 (*19%*)	109	19 (*17%*)	135	45 (*33%*)

* See footnote to table III.

The King's College Hospital series, consisting of 141 cases in 1949 (Peel and Oakley 1949) and 275 by June, 1953 (Oakley 1953), carried an unaltered over-all fœtal mortality of about 25% The patients attended the diabetic clinic and were treated as outpatients They were controlled by different, though fewer, doctors, but no attempt was made to bring the blood-sugar to the physiological level Pregnancy was terminated between the 33rd and 38th weeks, and in 75% of cases cæsarean section was done (Oakley 1953) In 56 of 129 cases treated between 1949 and December, 1953, stilbœstrol and ethisterone were given by mouth (Peel 1954) This hormone therapy was not thought to reduce the fœtal mortality Oakley and Peel have not reported their fœtal mortality classified according to the stage of pregnancy at which the patient first attended the clinic, but 18 5% of the infants born by cæsarean section died in the neonatal period (Oakley 1953)

The Medical Research Council's (1955) series was designed as a controlled trial of the value of giving stilbœstrol and ethisterone by mouth during pregnancy The series comprises 136 viable infants distributed among nine centres Apart from the hormone treatment and some general rules (termination of pregnancy between the 34th and 38th weeks by the method most desirable on obstetric grounds, and keeping the babies in oxygen tents for at least 48 hours after birth) the treatment was not strictly regimented The series was treated by different physicians, obstetricians, and pædiatricians Half the mothers were given hormones by mouth during pregnancy, and the average stay in hospital before delivery was 2 3 weeks The average weight of the babies at birth was about 3 2–3 3 kg (7–7¼ lb) The fœtal mortality (stillbirths and neonatal deaths within a month after delivery) was 25% in both groups

TABLE VI—FŒTAL MORTALITY * FROM 1946 TO SEPT 30, 1955, IN WHITE'S CLASSES B, C, AND D

Treatment	White's classes					
	B		C		D	
	No of babies	Fœtal loss	No of babies	Fœtal loss	No of babies	Fœtal loss
Long term	41	2 (*5%*)	30	3 (*10%*)	50	4 (*8%*)
Short term	44	18 (*41%*)	42	5 (*12%*)	37	18 (*49%*)

* See footnote to table III

Table VII compares the treatments given in Peel's 1949–53 series (Peel 1954), the Medical Research Council's (1955) series, the series of Nelson et al (1953), and our long term series Two factors common to the treatments of the two series—that of Nelson et al (1953) and our long-term series—with the lower fœtal mortality are: (1) one attending physician and good medical treatment during pregnancy ("treatment of every abnormality"); and (2) experienced obstetrical management and infant care by a few persons To get a low fœtal mortality it is unnecessary to do a lot of cæsarean sections or to give sex hormones We deliberately use the word "unnecessary" of sex-hormone therapy because we are not in a position to judge whether this treatment is possibly beneficial To test this a controlled trial would have to be made with material having the lowest fœtal mortality by the classical treatment, and at present there does not seem to be any need for such a trial

TABLE VII—COMPARISON OF SOME PUBLISHED SERIES

Series	Years	No of *cases*	Fœtal mortality (*%*)	Treatment during pregnancy			Rate of cæsarean section (%)	No of teams in obstetric and in infant care
				Sex hormones (% of cases)	Last months			
					Strict medical	No of physicians		
Peel (1954)	1949–53	129	27	43	—	Few	75	One
Medical Research Council (1955)	?	136	25	50	—	Several	?	Several
Nelson et al (1953)	1950–52	128	10	ab 95	— —	One	70	One
Present long term treated series	1946–53	130	10	0	— — —	One	18	One

extradural hæmorrhage, it indicates that a tentorial pressure cone is developing and the patient's condition often deteriorates very rapidly

As Lewin emphasises, a localised bruise or laceration of the scalp is a very useful guide in identifying which side a hæmatoma is on, in 21 of his patients there was a local injury over the hæmatoma He stresses the importance of careful examination of the scalp, and the search should be repeated on the operating-table after the whole head has been shaved. In most cases there is radiological evidence of a fracture overlying the hæmatoma, though occasionally there is none[29 30] X ray examination may also show displacement of a calcified pineal body, and this is of course most valuable evidence of a hæmatoma But even a centrally placed pineal body does not exclude a hæmatoma, since in Lewin's series there were 2 patients with central pineals, in each the extradural hæmatoma was in an unusual site, one in the posterior fossa and the other under one frontal lobe Most extradural hæmorrhages are in the temporal regions but occasionally they may be found, as in these 2 cases, in the posterior fossa or under the frontal lobes, and this is one of the main reasons for the high mortality, since the accurate diagnosis of bleeding in these sites may be very difficult Lumbar puncture is not a great help in diagnosis and has the very definite danger of precipitating a tentorial pressure cone, puncture was performed in 13 of Lewin's patients and in 5 the pressure was normal It is by no means certain why the pressure is normal in the presence of a large extradural clot, but it is important to realise that it may be so, otherwise the possibility of a hæmatoma may be dismissed in spite of a suggestive clinical picture Schneider and Tytus[24] drew attention to another pitfall in diagnosis when there is profuse cerebrospinal rhinorrhœa or otorrhœa after a head injury extradural hæmorrhage may produce very little immediate signs of rising intracranial pressure

As Lewin observes, the important clinical pointers to the presence of a hæmatoma are deterioration in the level of consciousness once improvement has begun, the onset of symptoms and signs of cerebral compression, and the development of fresh neurological signs

COOPERATION IN TREATMENT OF CANCER

THERE has in recent years been a good deal of discussion about the best methods of securing cooperation between physicians, surgeons, and radiotherapists in cancer treatment In many centres the days are passing when a patient with cancer tends to be treated rather by the method most familiar to the first specialist he sees than according to his need, but the resources for investigation and treatment still differ widely between one hospital and another Joint cancer consultation clinics are greatly aiding selection and combination of treatment and, through joint follow-up clinics, have provided valuable opportunities for specialists to see what can be achieved by methods other than those in which each is expert A further advantage has been the concentration of clinical material and specialist experience for teaching purposes

In 1944 an interesting experiment on these lines was organised by the Royal Marsden Hospital (then the Royal Cancer Hospital) Joint cancer consultation clinics had been set up within the hospital just before the war and these were later extended to include other hospitals, starting with the Brompton Hospital for Diseases of the Chest and the Chelsea Hospital for Women, its immediate neighbours with which there had been a long unofficial association By 1945 these clinics had been extended further to include the Moorfields, Westminster, and Central Eye Hospitals, and the Royal National Throat, Nose, and Ear Hospital For four years the Royal Free Hospital cooperated in the scheme until its own radiotherapy department was re established, and another arrangement existed with the Princess Beatrice Hospital until it became part of the Westminster Hospital group At present the group of hospitals running joint cancer consultation clinics consists of the Brompton Hospital for Diseases of the Chest, the Chelsea Hospital for Women, Fulham Hospital, Moorfields, Westminster, and Central Eye Hospitals, the Metropolitan Ear, Nose, and Throat Hospital, the National Hospital, Queen Square (together with the Atkinson Morley Hospital and the neurosurgical unit of the Hospital for Sick Children, Great Ormond Street), the Royal National Throat, Nose, and Ear Hospital, the Royal Sussex County Hospital, St Mary Abbot's Hospital, St Peter's, St Paul's, and St Philip's Hospitals, St Stephen's Hospital, and the West End Hospital for Nervous Diseases

Over 1000 patients a year are now seen at the joint clinics held between these hospitals On May 11 and 12 this group is to hold its first general meeting, which will be open to the medical profession[1]

On Friday, May 11, starting at 10 A M, at the Royal College of Surgeons there will be a series of reports, mostly from the special postgraduate hospitals cooperating in the scheme, giving some account of the working of the joint consultation clinics of the way in which surgery or radiotherapy have been selected or combined in the treatment of special groups of patients, and of the results obtained over the past twelve years There will also be accounts of some of the joint clinical research projects initiated within the group An exhibition illustrating the work of the clinics will be on show in the council room An account will also be given of the cooperating hospitals cancer registry which has been set up to provide a direct registration and statistical service to each of the cooperating hospitals The scheme is designed to obtain complete cancer registration within this group of hospitals and for the registry to provide each individual hospital, and indeed each individual member of each staff, with any recorded information they may require about any group of patients seen, including the follow up

On Saturday, May 12, the Royal Marsden Hospital will be open from 10 A M to 1 P M, and demonstrations of special facilities available to the group and some of the clinical investigations, treatment, and research carried out will be on view

SOCIETY OF MEDICAL OFFICERS OF HEALTH

NEXT week this society is celebrating the centenary of its foundation At the opening meeting on Tuesday afternoon at B M A House Dr Huntington Williams, health commissioner of Baltimore, will deliver a message from the American Public Health Association and himself receive the honorary fellowship of the society from Dr C F White, the president The following day at 2 15 P M open fora will be held on public health problems of today, and at 4 30 P M Lord Adrian, O M, will deliver an oration on the Organisers of Health In connection with the celebrations, exhibitions will be held at the Wellcome Historical Medical Museum and the London School of Hygiene and Tropical Medicine The Lord Mayor and corporation of London are giving a banquet, and the London County Council and the British Medical Association receptions, in honour of the society

THE INDEX and title-page to Vol II, 1955, which was completed with THE LANCET of Dec 31, is to be issued next week A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W C 2 Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now

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[29] Turner J W A *Brit med J* 1941 ii 569

[30] Falconer M A Schiller F *Lancet*, 1942 i 532

[1] Copies of the programme may be had from the House Governor Royal Marsden Hospital Fulham Road, London, S W 3

TABLE II—PLASMA-VITAMIN-A LEVELS IN MARASMIC INFANTS

Case no	Disease	Age (mos)	Weight (kg)	Plasma vitamin A (I U per 100 ml)			
				Fasting (duplicates)		4 hours after the standard oral dose of vitamin A (duplicates)*	
1	Gastro-enteritis	1	3 1	95	110	165	150
2	Gastro-enteritis	2	3 6	50	—	415	—
3	Bronchitis	3	3 1	135	210	755	765
4	Mongol	4	4 0	Nil	—	Nil	—
5	Feeding disorder	4	2 6	130	115	105	100

* The standard oral dose of vitamin A was 12 500 I U vitamin A palmitate in arachis oil per kg of body weight

level after vitamin-A concentrates had been withheld for at least forty-eight hours

The plasma-vitamin-A level was estimated by spectrophotometry by the method of Bessey et al (1946) modified by the use of 2-ml plasma samples and the substitution of benzene for the kerosene-xylene mixture used to extract the vitamin A from the plasma The spectrophotometric readings were converted into I U of vitamin A by reference to a standard curve prepared from pure solutions of vitamin-A acetate in benzene

Results

The results are shown in tables I, II, and III The infants with idiopathic hypercalcæmia had higher fasting plasma vitamin-A levels than either the infants marasmic from other causes or the healthy children, they also had higher plasma-vitamin-A levels four hours after the standard test dose Cases 12 and 13 are exceptions, but beginning recovery from the disease may explain their normal results, they had been under medical supervision for four months and five months respectively, and both were starting to thrive when their vitamin-A levels were estimated

TABLE III—PLASMA-VITAMIN-A LEVELS IN INFANTS WITH IDIOPATHIC HYPERCALCÆMIA

Case no	Age (mos)	Weight (kg)	Serum calcium * (mg per 100 ml)	Plasma vitamin-A (I U per 100 ml)			
				Fasting (duplicates)		4 hours after the standard oral dose of vitamin A (duplicates) †	
6	8	5 6	15 5	245	280	3590	3480
7	14	6 3	15 3	280	430	940	905
8	11	7 0	15 2	225	210	1320	1365
9	8	6 6	15 1	365	435	1720	1810
10	4	5 4	14 8	355	355	3230	3375
11	10	5 8	13 5	255	—	1215	—
12‡	9	5 5	13 3	160	155	605	595
13	7	6 5	12 4	120	235	975	1095

* The serum-calcium levels were estimated within a few days of the plasma vitamin A levels

† The standard oral dose of vitamin A was 12 500 I U of vitamin-A palmitate in arachis-oil per kg of body weight

‡ This patient was given 20,000 I U of vitamin A per kg of body weight

The plasma vitamin-A levels of the infants with idiopathic hypercalcæmia were compared by statistical methods with the corresponding levels, of the healthy children These calculations showed that both the fasting levels and the levels four hours after the standard test dose were significantly higher in the infants with idiopathic hypercalcæmia The mean plasma-vitamin-A levels are shown in table IV The calculations were made only on the duplicate estimations to eliminate the variations between children—e g, a variation from an average value of 3545 I U per 100 ml of plasma four hours after the standard test dose in one infant with idiopathic hypercalcæmia to 600 I U per 100 ml of plasma in another

Discussion

Aron (1949) has shown that the plasma-vitamin-A level of a healthy person is kept almost constant despite variations in the dietary intake of the vitamin He considers that this is due to the existence of a mechanism for controlling the level of vitamin A in the plasma, and that the liver plays an important rôle in this regulatory process In apparently healthy infants a high oral intake of vitamin A daily for several weeks will raise the plasma-vitamin-A level, but this returns to normal within a few days of reducing the intake to that contained in a normal diet (Josephs 1944) None of the infants with idiopathic hypercalcæmia in the present series had a high vitamin A intake immediately before the date on which the estimations were made, hence vitamin-A overdosage was not responsible for the high fasting plasma-vitamin-A levels of these infants Various diseases are associated with alterations in the plasma-vitamin-A level, which is low in febrile states (Clausen and McCoord 1938, Lindquist 1938) whereas it is high in chronic nephritis and in the nephrotic syndrome (Clausen and McCoord 1938) Idiopathic hypercalcæmia appears to belong to this group of diseases Aron (1949) has suggested that such diseases interfere with the mechanism normally responsible for maintaining a constant plasma-vitamin-A level

TABLE IV—MEAN PLASMA VITAMIN-A LEVELS
(Calculations made only on duplicate estimations)

—	Plasma vitamin A (I U per 100 ml)	
	Fasting	4 hours after the standard oral dose of vitamin A*
Infants with idiopathic hypercalcæmia	275	1786 1
Healthy children	130 6	648 1

* The standard oral dose of vitamin A was 12 500 I U of vitamin-A palmitate in arachis oil per kg of body weight up to a maximum of 250 000 I U of vitamin A

McCoord et al (1948) showed that, after a standard oral dose of vitamin A, the rise in the plasma-vitamin-A level of malnourished infants is smaller than in healthy infants This finding has been confirmed in the present investigation It contrasts with the greater than normal rise observed in the infants with idiopathic hypercalcæmia The height to which the plasma vitamin-A level rises after a large oral dose of vitamin A must depend on the rate of absorption and the rate of storage It is impossible, however, to determine from the present data whether there is increased absorption or diminished storage of vitamin A in idiopathic hypercalcæmia

A disorder of vitamin-A metabolism similar to that found in idiopathic hypercalcæmia has been described in the nephrotic syndrome (Kagan et al 1950) Moore and Sharman (1951) have drawn attention to this and to other evidence which appears to connect urinary diseases with vitamin-A deficiency and with abnormalities of vitamin-A metabolism It is of interest, therefore, that idiopathic hypercalcæmia, in which renal calcinosis sometimes develops, provides a further example of this association

Since vitamins A and D are both fat soluble, an abnormal vitamin-A metabolism in idiopathic hypercalcæmia is a further indication that vitamin-D metabolism may be abnormal in infants who develop this syndrome

Summary

In 8 cases of idiopathic hypercalcæmia the plasma-vitamin-A levels were estimated before, and four hours after, a standard oral dose of vitamin A The results

of hospital privileges, but British patients expect to be referred to specialists for major procedures and they do not think less of their own doctor because of this. In contrast, general practitioners in small towns in Western Canada do much surgery, partly because this is often essential, and partly on the assumption that their patients expect it of them. A demand by the general practitioner for hospital work or some form of specialised practice is reasonable if this will fill a local need, but it should not be allowed to prevent him giving adequate time to the rest of his patients.

The general practitioner is taught as a student principally about diseases which are best treated in hospital, and he tends to think that hospital practice is the most important aspect of medicine. This is bad because he will be frustrated at being unable to practise the sort of medicine he was taught, and also because, in his quest for hospital privileges and impressive equipment, he may be diverted from his rôle of adviser and friend to his patients.

The overwhelming part played by the hospital and its specialist staff in our education deeply affects our ideals of medical practice. We spend so much of our early career inside one that it is difficult for us to see that a hospital in relation to present day medicine as a whole is only a specialised instrument—certainly a very large, important, impressive, and expensive instrument, and for this last reason one which must be reserved as far as possible for patients in a phase of their illness in which it is needed. Since the hospital is the scene of so much impressive, and by and large successful, medical endeavour, the student may be forgiven for thinking that it is the whole world of medicine that matters, in which the consultants are the heroes. The consultants have not been assiduous in discouraging this view. It is not surprising, therefore, that the doctor graduates as an indifferent specialist rather than as a general practitioner, and that he retains a respect for hospital privileges, access to impressive equipment, and technical skill.

The original concentration of medical teaching in hospital was necessary to break the unscientific traditions of the apprenticeship system, which still is often perpetuated in assistantships. But general practice has become increasingly effective, recently aided by chemotherapy and by diagnostic facilities such as the Public Health Laboratory Service. The extension of medical care to the whole community has only been possible through a great increase in the effectiveness of general practice ; similarly, the economical use of hospitals and the extension of medical care to the whole community are possible only because of the general practitioner's work outside hospital. If general practice is limited in scope, it is because medical education did not prepare the present generation of doctors for this type of work.

Introducing students to general practice is still in the experimental stage, and although this has been under way for some time in the United States and Scotland, English and Canadian universities seem to be approaching the problem more cautiously ; the colleges of general practice in England and Canada should speed this scheme.

The general practitioner has a continuous responsibility for his patients, although for a phase of an illness they may be in the hands of a specialist. In *fulfilling this* responsibility he encounters organic disease he knows how to diagnose and treat rationally, disease he can diagnose but must refer for treatment (which if he conducts his practice well need not constitute more than 15% of his cases), organic disease which neither he nor anyone else can do more than palliate, many disorders of a probable organic origin which do not fit into any distinct syndrome, and 30% or so ailments largely psychogenic. This is a sufficient challenge to any man's scientific and humane abilities for which he needs as much time as he can gain. Unfortunately his training has prepared him very unevenly for these various types of case. The young general practitioner not unnaturally tends to pay most attention to the types of case he has been taught about and is apt to think that patients who do not have syndromes he recognises are not really ill. Yet if he attempts to select those he will help and those he feels not morally entitled to help, he creates needless difficulty for himself and unhappiness and hostility in those rejected. Treatment of course does not necessarily consist in granting all demands, but may consist in a firm but polite explanation why none is necessary.

Until he has had much experience he tends to judge the quality of general practice by specialist *criteria*, and feels that he should be using methods appropriate to dealing with disease at the specialist level. Since he has to deal with comparatively large numbers of patients, inevitably part of his work consists in "screening" or selecting *those most suitable for specialist treatment*. This should cause no shame and is an important part of his function as part of the medical team. Specialists appreciate the general practitioner who uses them efficiently on behalf of his practice.

Conclusion

No rigid pattern for general practice should be devised. The general practitioner's work is decided by the needs of the society he serves, but his ability to fill this need is impaired if his *training gives him too* rigid a conception of medical practice ; for instance, in the small towns of Western Canada he is required to do much emergency surgery which in Britain he is not. General practice fills the very big gap between the medical needs of the *community and the capacity of hospitals and specialists* to meet them.

More doctors should be encouraged to become general practitioners ; and practices should be made smaller. They could then spend a greater amount of time in *consultations (at present brief* by Canadian standards) as friend and adviser to their patients.

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THE EFFECTS OF SEPARATION FROM THE MOTHER IN EARLY LIFE

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LARGELY through the work of Dr. John Bowlby, there has been much discussion in recent years about how children's personalities may be affected by stays in institutions or in hospital during early life. For the present study we chose, from among 141 backward children, the 25 who had been separated from their mothers for at least ten weeks during their first *four* years of life. Actually the average length of their separation was *over eighteen* weeks in the first year, nearly seventeen in the second, and for the whole of the first four years no less than seventy two weeks, or about one third of their lives up to that point.

Assessments of their emotional development were provided by their teachers on the comprehensive Bristol Social Adjustment Guide, and comparable information as to their domestic behaviour was obtained from interviews with the mothers or with the staff of institutions. Since emotional factors are very important for the understanding of backwardness, indications of the mutual affection between mother and child had been

BIOCHEMICAL DATA AND BLOOD-PRESSURE

—	Day of disease																	
	1	2	3	4	5	6	7	8	9	10	11	12	13	16	20	27	30	35
Hb (g per 100 ml)			11 5	8	7 7	7 7	7 4	8 7	7 1	7 1			7 4	5 9		9 9	10 5	
Urea (mg per 100 ml)					80	400	410	410	420	440			230		56			30
Serum-sodium (m eq per litre)					137 5	137 5	137 5	145	140	137 5			137 5					
Serum-chloride (m eq per litre)					103	104	104	107	105	105			106					
Serum potassium (m eq per litre)					5 6	5 7	4 6	5 5	4 9	4 75			4 6					
Plasma bicarbonate (m eq per litre)					26 2	25 7	22 3	28 5	23 2	21 4			27					
Serum bilirubin (mg per 100 ml)			5 0	4 8	5 0					0 2			0 2					
Urine (ml daily)				60	190	210	300	330	840	1020	1020	1830	2070					
Vomit (ml daily)				45	120	480	600											
Total output of fluid (ml daily)				105	310	690	900	330	840	1020	1020	1830	2070					
Fluid intake (ml daily)				1400	1200	900	1300	1300	1050	1980	1980	1200	2130					
Blood pressure (mm Hg)				130/85	135/85	135/70	110/70	110/70	130/70	130/70								

normal. At no time did the serum potassium level rise above 6 m eq per litre (normal = 4–5 m eq per litre) The blood-urea level was 56 mg per 100 ml on the twentieth day Since the anæmia still persisted (Hb 8 6 g per 100 ml) and Heinz bodies and fragmented red cells were still present, the patient was given a further transfusion of 1000 ml of packed red cells, which increased his Hb to 10 4 g per 100 ml

Convalescence was complicated by a recurrence of acute bronchitis and by a deep vein thrombosis in the left calf, from both of which he recovered rapidly He went home thirty three days after admission, and when seen again a month later he was very well His blood urea level was then 35 mg per 100 ml. and Hb 13 3 g per 100 ml, and his erythrocytes were morphologically normal

Discussion

The fatal dose of potassium chlorate varies greatly A. R Cushny (Grollman and Slaughter 1947) said that 1 g had proved fatal in a child, whereas adults had swallowed 40–50 g without developing serious symptoms, he remarked that poisoning was more likely in nephritics than in healthy people Witthaus (1911) stated that the minimum lethal dose was 12 g for an adult, 5 g for a child, and 1 g for an infant

The toxic effects of orally administered potassium chlorate are due to three distinct causes

(1) A non specific local action characterised by immediate nausea, vomiting, and mild diuresis

(2) The effect of the potassium ion on the myocardium, leading to hypotension, bradycardia, heart-block, and, in fatal cases, ventricular fibrillation

(3) The effect of the chlorate⁻ion, which denatures Hb with the production of Heinz bodies, and lyses the erythrocytes This reduces the oxygen-carrying capacity of the blood The hæm of the Hb thus liberated becomes attached to serum albumin, forming the brown pigment methæmalbumin (Fairley 1941), which is probably excreted as bilirubin by the liver Part of the liberated Hb may be excreted unchanged in the urine

The mass destruction of red cells has consequences similar to those found in the syndrome variously known as pigment nephrosis, transfusion kidney, tubovascular syndrome, and renal anoxia syndrome (Maegraith et al 1945) Potassium chlorate is metabolised slowly, and about 90% is excreted unchanged in the urine (Grollman and Slaughter 1947) It thus remains in the body during any period of anuria and continues hæmolysis

Acute potassium-chlorate poisoning has therefore a very characteristic course It begins with an attack of vomiting, followed by transient cyanosis due to the formation of Heinz bodies The onset of hæmolysis is rapid, and the consequent anæmia and jaundice are severe by the third day, when Hb, bilirubin, and urobilin are present in the urine and the risk of anuria is greatest Hæmolysis is likely to continue for several days, even after the flow of urine has been restored

Potassium-chlorate intoxication thus provides another example of oliguria due to renal damage Bigby and Avery Jones (1949), Bull and Joekes (1949), and Discombe (1954) have all emphasised that patients with this form of acute oliguria usually recover, provided that they are not *given* potassium salts, and that overloading of the circulation with parenteral infusions of saline solution, glucose, sucrose, or sodium sulphate is avoided Evans et al (1953) have pointed out that hyperkalæmia is the common cause of death, and that it is due to the breakdown of endogenous intracellular protein This process is accelerated by pyrexia, infection, and semistarvation, and is minimised by the prevention and cure of secondary infection and by providing a protein-free high-calorie diet (Bull 1955) These principles were successfully used in treating the present patient Since at no time did his serum-potassium level rise above 6 m eq per litre, ion exchange resins in the sodium cycle, as advocated by Evans et al (1953), were not used The anæmia, which may further impair renal function, was treated with transfusions of packed red cells Removal of the potassium-rich plasma lessened the danger of hyperkalæmia and averted disturbance of the fluid balance Control of the patient's respiratory infection and oral sepsis was achieved by systemic chemotherapy In retrospect such high dosage was not required in the presence of poor renal function 1 mega-unit of penicillin G given intramuscularly daily is all that is required (Bull 1955) Efforts to promote renal activity with oral potassium citrate and parenteral infusions were avoided because they are useless and indeed dangerous (Discombe 1954)

Summary

A case of Heinz-body hæmolytic anæmia following the accidental ingestion of potassium chlorate is reported

The hæmolysis persisted for twenty days and was complicated by oliguria lasting nine days

Potassium chlorate poisoning is yet another cause of renal damage with oliguria best treated by the Bull regime

I wish to thank Dr K. P Bull for permission to publish and for his encouragement, and Dr George Discombe and Dr Clifford Hoyle for invaluable advice and criticism in the preparation of this paper

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them as maladjusted children It is significant that all these again were unnaturally helpful towards their mothers There were also powerful additional factors, other than early illness or separation, which could account for their unsettledness One of these children was the twin of a girl in the well-adjusted group His unsettledness is of theoretical interest in that besides being badly scalded as an infant he suffered distressing experiences during the nine months' separation, while his stable girl-twin did not During his stay in a residential nursery, he was removed to hospital because of ringworm, and underwent what to a toddler must have been the terrifying ordeal of having his head shaved without his mother or other familiar person being there to comfort him

Another of this unsettled group well illustrates how the lack of a mother in the first years of life, while not making the child into a completely "affectionless character," may provide it with a mechanism by which it can cut itself off from affection This withdrawal will not be the dominant element in the personality unless the child feels itself unwanted and unloved in its contemporary life, but it reverts to a defensive attitude of "affectionlessness" when punished or is otherwise in disfavour

The boy in question was placed in an institution when 3 weeks old, and remained there until he was 3 The mother could not bear to visit him during most of this time, but accepted him gladly when, on her marriage, she had him to live with her When, preparatory to his homecoming, she visited him, he was "petrified of anybody and stayed in the middle of the room and screamed" At home "he was not a cuddly child, you couldn't pick him up on your knee, he didn't want it" Her constancy, however, won him over, and the only complaint she made of his home behaviour was that he had terrific tempers and got stubborn "for really nothing at all" This underpattern of withdrawal shows itself occasionally in children who have had to do without a mother in their early years, when they are crossed they go into a stubborn "freeze"

The Maladjusted

So far 21 of the 25 children are accounted for, which leaves only 4 really maladjusted ones One of these was a foundling child who had been in institutions all her ten years of life Little can be said of her except that she represented that mixture of hostility and anxiety for acceptance which is found as a type of maladjustment just as much outside as inside institutions

The second girl was put in an institution when she was $3^1/_2$ for some two years her mother was an invalid who later died After that she was passed back and forth among various relatives, with the result that she became virtually unmanageable, and could not be kept in a residential school, in a mental defectives' institution, or with a foster-mother—until finally an aunt by marriage took pity on her and heroically showed herself determined to keep her This child, after a year of this latter day security, was very friendly and attention seeking, but would become stormily defiant at the slightest provocation, and stole frequently as the pronouncedly anxious-hostile type are inclined to do

The third child was away from her parents, either in hospital or evacuated, until she was nearly 6 Her main preoccupation was expressed in her repeated question to her mother "If I am not a good girl will I have to go away?" This child was also of the defiant hostile-anxious type

The common element in these three girls' lives was that they had no permanent mother figure during their childhood, but had to make do with such affection as was offered by whoever was in charge of them for the time being Even then they were not affectionless they had a burning need for affection, alongside the rejection and hostility which they always kept ready at hand in case their need for love was not met Their maladjustment was the imprint upon them, not of any specific phase in their lives, but of their motherless state over large stretches of it

The last child comes nearest to the type of the "affectionless character" He had trained himself never to seek sympathy, and so he never cried when he hurt himself His mother often threatened to have him put away, especially over his stealing, in which he indulged shrewdly both at home and at school, but he showed no distress at the threat He was one of those children who, although reputedly of dull intelligence, could "tell lie after lie and look you full in the face" How is such a character made? His early history did not differ greatly from that of the other maladjusted and unsettled children Being exceedingly puny and underweight at birth he was retained in hospital for the first three months of his life When, at that age, he was returned to his mother she put him in a day nursery because she was in residential service At 1 year he had another three months in hospital with meningitis When he was 6 or 7 his mother, as she said, "tried to get him away but we could not do anything about it He was a drawback to me working in service" All this was related in front of the child in a matter of fact way It was evident that the child must have heard all the details of the steps she was taking to get rid of him Thus was progressively destroyed his faith in her loyalty as a mother It was this unnatural situation during the years between 6 and 9, rather than his early experience, that was making him seek refuge in affectionlessness But he helped his mother with the washing up, swept for her, and "starts to clear the table even before you have finished"—which shows that the term "affectionless character" in this as probably in most cases is an over-simplification, about which caution must be exercised in the diagnosis of maladjustment

Separation and Security

What conclusions can be drawn as to the effects upon these 25 children of long early separation from their mothers? The only definite one is negative in itself the separation certainly does not have the dire consequences that have been supposed, for, if it did, there would have been more than 4 maladjusted children among the 25 considered Furthermore their maladjustment, and the unsettledness of 5 of the other children, can be accounted for by a succession of other factors in their later lives The formula for maladjustment is to deny the child family security More exactly, this means that for stability of character a child needs to feel that it has reliable—that is to say permanent—human attachments It is not affection in the sense of fondling or treats or indulgence that counts, but affection in the sense of a loyalty which induces the parent or other adult to stick to the child through thick and thin and neither relinquish the child to other care nor threaten or appear likely to do so A child who has never enjoyed these loyalties from any adult at any time will become the so called "affectionless character"—the toughened rogue without loyalty or sense of decency But such children are exceedingly rare, and, certainly at the pre adolescent stage, the loss of feeling will still be incomplete and there will be at least a modicum of anxiety for acceptance

There is nevertheless some evidence that long separation can have a detrimental effect upon a child's emotional development In the total sample of 141 there were 9 children who had been separated a month or more under 4 years of age without, so far as was known, any serious illness or its equivalent Of these 5 were maladjusted (3 of them being mentioned above in the group of 25 separated ten weeks or more), and 4 were unforthcoming The quantitative evidence as to the effects of separation as such is thus scanty, but the indications

Relief of Symptoms

WALTER MODELL, F.A.C.P., associate professor of clinical pharmacology, Cornell University Medical College Philadelphia and London W B Saunders 1955 Pp 450 56s

IT is perhaps true, as Dr Modell believes, that, with the great advances in curative medicine, the relief of the patient's distress has come to be neglected Certainly, the proper use of symptomatic treatment calls for skill and judgment, and this book provides useful help It is written informally and readably, and reflects the wide practical experience of its author

The opening chapters discuss the general principles involved in the relief of symptoms and they contain much sound advice Important symptoms are then dealt with individually A final chapter describes the uses of cortisone and gives warning of its danger as a masker of symptoms There is a refreshing clarity and briskness in the writing

As a pharmacologist, the author is able to speak with authority about the use of drugs, and he mentions many substances recently introduced It is interesting to note that heroin receives little attention, either in the chapter on cough or elsewhere

Arthroplasty

SIR J D BUXTON, F.R.C.S., consulting orthopædic surgeon to King's College Hospital London Pitman Medical Publishing Co 1955 Pp 126 30s

WRITING in an easy and direct style, Mr Buxton gives an excellent historical review of the work on arthroplasty of all joints over the past fifty years, but it is only where the hip is concerned that he goes into sufficient detail to be of real help to the orthopædic surgeon He was one of the first in this country to make extensive use of the 'Perspex' femoral head, experience of this operation dates only from 1950 and recent reports on the late results, at least in this country, have shown that the durability of the perspex head is much less than had at first been hoped The pendulum is now swinging back towards the old operations, such as McMurray's osteotomy and Girdlestone's pseudarthrosis, where the maintenance or creation of a mobile hip is essential, and the indications for the Judet procedure are becoming relatively restricted

Nevertheless, this is an interesting monograph which will be enjoyed by many It is excellently produced and embellished with illustrations of the highest class, and there are very useful chapters on rehabilitation and record charts

Applied Medical Bibliography for Students

WILLIAM DOSITE POSTELL, medical librarian and professor of medical bibliography, Louisiana State University School of Medicine, New Orleans Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 142 32s 6d

SOME instruction in the use of libraries, much of it informal, has been given in America and in this country for many years, but there are very few medical schools in which medical bibliography has managed to win its own little corner in the curriculum Mr Postell, a librarian of great experience, has embodied the substance of his lectures on this subject into a book which medical students (and indeed all users of medical libraries) may read with interest and profit

The book starts with an account of the evolution of medical literature, which includes an excellent chapter on the history of medical periodicals Information is then given on the arrangement of the library, the catalogue, some of the classification schemes in common use, basic reference works, bibliographical tools, and the periodical collection The final part contains advice on medical writing and on the principles of bibliographical citation

There are few questionable statements of fact, but it is wrong to say that most of the earlier printed books were on parchment or vellum, and the author is also mistaken in his belief that a sheet folded four times is known as a quarto and one folded eight times as an octavo The information concerning the *Medical Directory* is out of date and the list of bilingual medical dictionaries is inadequate

A more serious criticism is that Mr Postell does not always seem to know whether he is writing for the student of medicine or for the student of librarianship Thus, the instruction regarding alphabetisation in catalogues may mislead the medical reader into expecting uniformity in treatment which he will certainly not find in practice Much of the space devoted to medical writing could have been more profitably given to certain forms of literature (such as governmen publications, theses, reprints, and congresses) which presen special difficulty to the inexperienced reader A more precis evaluation of some of the reference sources mentioned, and hints on the extent and peculiarities of the "literature" in the special departments of medicine would have added considerably to the value of the work The procedure fo looking up references on subjects such as tuberculosis o cancer is quite different from that for the "rare" diseases but distinctions of this kind are not mentioned

The difficulty of seeing the problems of bibliographica research from the reader's point of view is very great and although the author has compressed much valuable information and advice into a short book it can hardly be said that he has reached the heart of the matter

Die Hand des Kranken

Prof Dr MAX BURGER, Direktor der medizinischen Universitätsklinik Leipzig Munich Lehmanns 1956 Pp 445 DM 37

To doctors, as to artists, the hand must always be o interest, for it has much to tell the discerning physician Professor Burger has done good service in collecting so much of value in this unusual and stimulating book

He has not limited himself to mere lists of pathologica states of the hand, though there can be few if any of these that he has overlooked He has also described the norma hand, its anatomy and physiology, and added many interesting sidelights on such things as finger prints palmistry and even the deaf-and dumb language In his description of disorders and abnormalities of the hands he gives brief accounts of the general diseases underlying them, and the many bodily change in which the hand takes part The book is beautifully illus trated by some 200 pictures, mostly photographs and these alone tell a remarkable story of the manifold diseases of the hand.

No-one reading this book will fail to find much of interest in it—perhaps much that he has not known before

Thallium Poisoning

J J G PRICK, professor of neurology and psychiatry University of Nijmegen, W G SILLEVIS SMITT, professor of neurology, University of Utrecht, L MULLER, industrial physician, Enschede The Netherlands Amsterdam Elsevier London Cleaver Hume Press 1955 Pp 155 19s

THALLIUM is the active principle of many rat poisons and is easily obtainable In Great Britain all thallium salts are schedule-1 poisons and their sale is strictly controlled, but on the Continent thallium is rapidly superseding arsenic as the most common means of murder by poisoning This monograph was written because the symptoms and signs of thallium poisoning are not well known.

The symptoms are acute gastro intestinal upsets followed by signs of renal damage and peripheral neuritis If death does not occur in the acute stage, the peripheral neuritis progresses rapidly and baldness occurs after about twelve to fourteen days A butterfly shaped seborrhœic rash may develop on the face, and semilunar-shaped areas of discoloration of the nails may be seen

Professor Prick and his colleagues include in this useful study accounts of clinical cases, necropsy findings, and the results of animal experiments. The photographs of patients and photomicrographs of pathological tissue are of a high standard

Chirurgie du corps thyroide

SYLVAIN BLONDIN, chirurgien de l'Hôpital Beaujon Paris Masson. 1955 Pp 292 Fr 2600

THIS book is one of a series of surgical monographs edited by Professor Mondor The text is based throughout on the author's personal experience, sustained by a review of the literature which appears rather sketchy so far as British and American authors are concerned Operative procedures are described, though not in great detail The author has a strong preference for the use the greater will be the blow if the family loses its "mother." To a group of normal or stabilised children such a change can probably be overcome without harm, but for a maladjusted child, to take away the woman in whom it has learnt to trust may be absolutely disastrous. Such children should be placed in family groups which are likely to have a permanent mother-figure.

Assessment

The precise assessment of the influence of the events of early life upon emotional development obviously depends upon our having the means of diagnosing the nature and degree of maladjustment. In the past we have had perforce to rely upon subjective clinical assessments. These, however, are unreliable because they are weighted first by the interpretative preferences of the individual clinician and secondly by the fashion of the times. For example, psychopathic personalities and affectionless characters are at present being over-diagnosed. An alternative, and more objective, means of assessment has proved successful in the Bristol studies. This asks *the observer to furnish only data as to the child's* behaviour and attitudes, the interpretation of the latter being limited to a recognition of elementary emotional expression. *It has been found that the behavioural* data thus provided fall into fairly clear syndromes, indicating the existence of a small number of general maladjusted attitudes which serve as a basis for the diagnosis of maladjustment.

Summary

This has been a study, based on the case histories of backward children, of the effects of early adverse factors upon personality-development, with special reference to separation from the mother.

The mere fact of separation had a markedly small specific effect, but it contributed to unsettledness or unforthcomingness when other adverse factors were present. With short separation, the attendant circumstances of the separation and the maternal care received on return home were seen to be more important than the separation in itself.

The preventive indications are that, where a child has to undergo painful or frightening treatment, the mother should enter hospital with the child; for other hospital treatment frequent visits should suffice, together with guidance to the mother about the homecoming.

The minority of maladjusted children in the group of "separateds" owed their condition in the main to lack of a permanent parent figure throughout large parts of their lives, including their contemporary situation. Separation could predispose to "affectionless character," but this is due to a lack of maternal loyalty throughout life.

The most striking positive finding from the point of *view of personality-development was the high proportion* of early illness among the unforthcoming children. This was a general state of anxiety seen as chronic lack of confidence and over attachment to the mother. To this separation was only a minor contributory factor.

The Wider World

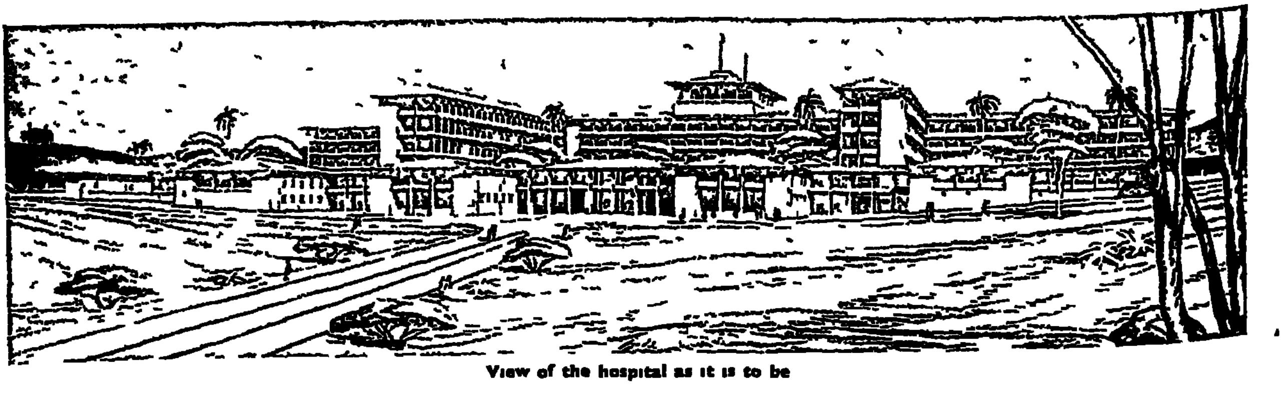
IBADAN

The New University College Hospital

Ibadan, visited by the Queen and the Duke of Edinburgh towards the end of their tour of Nigeria, is one of the most remarkable cities in Africa. Capital of the Western Province, with a population of more than half a million, it is the fourth or fifth largest city in the whole continent. But it is not so much for its size that Ibadan is likely to play an increasingly important part in the world as for its development in the past decade as a university town and a centre of African learning.

Since the late war, Nigeria has made notable progress alike in the political, the economic, and the educational fields. Politically, Nigeria is now a Federation with three component regions and the Trust Territory of the Cameroons. Both in the regions and at the centre political power is very largely in the hands of Nigerian ministers. Mainly because of favourable prices for produce the post-war period has been one of relative prosperity with expanding public revenues and much development both in the public and private sectors. But here, as elsewhere, civilisation and modern methods of communication have outstripped the available technical resources, with the result that the recruitment of trained professional people—always a difficult problem—presses with increasing urgency as the country advances. In particular Nigeria has a great need for doctors, of whom there are only 509 in the whole country, and it was the recognition by the Elliot and Asquith Commissions, whose reports were published in 1945, that the only solution of the problem lay in training Nigerians for positions of responsibility in Nigeria itself, which led to the founding at Ibadan in 1947 of a University College with faculties in arts, science, agriculture, and medicine.

Housed temporarily at first, the University College now has a fine new site just north of Ibadan with striking modern buildings erected at a cost of over £2½ million. But though the other faculties were soon well established, that of medicine had many difficulties to face. From its inception the University College was in special relationship with the University of London, which means that, with modifications to meet particular Nigerian requirements, the students are prepared for London degrees—an essential, in the initial stages, for recognition by the General Medical Council and the acceptance of training at Ibadan as the equal of that elsewhere. This arrangement, however, valuable though it is, brought immediate troubles to the young medical school, for the standards of London are high; and, though the facilities for preclinical training were soon recognised as adequate,

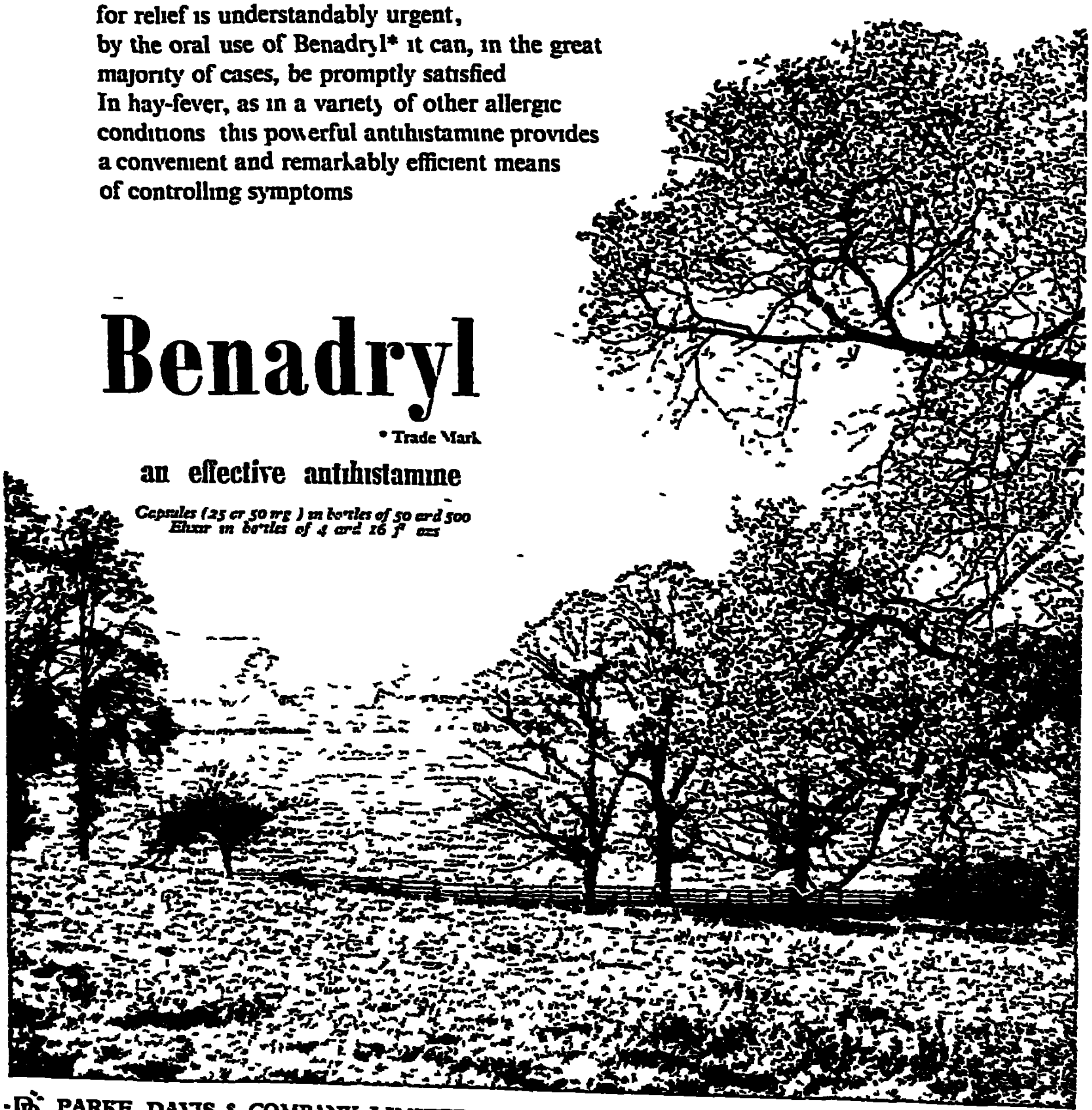


View of the hospital as it is to be

Nothing so active is as that which least seems so

Francis Thompson

A peaceful countryside scene but an active source
of intense discomfort for all those susceptible
to hay-fever, for now is the time of the year when
invisible air-borne pollens begin to take their toll
Incapacitated by continual weeping sneezing
and nasal congestion, the hay-fever patient s desire
for relief is understandably urgent,
by the oral use of Benadryl* it can, in the great
majority of cases, be promptly satisfied
In hay-fever, as in a variety of other allergic
conditions this powerful antihistamine provides
a convenient and remarkably efficient means
of controlling symptoms



Benadryl

* Trade Mark

an effective antihistamine

Capsules (25 or 50 mg) in bottles of 50 and 500
Elixir in bottles of 4 and 16 fl ozs

PARKE, DAVIS & COMPANY, LIMITED (Inc U S A) HOUNSLOW, MIDDLESEX Tel Hounslow 2361 stimulate entry into the profession and lay a firm foundation for the country's medical future

Most of the benefits, however, will not be immediate, and many difficulties remain to be faced—not the least of them staffing Though the first Nigerian medical graduates from the University are now returning and will play an increasing part, the medical faculty, the consultants, and many of the residents and nurses must at first be drawn mainly from Britain—an arrangement facilitated by an agreement recently concluded with the Ministry of Health by which doctors, nurses, and technicians may accept engagements at Ibadan for periods not exceeding six years without losing their position under the National Health Service superannuation scheme

The hospital board of management has repeatedly expressed its lively appreciation of the practical help and interest of the University of London and other British universities and of the valuable contacts which have been established with individual medical schools and teaching hospitals The outstanding need is to secure a medical staff, consultant and non-consultant, of the right size, composition, and quality The opportunities which Ibadan offers for an interesting and rewarding medical career are manifold, and good progress has already been made in building up a suitable staff of resident medical officers and registrars Broadly speaking, the consultant medical staff are recruited and employed by the University College, though they hold honorary appointments under the hospital Important and interesting vacancies exist, or are impending, in this group

* * *

It is not the least of the results of the Royal visit to Nigeria that there is in Britain an increased consciousness, not only of our unity with her peoples, but also of the extraordinary progress which they are making towards their development as a self governing nation To this progress the new University College Hospital will make an important contribution in the years to come

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Public Health

BACTERIAL RODENTICIDES AND INFECTION WITH *SALMONELLA ENTERITIDIS*

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EVIDENCE is presented here that the jena and danysz varieties of *Salmonella enteritidis* are pathogenic to man and animals, and that disease in man and animals is sometimes caused by rodenticides consisting of living cultures of one or both of these organisms

Table I shows that both the jena and danysz varieties of *S enteritidis* cause sporadic cases and outbreaks of food poisoning, including some fatal cases in this country These findings support similar evidence from other European countries and from the U S A The use of *S enteritidis* for destroying rodents is unjustified because man has been accidentally infected in the past and may be so again An outbreak in Stoke on-Trent, due to the jena variety, caused 6 deaths in about 30 people affected 'Liverpool Virus' was suspected of being the source of infection, but complete proof was lacking

An outbreak in 1944, described by Dathan et al (1947), showed conclusively that infection of 4 children was due to the use of a "virus" preparation In this outbreak a child was seen handling an empty bottle of the "virus" preparation *S enteritidis* var *jena* was isolated from this bottle, from the child, and from 3 other children in the household

A large outbreak due to the danysz variety reported privately by Avent showed conclusively that human illness was caused by infection with this organism In an outbreak associated with vanilla slices only 2 persons were known to have had symptoms, and *S enteritidis* var *danysz* was isolated from the mice in the bakery concerned The bakery had been baited with *S enteritidis* var *danysz* to clear it of vermin a month earlier (Ministry of Health 1955)

Scott (1933) described an outbreak, affecting 38 people and causing 1 death, in which food was probably infected by mice A "virus" preparation containing *S enteritidis* had been used in the establishment, and this organism was isolated from apparently healthy mice on the premises These mice were probably infected by the "virus" and became healthy carriers

So far the emphasis has been placed on infection in this country, but there are many reports of outbreaks and deaths in other countries Leslie (1942) reviewed the published cases of human infection, due to the use of "virus" preparations, in Denmark, Germany, the U S A, and other countries

The use of bacterial rodenticides raises many problems The rodents, as a result of eating bait, develop gastroenteritis and, if it is fatal, die of septicæmia (Bahr 1947) During this illness the organisms are excreted in the fæces, which may infect food As in all salmonella infections, some of the rodents become infected and remain healthy or recover from the infection Branham and Robey (1929) showed that mice infected with *S enteritidis* may excrete the organism in the fæces for up to 21 days, Welch et al (1941) have shown that experimentally infected rats may excrete the organism in fæces for up to 148 days, and Price Jones (1927) showed that *S enteritidis* could be isolated from the organs of such apparently healthy animals, which initiated an outbreak when mixed with non infected stock It is obvious that these apparently healthy rodents may also infect food

During the acute septicæmia in rodents fleas feeding on them become infected (Eskey et al 1951) and may be a factor in spreading infection among other rodents Possibly fleas from the dead rodent may even bite and infect man, as in the spread of plague, but there is no evidence that this has ever happened

The bait used with these "virus" preparations is laid where there are runs, these may be where cockroaches abound Mackerras and Mackerras (1948) have shown that, in a hospital ward where there was an outbreak of salmonella infection, the cockroaches became infected Mackerras and Pope (1948) have shown that infected cockroaches may continue to excrete salmonella in the fæces for 14 days or more Cockroaches may also become infected from the "virus" baits and spread the salmonella This danger may be very real, as in the outbreak affecting 123 people, described by Spray (1926), who concluded that organisms were probably transferred by flies or ants from the rat "virus" to milk and cream This outbreak was due to *S enteritidis*, and tests seem to indicate that the organism was the danysz variety

Another way in which human infection has arisen was described by Lütje (cited by Hohn and Herrmann 1935) in an outbreak affecting 126 people The infection was traced to a pig infected with 'Ratinbazillen' which became ill, was slaughtered, and was passed as suitable for human consumption Table II shows that various animals may be infected with *S enteritidis* of either the jena or danysz varieties and so increase the chance of both human and animal infection

Kristensen (1946) surveyed *S enteritidis* var *danysz* infection in Denmark from 1926 to 1945 inclusive During

THE LANCET

LONDON SATURDAY MAY 5 1956

Freud

Seldom has one man been so incontestably the creator of a new field of thought as **Freud** was of psycho-analysis Whether we accept it as a profound new science or doubt it as a far-fetched speculative system, we must wonder at the massive and daring product of one fertile original mind, working with intense concentration through more than forty years Now, a century after **Freud**'s birth there is still dispute about the value of his achievement, but hardly about the force of its impact on contemporary thought It can be said of him (as it was of another notable disturber of pleasant illusions concerned in part, with the sexual impulse) that he dug into the mine of truth bringing up ore mixed with dross to such purpose that he did not leave opinion where he found it his theory provided " a ground on which to fix the levers that may move the world "

Psycho-analysis is, of course not only a theory but also a therapy. It took its origin in efforts to cure hysteria, and almost all its medical expositors and investigators have been dependent on the practice of psychotherapy as a source of evidence and experience, and generally as a means of livelihood This has influenced the development of the subject, and its critical study Whether the effect has on the whole been for the good of psycho-analysis as a branch of medicine is hard to say No one has succeeded in amassing statistical evidence that it is more effective in the treatment of neurotic or other mental illness than other methods, though in the opinion of many people statistics has not the final say in this matter **Freud** himself saw some of the inherent obstacles to statistical evaluation—small numbers of patients, heterogeneity in form and severity of illness mutability of technique, premature termination of treatment—and he asserted that in any case the therapeutic aspect of psycho-analysis was not the most important

It is one of the many paradoxes in **Freud**'s career that he was deeply indebted to his medical training yet rejected it in retrospect ' I have never really been a doctor in the proper sense I became a doctor through being compelled to deviate from my original purpose, and the triumph of my life lies in my having after a long and roundabout journey, found my way back to my earliest path ' It is impossible to tell what he would have done if his training had been in philosophy or in psychology, as psychology was then. What seems clear is that his earliest researches, in neural structure, the action of cocaine aphasia and the paralyses of children confirmed him in habits of minute observation, organisation of diverse material deduction and lucid expression which served him well in the bolder studies that occupied his mature years In this matter he was unjust to his own achievement and his self-estimate erred on the romantic side ' I am not really a man of science, not an observer, not an experimenter and not a thinker I am nothing but by temperament a Conquistador—an adventurer if you want to translate the word—with the curiosity the boldness and the tenacity that belongs to that type of being His excursions into fields of human endeavour remote from clinical medicine derived from his overmastering desire to understand human nature Medicine gave him, in psychotherapy the springboard from it he plunged into literature, sculpture history, and anthropology, seeking always to find the ulterior meaning of men's conduct and the motives of creative action In these audacious forays cautious deduction which his teacher **Brücke** had once commended in him was a quality hard to find he took risks and made mistakes as any amateur must But these counted for little, when set against the stir he caused the incitement to fresh inquiry the lively light cast into dull-seeming corners and neglected depths Our ideas about education, religion crime, and many other human concerns have been shaken about by the impact of this restless, penetrating subtle mind. Techniques of which **Freud** had no inkling or for which he would have no sympathy are now being deployed to test the validity of his theories and suggestions not only in dynamic psychology and psychiatry, but in the social sciences at large

It is appropriate that **Freud**'s centenary should be commemorated with especial regard in this country, for it was here that **Freud** came as a young man (on a journey that he said had a decisive influence on his whole life), here that he thought of settling and here that he found refuge when driven from Vienna by the Nazi occupation He probably owed some pregnant ideas to 19th-century English thinkers—notably **John Stuart Mill** and **Hughlings Jackson**—and he found in an English disciple his faithful and gifted biographer. Though his work transcended frontiers and was accepted in some other countries particularly the United States, more readily and eagerly nowhere more than here can there be respect for the courage and intellectual integrity which led **Freud** along strange paths, on a noble and endless quest

Methionine and Hepatic Cirrhosis

The mental disturbances that may be associated with hepatic cirrhosis include clouding of consciousness confusion, apathy personality changes abnormalities in behaviour, and finally, delirium and coma [1] Signs may appear in the motor system such as spasticity, increased limb reflexes involuntary movements, and a peculiar flapping tremor [2] consisting of a series of rapid flexion-extension movements at the wrist and metacarpophalangeal joints best demonstrated with the arms outstretched and fingers separated It is important to appreciate the diffuse nature of the cerebral disturbances and their connection with liver disease since, as **Sherlock** and her colleagues have pointed out,[3] the patient may all too easily be admitted to a mental hospital before the true diagnosis is reached

These complications arise in patients with hepatic cirrhosis who have large collateral channels between the portal and systemic venous systems, and they

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[1] Walshe J M. *Quart J Med* 1951, 20 421

[2] Sherlock S Summerskill W H J White L P, Phear E A *Lancet* 1954, ii 453

[3] See *Ibid* 1955 i 1023

TABLE III—RODENT VIRUS INVESTIGATIONS

Year	Preparation (bottles)	Organism	Single colony	Organism
1944	Liverpool Virus (mice)	Jena		
"	" " (rats and mice)	Danysz		
1945	Liverpool Virus (blue label)	Danysz		
"	" " (yellow label)	Danysz		
"	" " (green and yellow label)	Danysz		
1947			Ratsouris	Jena
1948	Ratsouris	20 % Jena 80 % Danysz	Bait (Ratsouris)	Jena
			Bait (unknown)	Danysz
			Bait (probably Ratin)	Danysz
			Bait (Ratsouris)*	Danysz 66%, Jena 33%
1949	Ratsouris	Jena	—	
1950			Bait (unknown)	Danysz
1951			Bait (Ratin)	Danysz
1952	R R R	Danysz	Bait (unknown)	Danysz
"	Virus contagieux (Pasteur)	Danysz	Bait (unknown)	Danysz
"	Ratin (British Ratin Co)	Danysz	Bait (unknown)	Danysz
"	Rat Poison (Scottish Ratin Co)	Danysz		
1953			Bait (unknown)	Danysz
1954			Bait (unknown)	Danysz
			Bait (Ratin)	Danysz
1955	Virus contagieux (Pasteur)	Danysz	Bait (Disinfestation Ltd)	Danysz

*Six colonies from a single bait

Inquiries at the butcher's shop and at the slaughterhouse did not throw any light on the case, and the means by which the organism got into the food and what component of the food was responsible, has not been elucidated

The organism concerned was of the danysz type, used in certain rat poisons, but inquiries failed to establish that such poison had been used anywhere near the food

From the explosive and widespread nature of the outbreak it seems probable that the food—most likely the meat used for the "savoury mince"—was somehow heavily infected before reaching the depot Both in the refrigerator and in the oven the centre of the mass of mince probably did not reach a temperature sufficiently low or high to inhibit the growth of the organism, which therefore multiplied all the time (24 hours)

The standard of hygiene at the depot is very good, and I am satisfied that no blame can be attached to the staff for this occurrence

The incident is an example of the increased risk of such outbreaks under present conditions, with large numbers of people depending on communal feeding arrangements, and the necessity for all possible care on the part of those handling food at any stage

Outbreak Due to S enteritidis *var* jena

This outbreak was reported in *The Lancet* (1945) At Stoke on Trent a small lock up cook shop, supplying meat sandwiches, meat, potato pies, and cooked dinners off the premises, carried on in addition a small grocery business The premises were infested by mice, and the occupier had been in the habit of using Liverpool Virus An outbreak of food-poisoning occurred in relation to food sold in this shop, affecting more than 30 patients, of whom 6 died From the patients investigated *S enteritidis* var *jena* was isolated Food taken from the premises was examined, but no salmonella was isolated *S enteritidis* var *jena* was isolated from a partially consumed sandwich found in the pocket of one of the patients The Liverpool Virus used on the premises was not available for examination A sample of this preparation was obtained and proved to be a pure culture of *S enteritidis* var *danysz* Samples of Liverpool Virus had been examined in 1944 and found to contain the jena variety (table III), and possibly the preparation used in the shop was of the same type

Animal Infections

Both the jena and the danysz varieties may affect animals, as shown in table II

Rodent Virus Preparations

From 1944 onwards various preparations have been investigated to determine the species and variety of salmonella organisms present In some instances the "virus" preparation was examined in this laboratory, in others the "virus" preparation or a "virus" infected bait was examined elsewhere, and a single colony culture sent for examination For this reason the data are presented under two headings in table III, which shows that, certainly as late as 1949, both the jena and the danysz varieties were used in "virus" preparations Since that time only the danysz variety has been isolated from material or cultures of material received here

In 1945 it was possible for anybody to buy "virus" preparations from retail shops, but this is now impossible "Virus" preparations are still used by the representatives of some firms undertaking pest control At present anyone may buy Institut Pasteur "virus" by writing to the Pasteur Institute, payment being made on an international reply coupon

Although the only salmonella found in "virus" preparations in recent years has been *S enteritidis* var *danysz*, there appears to be no official control of the varieties of organisms employed It has been shown that the jena variety was in use until 1949, and Bainbridge (1909) refers to the use of *S typhimurium*

The data show that the jena and danysz varieties of *S enteritidis* are pathogenic to both man and animals Some of these infections have been traced to the use of bacterial rodenticides both at home and abroad

There are other more effective methods in use for the destruction of rats and mice The Ministry of Food (1946) recommends certain methods of control but doe not include bacterial cultures Bainbridge (1909) reported a death rate of 20-50% from bacterial cultures It is believed that chemical poisons give a higher death rate, and their use is recommended by the Ministry of Agriculture and Fisheries Moreover, the chain of spread of salmonella infection, which may be through man animals, and insects, does not exist in the case of chemical poisons

A Working Party, of which Prof S Zuckerman was chairman, set up by the Ministers concerned to advise on precautionary measures against toxic chemicals used in patients with coexisting cerebral arteriosclerosis[14], but it should also be borne in mind with less severe attacks in younger individuals[15] Experimental[16] and clinical[17] pathologists have been able to demonstrate organic cerebral damage, and psychiatrists have detected mental deterioration, using intelligence tests and electro encephalography,[18] after repeated hypoglycæmic episodes This is certainly a danger to be weighed against the advantages that can be attributed to long-term strict diabetic control, which for this reason should not be expected to attain chemical standards of normality[19] SOMOGYI attributes[20] some of the wide and seemingly spontaneous swings in blood sugar in so-called "brittle" diabetics to the hyperglycæmic reactions to episodes of hypoglycæmia and to the tendency to treat these hyperglycæmic peaks with more insulin The increasing reliance on single daily injections of long-acting insulins has increased the risk of hypoglycæmia not only because errors of overdosage are concentrated into single injections, but because the blood-sugar is often at its lowest during sleep (especially with protamine zinc insulin), when prompt treatment is unlikely For this reason it is probably unwise to give insulin in single long-acting injections to a patient who needs large doses, especially if his insulin needs are known to be variable And this is also why patients on long-acting insulins are advised to take bedtime snacks containing a proportion of protein to sustain the blood sugar longer than would be possible with isocaloric amounts of carbohydrate

When hypoglycæmic attacks occur in hospital confirmatory evidence is often sought from the blood-sugar, and not uncommonly this is found to be unexpectedly high,[21] thus casting doubt on the assumption that hypoglycæmia was the cause of the symptoms The situation is complicated because, by the time the blood is withdrawn the patient may be in the phase of rebound hyperglycæmia attributed to adrenaline-induced glycogenolysis Indeed many of the classical symptoms of hypoglycæmia may be traced to adrenaline, for diabetics taking ganglion-blocking methonium compounds may slip into hypoglycæmic coma without such warning manifestations[22] Vasoconstriction due to the release of catechol amines may serve to intensify hypoglycæmic symptoms by adding an element of anoxia to a perhaps already impaired cerebral circulation Thus vasodilator drugs have been shown to improve hypoglycæmic manifestations when given without sugar[23] If the blood-sugar level is falling very rapidly then the brain may be shorter of glucose than is suggested by a blood-sugar which seems relatively normal[24] JOSLIN[25] was one of the first to draw a parallel between the effects of hypoglycæmia and those of anoxia Different parts of the brain are involved in the same sequence, and both processes have the same end-result of reducing cerebral metabolic activity, since glucose, even in the untreated diabetic, is the only fuel burned by the brain Thus it is that chronic mild cerebral anoxia may promote the development of clinically apparent hypoglycæmia, just as coronary atheroma may give rise to typical anginal pain during mild hypoglycæmia[26] JONES[13] has described as 'hypoglycæmic encephalopathy' the cerebral damage following hypoglycæmic attacks thereafter the brain may be more liable to similar attacks even at higher blood-sugar levels[21] The surest confirmation that an attack is hypoglycæmic lies in its response to intravenous glucose

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[14] Lindsay J W Rice E C Selinger M A Mish K H *Ann intern Med* 1937 10 1892
[15] Goodman J I *Metabolism* 1953 2 485
[16] Weil A. Liebert E Heilbrunn G *Arch Neurol Psychiat* 1938 39 467
[17] Lawrence R D Meyer A. Nevin, S *Quart J Med* 1942, 11 181
[18] Gardner L I Reyersbach G C *Pediatrics* 1951 7 210
[19] Himsworth H P *Brit med J* 1937 i 541
[20] Somogyi M. Weichselbaum T E Heinbecker P *Proc Soc exp Biol N Y* 1937, 37 62
[21] Fabrykant M Bruger M. *Amer J med Sci* 1948 216 84
[22] Laurence D R Stacey, R S *Lancet*, 1951 ii 1145
[23] Sindell J A *J nerv ment Dis* 1947 105 616
[24] Conn, J W *J Amer med Ass* 1947 134 130
[25] Joslin E P The Treatment of Diabetes Mellitus Philadelphia 1928 p 49
[26] Murdock T P *Conn St med J* 1951, 15 1084

Annotations

THE WELFARE OF SPASTICS

THE organisation of a national scheme for the welfare of children and others suffering from cerebral palsy was curiously neglected in this country until after the second world war In 1946 at a meeting in the London School of Hygiene and Tropical Medicine, the British Council for the Welfare of Spastics was formed with a broad basis of representation from medical, educational and other professional interests The aims of the council were to act as a central advisory and coordinating body for all activities directed to the well being of spastics, to assist in the early ascertainment and classification of spastics and in establishing schools and clinics, to promote research, and to help the parents of spastics by publishing informative books and pamphlets As time went on, the council established useful contacts with voluntary bodies abroad, especially in Australia and the United States, and they cooperated successfully with the Ministries of Education and Health in plans for training staff in the best known methods of education and social welfare The council's initiative helped in the establishment of residential and day schools, and they were closely concerned with the setting up of regional and local parents' associations In this and many other ways they broke new ground, but lack of funds and a certain reluctance, not uncommon in professional bodies to engage in widespread appeals to parents and the public made progress rather slow and formal.

The parents of spastic children, however, once their imagination had been fired, were in a hurry They were not content to jog along under professional guidance, they were determined to take the wheel themselves In this ever growing enthusiasm a number of parents, spastics, and their friends began to press for an immediate improvement of the conditions under which children suffering from cerebral palsy were receiving education, medical care, and the special forms of speech training and physiotherapy which have proved so valuable The National Spastics Society was formed in 1952 and immediately began to form parents' associations on a nation wide scale The brilliant publicity campaign organised by the central body through the press, the wireless, and the theatre still further stimulated the enthusiasm of parents and the formation of local associations, and large sums of money were collected by house-to-house visitation The National Spastics Society have in fact scored a resounding success, and honour is due to them for their courage and resourcefulness

Nevertheless, the situation has its own embarrassments in the process of the campaign the essential problems of the spastic have been oversimplified, and

The Widdicombe File

XXXIII. ON A PERSONAL NOTE

MY DEAR WHIDDON,

Things are coming to a pretty pass indeed! Your precious Management Group Secretary has the nerve to claim that every letter I write to you about a patient automatically becomes the property of his hospital. It does not seem to matter even if I mark it "Private and Confidential": it is filed with the hospital records just the same. Damned presumptuous, I call it.

On the contrary, persists the Group Secretary, every general practitioner who writes a letter to a hospital consultant knows what is customarily done, and thus he implies consent for his letter to be included in the records. Stuff and nonsense, I retort; not one general practitioner in a thousand bothers to think about the consequences of writing friendly notes to help his professional brethren or his patients. More fool them, shrugged the Secretary. And that is where you come in, *my dear Whiddon, for it cuts both ways.*

If it is worth writing a letter at all, it takes two people to make it a success. Unless there is implicit confidence between us, the text of the letter and its sincerity will not be worth the paper it is written on, never mind the 2½*d.* stamp. None of us in our right senses are going to put down all that is in our hearts if we suspect that the fellow at the other end is allowing a bunch of strangers to peep over his shoulder. Still less are we going to be happy about the risk of our letters being bandied about by all and sundry, some of whom may be bloody-minded towards us in these compensation-worship days. Such suspicions gnaw at the very basis of the traditional confidence which ought still to exist when one doctor writes to another about a patient.

They tell me that in theory the copyright of a letter remains with its author; and, though I don't suppose many general practitioners make a habit of endorsing their letters to you "All Copyright Reserved," this could be a point worth remembering. It might prove helpful in these days when hospital records are lent to Government departments, and, on strange occasions, may even fall into the hands of the patients themselves and their legal advisers.

If we were to take a firm stand on copyright, might it not become obligatory to ask each writer for his consent before publishing his letter to any other party? That would shake the Group Secretary's office! At present they get away with their self-chosen practice of asking the consultant in charge of the case to review the records and say whether the notes can be borrowed by the laity. Now, my dear fellow, I would trust you with all my heart to do that; but I can think of one or two of your colleagues who might not be quite so acceptable, human nature being what it is. I certainly would not approve of the hospital nominating an official scrutineer for the purpose. Confidence has a personal quality, like a delicate flower to be cultivated and tended.

Delicate flowers remind me of my old Uncle George. Do you remember meeting him at the Chelsea Show before the war? He was not only an expert on orchids, he was a damned good lawyer as well. I always remember him holding forth on the subject of qualified privilege in correspondence. He used to say that a qualified privilege existed when the person who makes a communication has an interest or a duty—legal, social, or moral—to make it to the person to whom it is made, and that the person to whom it is made has a corresponding interest or duty to receive it. I think that you and I easily satisfy those conditions when I write to you about Mrs Popplecorn. Whether I have a legal duty to do so under the mass of N.H.S. legislation I would not know without rummaging out my desk; I am sure that I must have a social duty in this age of social medicine. I certainly have a moral duty not to spin you half a tale.

But old Uncle George was careful to point out that our qualified privilege will be lost if the communication was actuated by malice. Goodness knows, there has been a wealth of gentle malice in some of my notes to you. Mrs Popplecorn suffered far less pain in her neck than I did when I attended her. Old Colonel Firebrace was a left-handed gift to your consulting room. Was it really malice on my part to betray their hideous characters, or was it my compassion to spare you ferreting out the truth for yourself? Perhaps we need bother no more about those finer ethical points, for Uncle George showed us that we could rebut the presumption of malice by proving that the publication to another party was made without the writer's authority or knowledge. Uncle George has been pushing up the daisies for a long time now, and maybe the law has changed since then; but all the same I think he has left us a few good tips.

When I look back I can think of some notes to you that would not have done me much good in a court of law. Do you remember the odd mistakes of my early days which I sent along to you to put right? Just fancy what would have happened if one of those got back to the patient! Somehow I feel it was better to have owned up to you about them than to subscribe to this present-day creed of writing notes for the main purpose of squaring one's own yardarm, or, in the less polite language of the Civil Service, of keeping one's nose clean. I can see that you consultants are having the same difficulties with your letters to us. Your phraseology is becoming tainted with a brand of dour caution inspired by the shadow of the Legal Aid Fund. Not only is there a danger of losing confidence between consultants and general practitioners, there is also a danger of losing the more civilised techniques of self-expression.

What, Whiddon, do you think we ought to do to protect and restore that confidence? What can we do to preserve intact the free and full exchange of information and opinion between doctors? Can we beat the enemy at their own game? I suppose that the endorsement "Private and Confidential" carries no special significance, for are not most medical documents contemptuously so marked? "Copyright Reserved" is perhaps rather too pedantic. I have a theory that a simple endorsement "Personal" might suffice to rescue my confidences from the clutches of the lay administrators; but of course you will have to put up with having your jacket pockets bulging with papers unless you adopt some memory-man technique and swallow the notes like a first-class spy.

Another bright idea might be to copy the lawyers' device of endorsing their more scurrilous communications "Without Prejudice"; and what they get away with under that umbrella is just nobody's business, not even the court's. A system of dual letters in parallel, one stating the truth for your private eye, and the other providing eyewash for the hospital records, seems a little too schizophrenic, and fraught with the horrible possibilities of intermixture under stress in the witness-box. It would be simpler to devise a secret code if we were not so involved with security scares over atomics and space satellites.

I don't know just what the answer is, but it will be a sorry day when you and I have to write to each other about Mrs Popplecorn on notepaper which carries on the reverse side a schedule in small type setting out the conditions of communication between us. It may give some gratification to the administrators to see us using the appropriate form. But one person at least is likely to lose rather than gain—and that person, as I need hardly say, is our Mrs Popplecorn.

Still very hot under the collar,

Yours sincerely,

WILL COBBLEIGH

gained favour, ousting plombage and largely replacing thoracoplasty

The present position of plombage has been reviewed by Jackson and McCann[8] Although in their series of 203 operations in 191 patients, infection was relatively uncommon compared with some other reported series, they nevertheless conclude that the problem of preventing such infection remains unsolved and that the trend of surgery in pulmonary tuberculosis is towards removal of the tuberculous focus rather than its collapse They still advocate plombage in certain circumstances (for example, for patients in whom resection is considered unwise and thoracoplasty dangerous, and for those with bilateral disease where the conservation of the greatest possible respiratory function is essential) It is also of value at times in thoracoplasty, the plomb being removed at the second stage Time will tell whether long-term chemotherapy is not a better line of treatment in patients who are doubtful surgical risks, but the indications even for resection appear to be contracting, for plombage, many think, they have already disappeared, particularly since modified one stage thoracoplasty[9-11] is being perfected, which offers most of the advantages of plombage without its dangers

PROGNOSIS IN ADDISON'S DISEASE

Few therapeutic advances in recent years have been more impressive than the development of endocrine therapy in Addison's disease A condition which was almost inevitably fatal a quarter of a century ago now promises to be compatible with a normal lifespan[12] As Dunlop[13] pointed out, there have been four eras in the treatment of this disease In the first era (1849–1930) there was no really effective treatment The average length of survival in tuberculous cases was only just over a year from the onset of symptoms, in simple atrophy it was just under three years Only a few patients survived for a number of years—the longest recorded survival being eighteen years[14]—and one or two recovered partially or even completely[15 16] The second era opened with the introduction of Swingle and Pfiffner's cortical extract[17 18] This produced immediate benefit but the long-term results showed little improvement, 23 of Dunlop's 30 patients still died within one year of diagnosis Using Swingle's extract continuously, with a high intake of salt, Rowntree[14 19] was able to keep 5 out of 8 patients alive and well for an average of ten years from the onset of symptoms, and 4 were still alive in 1955, having survived an average of nearly seventeen years 2 of these 4 patients had received additional deoxycortone acetate for four and ten years respectively, and the other 2 had had small doses of cortisone during the past three years[15]

The third era extended from the introduction of deoxycortone in 1938[20 21] to the use of cortisone in 1950 Thorn[22] reported that 48% of a group of 158 patients survived for an average of ten years under treatment with deoxycortone—supplemented from time to time with whole adrenal extract—whereas before 1930 50% had succumbed within one year Many of the patients were maintained in good general health with regular implantations of deoxycortone pellets, and the use of cortical extract during crises, but they remained unduly susceptible to infections, many of which proved fatal

The fourth therapeutic era opened with the introduction of cortisone as a regular medication, and of intravenous hydrocortisone in crises This so much improved the prognosis that Thorn et al think that "at present the well supervised patient with Addison's disease should have a nearly normal lifespan"[12] Good supervision, in their view, involves imposing on patients conditions similar to those commonly applied to diabetics Not only should they receive regular cortisone and deoxycortone, but they should carry emergency supplies of cortisone acetate tablets and suspension, deoxycortone in oil, and sodium chloride capsules. Thorn et al also recommend that each patient should carry a card giving (a) the diagnosis, (b) the name, address, and telephone number of his doctor and next-of-kin, and (c) instructions to give the patient 25 mg. cortisone acetate by mouth—or 100 mg intramuscularly —if found collapsed, and to notify his doctor immediately Patients should also be instructed to take an extra 50–100 mg cortisone daily in the presence of infection, and likewise to notify their doctor A supply of a broad-spectrum antibiotic might well be added to this "iron ration" of cortisone and deoxycortone which Thorn et al recommend

Only by regular supervision, and by education of the patients and the profession along these lines, will unnecessary deaths be avoided and patients given the best chance of a full lifespan

EXTRADURAL HÆMATOMA

The mortality of traumatic extradural hæmorrhage is high Spurling[23] put it at from 30 to 50% in large centres in the United States Schneider and Tytus,[24] of Ann Arbor, have recently analysed some of the factors in the high death-rate, and Lewin,[25] in a Hunterian lecture some years ago, studied the problem in detail The classical clinical development of middle meningeal hæmorrhage and the need for operation have been recognised since the descriptions of Percivall Pott,[26] Jacobson,[27] and Hutchinson,[28] but by no means all patients present the typical picture Lewin analysed 34 cases admitted between 1940 and 1949 to the Radcliffe Infirmary and the Military Hospital for Head Injuries, and in 20 the illness conformed to the classical description, with minor variations The head injury may be slight without loss of consciousness (as in 7 of Lewin's cases) and it is often a blow on the temple, but sometimes (in 9 patients in this series) the head injury is severe and there is no lucid interval of recovered consciousness before cerebral compression develops In this group diagnosis may be difficult, since the signs of cerebral compression appear on a background of cerebral contusion Considerable importance is usually given, in the diagnosis of extradural hæmorrhage, to dilatation of the ipsilateral pupil, later followed by changes in the opposite pupil, but in nearly half Lewin's patients there were no abnormal ocular signs, and they should be regarded as a late and inconstant feature of the condition A unilaterally dilated and inactive pupil following a head injury may be due to traumatic mydriasis or injury of the oculomotor nerve, but in these conditions the pupillary abnormality will be present from the time of the injury When the pupil dilates as the result of

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[8] Jackson C A., McCann, J J *Tubercle*, 1956 37 36
[9] Bjork, V O *J thorac Surg* 1954 28, 194
[10] Holst J *Nord Med* 1952, 48 1288
[11] Sellors, T H, Jackson J, W, Callanan, J G *Thorax*, 1955, 10 191
[12] Forsham P H Thorn G W *In* Textbook of Endocrinology by R H Williams *Philadelphia and London 1955 p 270*
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[14] Rowntree L G *Acta med scand* 1947, suppl 196, p 90
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[17] Swingle W W, Pfiffner, J J *Science* 1930 71, 321
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[19] Rowntree L G *J Amer med Ass* 1940, 114 2526
[20] Simpson, S L *Lancet* 1938 ii 557
[21] Thorn G W *Amer J med Sci* 1939 197 718
[22] Thorn G W The Diagnosis and Treatment of Adrenal Insufficiency Springfield, Ill 1951
[23] Spurling R G Surgical Treatment of the Nervous System Springfield Ill 1946
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[25] Lewin W S *Ann R Coll Surg Engl* 1949, 5 240
[26] Pott P Observations on the Nature and Consequences of Wounds and Contusions of the Head London 1759
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[28] Hutchinson J *London Hosp Rep* 1867, 4 28

Letters to the Editor

REVISION OF THE CURRICULUM

SIR,—Professor Wyburn's letter last week is profoundly disappointing As an advocate of radical reform of the curriculum he must surely know that such reform is impossible anywhere in this country except on the instructions of the General Medical Council, or by its permission Both because the G M C is a conservative body and because it has liberal traditions, we can rule out the possibility of radical reform being undertaken on its instructions it is never going to adopt an "experimental" curriculum and impose it on all medical schools Hence the only hope of getting anything done, after so many years of talk, is to persuade the G M C that it can safely allow teaching authorities liberty to experiment for themselves To say that the council is being asked to "abrogate its function as guide and supervisor of the training of medical students" is untrue it is being asked to exercise this function in a different way, relying on advice to individual schools rather than on general directions to all

This approach should surely have the support of all who want alterations of any kind whether (like the Royal College of Physicians) they favour a basic medical education or (like Professor Wyburn) they prefer a more vocational and utilitarian training For they will get neither unless the council accedes to the college's request

If it does so, and if major reform of the curriculum becomes at last a practical possibility, it will then be important to decide in each medical school whether and how far the teachers can agree on general educational objectives Professor Wyburn may then be able to carry the day in his own school, without having to enforce his views throughout the country This would be greatly to the satisfaction of those, such as myself, who are not so convinced as he that there is only a single remedy I do not believe that a curriculum is ever likely to be perfect in concept or application in any school, and I therefore am wholly in favour of the "interminable 'research'" that he condemns He may be correct that the training for lawyers is not so subjected, but the law does not change so rapidly as medicine On the other hand, if true, it is distressing to hear that the trainings for engineers and for scientists are not regarded as being in need of constant review aimed at improvement I do not personally consider that our knowledge of learning processes or our application of it justifies such complacency

It is, of course, entirely untrue to state that the curriculum is not considered by those whom Professor Wyburn describes as "best suited to advise"—the general practitioners Clearly he has not seen fit to study the published opinions of the College of General Practitioners This is extremely unfortunate, for had he done so he would have discovered that not all who are actually engaged in this branch of medicine regard themselves as merely skilled technicians Nor do they all favour a purely utilitarian training—irrespective of the fact that were it to be adopted for all, some 50% of students (who do not later enter general practice) would thereby be given a curriculum much of which might, as Professor Wyburn claims is the case at present, be "wholly irrelevant to the work subsequently undertaken"

Furthermore it appears to me that many general practitioners do not find "the job" easy to define dogmatically, but are convinced that what the people need is a doctor who is not only conversant with the common knowledge and proficient in the common techniques that are current at the time of his registration, but is also capable of learning new knowledge and new skills (It must be admitted that the general practitioner is at least as well placed as a professor of anatomy to know what "the people want") Perhaps Professor Wyburn's own single positive contribution—that the education of the medical student should "include, from an early stage, a concurrent and remunerated apprenticeship"—is intended to achieve this aim, but as it stands it is no more than a bare "pronouncement," and does not even make it clear whether the remuneration should be *additional to the present system* of grants and subsidies

The Royal College of Physicians was asked to amplify its original memorandum,[1] and it has done so It has reiterated its request that the G M C should abandon control by prescription *in order to foster experiment*, and Professor Wyburn is entirely wrong in suggesting that the college has done this in order to impose a "model curriculum" of its own upon anyone

To me he seems equally wrong in suggesting that the college has nothing else positive to add to the pronouncements so often made in the past He may note that, in describing the kind of framework within which it thinks the schools should design their own curriculum, it says that preclinical studies should not start till 18, and that exemption from the 1st M B should be obtainable by students taking only two scientific (and one non scientific) subject at advanced level in the G C E In discussing the implications of a basic medical education, it points out that any school which wants to integrate preclinical and clinical studies will have to be prepared to alter the 2nd M B, and it asks the council to refrain from issuing any general instructions on the content or timing of examinations, because this "might prevent the development of a method of progressive assessment which could be an alternative to the present examination system" There are *many* in the profession who share the college's belief that "at all stages of medical education, examinations now exercise an unhealthy dominance over the students' work and thought" Do they realise that nothing can be done about this dominance until a progressive medical school has been allowed to demonstrate that equally good (or better) doctors can be produced on some different system ?

The college is asking that if the teachers of any school believe they can improve their course—and can agree on how to do it—they shall have freedom to try Does Professor Wyburn really want to dissuade the General Medical Council from taking what has been rightly called the "essential first step towards reform"?

London Hospital, E 1 JOHN R ELLIS

SIR,—The letter by Professor Wyburn will be widely read with gratitude for its authoritative and robust common sense How refreshing to read that crucial statement "the people want a doctor who knows his job" So many of our academic medical ornaments seem to discover the truth of the statement only when they, or their families, fall ill Again, the manifestly true, but politically most dangerous, conclusion that "the present training of the medical student is unsatisfactory, uneconomic, and much of it wholly irrelevant to the work subsequently undertaken by the great proportion of medical graduates" leads one to fascinating musing on the theme what happens if public money voted for one object is used for another—however desirable in itself and even if this object be removed from critical appraisement by the inhibitory label "research"

Again, medicine is "not a science" but "a skill, much of it still empirical" and the inevitable conclusion, clearly stated—"apprenticeship" Great is the truth —may it prevail

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[1] *Lancet*, 1955, ii 162

Special Articles

HE PATTERN OF GENERAL PRACTICE

A G RICHARDS
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ASSISTANT PHYSICIAN,
SASKATOON SANATORIUM, SASKATCHEWAN, CANADA

MOST doctors visiting Britain from Canada and elsewhere have kind words for British consultant and specialist practice, but usually they are not so favourably impressed by general practice, of which Collings (1950) made a detailed and critical survey This unfavourable impression is created partly by conditions which individual practitioners could rectify, and by certain provisions of the National Health Service Act But the pattern of general practice is largely determined by factors not easily modified by doctors or legislators—e g, density of population ease of communications, capital resources, and the prosperity of the community Whereas specialist practice is basically the same the world over, general practice must adapt itself to local circumstances

To be constructive criticism should be directed against conditions of general practice that can be modified, and against failure to adapt to those conditions that must be accepted. To set before future general practitioners an ideal type of practice which is unattainable is unfair and also a disservice to their patients

Existing Patterns

A much-criticised aspect of British general practice is the limitation of scope in the treatment of organic disease particularly that imposed by lack of hospital privileges

In the country districts of Canada and the United States, most communities provide general practitioners with X-ray equipment, electrocardiographs, and hospitals which in Britain and Europe would be confined to large cities Furthermore, owing to the dispersal of the population in such large countries many general practitioners work far away from medical centres and specialist help, and they must deal with all surgical and medical emergencies But even in the cities the ideal of the self sufficient practice is pursued Since specialists in North American cities usually do not confine their practice to referred cases they are in direct competition with general practitioners who therefore, even more than their British colleagues feel a need for the prestige value of equipment and hospital privileges

In Britain a much lower proportion of the country s capital resources is devoted to general practice and to hospitals than in Canada and the United States Premises suitable for general practitioners, and even general practitioners themselves are scarce in some areas. Because of the shortage of hospital beds the British general practitioner spends much time visiting and treating patients in their own homes much of his visiting is in effect a vast ward round Because of the shortage of practices these are large—there is an average of over 2000 patients per doctor (Hadfield 1953)—and in cities they tend to be very large Shortage of hospital beds and the large size of his practice combine to fill the general practitioner's day with work outside the hospital

Nevertheless, because Britain is densely populated a reasonable standard of medical care is possible despite these shortages, for frequent visiting is feasible, and patients need not be admitted to hospital merely because they live too far away for supervision, as is often the case in Canada Furthermore in Britain visiting is eased by the good roads, universally tarred or "paved." Specialists are within easy reach, and the amount of major therapy which a general practitioner is justified in undertaking is therefore greatly reduced

The Canadian doctor, except in the largest cities, minimises the distances he travels by having his house and office within easy reach of the hospital, by commonly advising his patients by telephone and by visiting patients in their homes only when he must His practice is therefore limited only by the distance patients travel to see him, which may be 40 miles or more In Britain, because home visits constitute such a large part of his work the general practitioner must restrict his practice to a convenient area A hospital serves an area containing many practices of which only a few will be near to it A doctor whose time is filled by travelling about his practice may find it difficult to fit in a long journey to see a patient in hospital This was my experience in a semi-rural practice in Lincolnshire a small hospital was available to some 10 general practitioners, but in fact only 4 of us whose practices included the hospital geographically used it to any extent

THE HOSPITAL

It was my experience in Britain that the patients for whom I was responsible in our small general-practitioner hospital would have benefited from the care of a doctor who, if not a specialist at least spent most of his time doing hospital work and I had a suspicion that my patients would have been more efficiently managed in the fully equipped hospital with resident staff 16 miles away. Doctors in large practices with several partners can afford the time for regular hospital work but the single practitioner or member of a small partnership finds that his few hospital patients cost him a disproportionate amount of time, effort and worry A doctor who does most of his work in hospital is not bothered by the feeling that he should be elsewhere, but the practitioner attached to a hospital is always having to consider conflicting priorities and an emergency in hospital may coincide with one outside Hospital work requires not only skill in certain procedures and experience in interpreting special investigations but the establishment of harmonious personal relations with all members of the staff A hospital is an instrument, and as with other instruments, a certain critical frequency of use is needed to maintain proficiency The doctor who combines hospital work with a busy general practice is continually having to make the effort to change his mental orientation to a different pattern of work This adds to his burden and impairs his efficiency

An objection to the reservation of hospitals for specialists is that patients lose the continuity of care and personal interest of their family doctor but the wise patient prefers to be operated on by an experienced surgeon even if he is a stranger A further objection is that doctors lose sight of their most interesting cases through admission to hospital But why do doctors think these cases so interesting? Surely because they are cases of disorders about which they were taught as students in hospital, whereas the majority of patients seen in general practice are not The late Sir James Spence drew attention to the large number of illnesses seldom dealt with in hospital teaching (Spence et al. 1954)

This division of labour between hospital practitioners on the one hand and non-hospital practitioners on the other makes for effective use of doctors in densely populated areas Unhappily because of our undergraduate training we find it hard to accept this situation and make the best of it There is a risk that general practice may be forced into a form to suit our training instead of our modifying it in the best interests of patients and the profession.

General practitioners usually attribute the small number of hospital beds available to them to arbitrary regulations or selfishness on the part of specialists rather than to an inherent feature of British medical practice Many doctors feel that their prestige is impaired by lack basic method of treatment It has the advantages of precision and the immediate correction of possible diagnostic errors, and it preserves that sense of urgency in treatment on which early admission to hospital depends Conservative therapy has been used in those mild cases diagnosed as "leaking ulcers," and in others where the early diagnosis has been in doubt Some of these have been acute exacerbations of peptic ulceration or of antral gastritis, without perforation

Primary partial gastrectomy has been preserved for perforation in chronic ulcers in selected patients whose general condition has remained good and in whom diffuse peritoneal soiling has been absent, but the ultimate decision to proceed with this operation may have to be abandoned when the ulcer is exposed if conditions are unfavourable The plea is, therefore, for an accurate assessment of each case and the adoption of the procedure calculated to give the best results in the experience of the surgeon concerned

The claim that conservative therapy in perforated acute ulcers protects against relapses is one which only time can confirm, but it seems contrary to the nature of the disease

Newcastle upon Tyne JOHN GILMOUR

INFLATABLE POSTNASAL TAMPON

SIR,—Mr Mawson describes (April 21) an inflatable postnasal tampon There are two points in which this apparatus might be improved

For many years I have used a fine metal tube, over which is tied a large-size rubber finger-stall, this can be inserted into the nose and inflated to control hæmorrhage A spring-loaded valve, similar to a motor tyre valve, is incorporated in the proximal end of the fine tube and housed in a small light aluminium cylinder measuring 1 in by $^1/_4$ in This is, of course, self-closing after each puff of air is introduced and avoids the necessity of closing a piece of rubber tubing with a cross-action spring clip, or with a rubber cap, and is much more comfortable to wear

The second point is that if a double bulb is used for inflation similar to that employed for inflation of a cuff on an endotracheal tube, the pressure in the balloon or finger-stall can be more easily gauged This apparatus may be obtained from Messrs A L Hawkins, of New Cavendish Street, London, W 1

Royal Free Hospital,
London, W C 1 W G SCOTT BROWN

RESTRICTION OF ANTIBIOTICS

SIR,—I was very surprised by the opinion expressed in your annotation (March 3)

In point of fact, restriction on commercial distribution of an antibiotic seems to me detrimental to the public health The object of pharmaceutical firms is to supply the physician with new medicines, and *it is up to these* to choose the antibiotic best suited to each particular case The clinical and, more specially, the laboratory data (antibiograms) supply precise information Consequently, it appears to me that the more antibiotics a doctor has at his disposal, the easier it is for him to apply rational and effective treatment

If we adopt the course you favour, on what basis, and when, can a new antibiotic be placed at the physician's disposal ?

You mention an antibiotic on sale in France with, you say, *insufficient reason* Spiramycin (it is obviously to this antibiotic that you allude) has effective antibacterial properties rather similar to those of erythromycin, but clinical and laboratory data have shown that the similarity is not complete

I studied 50 different pathogenic staphylococcal strains, of which 42 were equally sensitive to each of the two antibiotics, 6 were resistant to erythromycin and sensitive to spiramycin, and 2 were sensitive to erythromycin and resistant to spiramycin Similar studies by other workers confirmed this, and it seems that 10% of staphylococcal strains are sensitive to spiramycin and resistant to erythromycin This discrepancy was borne out clinically, and there is evidence of success with spiramycin after failure with erythromycin

In our experience, spiramycin is better tolerated both digestively and generally at a daily dose of 3 g than erythromycin at 2 g daily This advantage was pointed out also by Sureau et al[1] who compared the results of treating scarlet fever by spiramycin and erythromycin

This justifies my point of view and the therapeutic interest in this new antibiotic *In combating infectious* diseases, each new weapon must be well known by the practitioner and placed at his disposal for his discerning use And obviously a patient infected with an erythromycin-resistant and spiramycin-sensitive organism (which from French observations will be once in about every ten cases of staphylococcal infection) would be extremely glad to benefit by this effective and well tolerated medicine

Tassin La Demi Lune
Rhône France J PELLERAT

*** As we see it, hospitals are experiencing an epidemic of antibiotic-resistant staphylococcal infection, which may spread to the general population In the face of such a threat to the public health we do not think that the policy of laissez-faire advocated by Dr Pellerat will be indefinitely acceptable either to peoples or to their governments Our plea is that the medical profession and the pharmaceutical firms should cooperate voluntarily *in measures to discourage the emergence of resistant* strains —ED L

HORMONAL EFFECTS OF TRANQUILLISERS

SIR,—The interesting letters of Dr Sulman and Dr Winnik and of Dr Marshall and Dr Lieberman (Jan 21) accorded with certain of our own observations During the past month, while examining a Papanicolaou smear obtained from the cervix uteri of a 68 year old patient who had had some recent bleeding episodes, we were amazed to find cornification of vaginal epithelium to a degree which suggested that the patient was receiving œstrogen therapy That, we were assured by her doctor, was not the case The patient had for some months been receiving only rauwolfia alkaloids, and it turned out that the bleeding coincided with the exhibition of *this medication*

In an investigation by one of us (R D B) of the tranquilliser, meprobamate ('Miltown,' 'Equanil'), in patients with inoperable neoplastic disease,[2] a patient with mediastinal and cervical Hodgkin's lymphadenopathy, previously responsive to hydrocortisone and to oxytetracycline in successive courses, but now refractory to both, showed progressive detumescence of the enlarged nodes in the first three weeks of sustained administration of miltown (400 mg by rectal suppository four times daily) administered for the control of anxiety This response was reminiscent in all respects of prior responses to adrenocorticotherapy or mycin antibiotics—in the case of one of which (chlortetracycline) humoral action *has been confirmed*[3] *It may be recalled that an* "adrenocorticomimetic effect" of this class of antibiotics has often been suggested to explain certain effects in diseases which are not *classically* "infective"

Experience with meprobamate indicates that the humoral effects of tranquillisers may not be confined to an anti-histamine or parasympatholytic one, as with chlorpromazine Nor is it certain that such effects do not noted wherever possible. The study was therefore likely to reveal, among other maladjustment, any examples of the "affectionless character" which is said to result from early separation.

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[1] Sureau B Chabbert Y, Veron M, Martin E, Cayla, F *Pr med* 1955 63 1615

[2] Kessler L N, Barnard R D *Med Times N Y* (in the press)

[3] Trams E G Kashiwa H K, Cornman, I Klopp C T *Antibiot Med* 1955 2 677

Four Groups

The Well-adjusted

Of the 25 children, 8 were normal and generally well adjusted in their school life, while at home they were (if one can put it that way) better than normal. They were very affectionate and thoughtful towards their mothers, so much so that they helped in the home without being asked. 3 were eminently stable, but they had not been separated from their mothers until they were 3–4 years old, and for less than a year. All these 8 children had mothers who cared for them, although the mother of one of the girls was rather a cold type of woman who had never kissed or cuddled her children.

One is bound to ask—when one has had experience of completely secure and stable children—whether this helpfulness in the home was as desirable as it sounds. Of a girl of 15 her mother said typically "she wants to do more but I won't let her do it." It would seem that these 8 children, although well adjusted and in school indistinguishable from ordinary children, were rather unnaturally anxious to keep in their mothers' good books. They had to make themselves useful in order to make doubly sure of having a mother.

The Unforthcoming

The next group (again of 8) came in the category of unforthcoming children. At school they were of the well-known type of "timid mousy" backward child, and this trait was really the key to their backwardness, for they lacked the confidence to face the uncertainties of learning. These 8—except the one who was still in a children's home—were even more anxious to help their mothers than were the first group.

It was quite evident that these children's efforts to please their mothers had reached the stage of anxiety. What is more difficult to decide is whether this was due primarily to their separation from their mothers in early life or to their early illnesses and other hardships. Among the sample of 141 backward children there were also 28 who had had severe illnesses in their early years *without* going into hospital or being otherwise separated. 15 of them had the same sort of unforthcoming characters as the separated children and 8 more were maladjusted or unsettled. That is to say, the non-separated children happened as a group to be about as maladjusted and somewhat more unforthcoming than the separated ones, but in a small sample such differences would be hardly significant.

The large overlap between children who had early illness and those who had been separated from their mothers makes it impossible to do more than sense which of these experiences is primarily responsible for the emotional maldevelopment. In the whole group of 141 "backwards," 51 were assessed as unforthcoming characters. Of these 20 were separated, for one reason or another, for at least one week in their first two years. In the same period of their lives 33 had at least one serious illness or its equivalent (born weakly or ill, needing medical attention owing to failure to gain weight in first months, gross physical neglect, convulsions or a fairly serious accident, burn or scald). In 16 of the "unforthcomings" there was neither separation nor serious illness under 2 years, but in these some of the above *factors* occurred after that age, and in others there was a history of changes of mother-figure, divided maternal attachment, or other anxiety-producing family situation. (The quantitative data on which this paper is based are summarised in the table.) In weighing the relative influence of early separation and early illness it is relevant that of the above 51 "unforthcomings" only 2 were separated without being ill, while 15 were ill without being separated. This suggests that the early illnesses more than the separations were responsible for the later unforthcomingness and anxious over-attachment to the mother. People are normally lacking in "go" after being ill; with these children the severe early illnesses may have robbed them of assertiveness and made them mother-dependent over most of their childhood.

To return to the group of unforthcoming "separated" children under consideration, one noticed in 2 of them that, while being very helpful, they were not demonstratively affectionate to their mothers.

A girl of 12, who was in hospital for four months from 1 month old, was described as "never a cuddlesome baby at all." "She has always been a child to creep into a corner on her own." In her case the mother had three children in close succession, and this child was the middle one, with a sister eleven months older and a brother ten months younger. The mother admitted that with three babies so much of age "You can't give individual attention." Thus the child, who was discharged from hospital still poorly and covered with sores, probably did not get the subsequent mothering that a sick child needs.

With a boy of 13 there were more serious indications of affectual inhibition. As a toddler he had been some eighteen months in hospital and convalescent home, where he forgot his mother and became attached to a nurse. Afterwards he would not take to his mother, went down the garden as far as he could go to play on his own, became a wanderer, and got a bad reputation in the neighbourhood for destructiveness and pilfering. But his mother had given birth to another child the very day he returned from his long stay in hospital, so that the homecoming must have been inauspicious. Also she had the unfortunate habit of using threats to put him away when he was naughty, and for two years he had been waiting to go to a residential school. It would thus seem that there was enough insecurity about his situation, as it was then, to account for his unsettledness at home, although his early separation is likely to have made him more sensitive to his mother's threats and to the prospect of being separated from her again.

The Unsettled

The next group, of 5 children, were unsettled both in school and in their homes—i.e., they showed definite signs of maladjustment, though not enough to justify classifying

SUMMARY OF QUANTITATIVE DATA

Total sample of backward children of ages 8–15 years	141

Social Adjustment *
(contemporary)

Maladjusted	34 (24%)
Unsettled (lightly maladjusted, very restless, &c.)	20 (14%)
Unforthcoming	51 (36%)
Specific tension with otherwise fairly good adjustment	5 (3½%)
Stable	31 (22%)
	141

* Assessment of adjustment made on the Social Adjustment Guide (Day-School edition).

Early History of 51 "Unforthcomings"
(0–2 years)

Separated from mother at least one week	20
Serious illness or equivalent	33
Neither of above	16
Separated without being ill	2
Ill without being separated	15

Social Adjustment and Long Separation

Separated from mother at least ten weeks in first four years (mostly in hospital)		Seriously ill in first two years but not separated from mother	
Stable	8 (0)	Stable	2
Unforthcoming	8 (0)	Unforthcoming	15
Unsettled	5 (1)	Unsettled	3
Maladjusted	4 (3)	Maladjusted	5
Total separated	25	Total ill but not separated	25

The figures in parentheses give the numbers separated under 4 years of age, but without being seriously ill so far as is known—except for physical neglect. 9 children were separated a month or more under the age of 4 without serious illness. Of these 4 were unforthcoming and 5 were maladjusted.

appointed themselves by opening up a single-handed practice, while a small number came into the service through vacancies advertised by local executive councils Over 60% of doctors in general practice in the service were working in partnership and they appointed their own successors and their own replacements Single-handed practices, which were large enough to be retained as such, were advertised and went to doctors in open competition Clearly it could not be laid down that any particular doctor, employed or otherwise, must have an automatic right to a vacant practice

The number of doctors in practice was certainly not decreasing In 1955 259 practices had become vacant owing to death, retirement, or resignation 117 successors were appointed, 17 practices were amalgamated with other small practices, leaving a residue of 125 dispersed Some of these were single-doctor practices which had been given up owing to the death of the doctor Of the practices dispersed, 40 had no patients on their lists, 51 had under 300 patients, and 14 had lists of 700 or more, but in most of them certain significant factors applied, such as diminishing population During the year 613 doctors were admitted to the list to practise in partnership Of these, 297 were assistants entering into partnership in practices where they were already working

Most of the doctors recently registered for unemployment benefit were registered for under 13 weeks and only 2 for over 26 weeks There were great difficulties in finding vacancies for some of the 35 unemployed doctors Some were severely disabled

In some spheres, however, there was still a shortage of doctors The number of doctors employed in the hospital service in England and Wales which it was estimated was about 13,500 in 1949, had risen by 3000, and was still rising In many areas it was difficult to find registrars, junior hospital medical officers, senior house-officers, and house-officers Some senior registrars had had difficulty in obtaining consultant appointments, especially in general medicine, general surgery orthopædics, and obstetrics and gynæcology In anæsthetics, radiology, and mental health there was still a shortage of candidates for consultant posts

While there was evidence of some maldistribution of medical man-power as between the specialties there was no evidence of any real unemployment among doctors generally The Waverley report made it clear that the medical branches of the Armed Services had been unable to recruit enough medical officers for regular and short-term commissions In England and Wales in 1955 there were 84 advertised vacancies in general practice and the average number of applicants was 43 Many of the applicants were already in practice and were applying for what they thought was a more favourable area In the north of England there were often as few as 10 applicants for a vacancy, in the south the number might reach 100 There were only about 1500 assistants working for general practitioners in the service and it was clear that the turnover from assistant to principal was normally quite fast Of the assistants who had been in post for one year or two years in 1954 there were 53% who changed their status Nearly 75% of the assistants were in the age-group of 30 to 35

Because of the future possibility of an over-production of doctors a committee on medical man-power had been set up under the chairmanship of Mr Henry Willink to study the future needs of the service, and perhaps the expansion of certain specialties, such as mental health But the evidence which the Ministry had at present did not warrant the suggestion that there was severe unemployment among doctors

QUESTION TIME

Fall in Milk Consumption

Replying to a question, Mr HEATHCOAT AMORY, Minister of Agriculture, Fisheries, and Food, said that production of milk in the first three months of this year had increased much more than consumption and the amount of milk becoming available week by week was causing anxiety to the Milk Marketing Board The average monthly consumption of fresh milk in 1951 was 130 57 million gallons and in 1955 126 36 million gallons The Milk Marketing Board, through the National Milk Publicity Council, were taking vigorous steps to encourage sales of milk and the Government were supporting the Council In answer to a further question, he added that the Government felt they could not justify subsidising an article, even an article as good nutritionally as milk, to the extent to which they had been subsidising it to every man, woman, and child in the country, regardless of means and needs

Milk Tablets in Schools

Replying to a question, Mr DENNIS VOSPER, parliamentary secretary to the Ministry of Education, said that 129 schools were now being supplied with milk tablets as a substitute for liquid milk Apart from 18 small isolated schools which no one was prepared to supply, 111 were in Blackpool and Newport where the local education authorities had been unable to obtain fresh milk at a reasonable price It was the desire of the Minister that liquid milk should be supplied, but there were cases where this was not always possible

Pensions for Elderly Doctors

Replying to a question, Mr R H TURTON, Minister of Health said that about 800 National Health Service doctors were still in practice who were over 61 years of age when the National Health Service Act came into force These doctors could not satisfy the ten year qualifying period for a pension Those with five years' service might, however, qualify for a lump sum retiring allowance Under the regulations he had no power to do anything for those with less

Abolition of Flogging

Replying to a question, Major GWILYM LLOYD GEORGE the Home Secretary, said that the tendency was definitely for the crimes for which flogging was formerly awarded to drop Though there were queer fluctuations from year to year this tendency persisted Before corporal punishment was abolished as a judicial penalty in September 1948, the principal offences for which it could be imposed were robbery with violence, armed robbery, and robbery in company with others The number of these offences known to the police since 1946 were

1946	804
1947	842
1948	978
1949	860
1950	812
1951	633
1952	790
1953	754
1954	604
1955	578

Average Cost of Prescriptions

Replying to a question, Miss HORNSBY SMITH said that the average cost per prescription in England and Wales was *4s 4 87d* for February, 1956, compared with *4s 2 09d* for *February, 1955*

Certification of a Mental Defective

Dr BARNETT STROSS asked the Minister whether he had noted the case of Vivienne Donger, now at Stallington Hall Stoke on Trent, who was alleged to have been certified as a mental defective at the age of 11 years, only because her parents had parted and she later was considered to be educationally backward, and if he would bring these facts to the notice of the Board of Control —Miss HORNSBY SMITH replied The grounds for certification in this case were that the girl was mentally defective and the subject of a report under the Education Acts that she had been found incapable of receiving education at school The Board of Control are satisfied that for the present she needs the care and training provided under the Mental Deficiency Acts Dr STROSS Has the hon Lady seen the type of letter which this girl is alleged to have written and which was published recently in a Sunday newspaper? If so, does she think it is the sort of letter which a mental defective could write?—Miss HORNSBY SMITH I have seen the press item referred to This girl is being tried out on employment in domestic service, and if that is satisfactory further consideration will be given to the case Dr STROSS If there be substantial grounds for believing that this girl was wrongly certified, how are we to have any protection to ensure that this type of thing does not take place frequently?—Miss HORNSBY SMITH The hon Member has missed the point I made in my initial reply This girl was certified as a mental defective after being found incapable of receiving education at school, which is the normal process The procedure was not on the basis which the hon Member implied are that it acts as a predisposing factor to anxiety. Without other adverse factors the child may become oversensitive to the loss of its mother and its family—that is to say, develop into an over good, over-helpful, over-loving anxious child. If other adverse factors are present the early separation seems to contribute to the maladjustment, or to reinforce the unforthcomingness resulting from severe early illness. The effect of a spell in hospital or in an institution, provided it is not unduly long, seems to depend largely upon attendant circumstances—notably traumatic events such as painful or terrifying experiences, pre-existing anxiety about loss of the mother, or inadequate mothering in the immediate post-hospital period. In short the context of the separation in the child's emotional development is more important than the bald fact of separation in itself.

The effect of *long* separation seems to be no more and no less than that of a period in the child's life when it is deprived of family security. There is nothing special about it which takes it out of our formula, except that the earlier a bad experience the greater impression it would presumably make upon the child. It was seen with the first group of stable children that even a long period of separation in early life may have few upsetting effects if the mother has given good affection and has been loyal to the child during the remainder of its life. With the unsettled group the separation appeared to be partly responsible—perhaps as a starting-point of insecurity because circumstances were unfortunate, perhaps as a contributor along with other unfavourable factors. In these cases there was evidence of the child having suffered from the early separation. It was on the other hand noticeable that serious unsettledness or maladjustment pointed to something being wrong in the child's contemporary life. We may conclude that early unfavourable experiences may make a child temperamentally sensitive, insecure, and lacking in confidence, and possibly even leave it with a capacity for effectional inhibition; but it is what has been happening to a child in more recent years that makes it maladjusted.

There is consequently no need for undue alarm and anxiety about separating children from their parents when this is necessary. At the same time the potential harmful effects should be recognised and minimised.

Preventive Measures

In such preventive work it may be useful to consider three categories of children.

Short Separation

In the first are those who will normally return within a few weeks or months to their own homes. These include children in residential care for a special reason, such as an illness or nervous breakdown of the mother. Children who go into hospital for a relatively long time will also be in this category. With the latter the ideal solution is that the mother should go into hospital with the child; and though this is usually difficult for domestic reasons it should be arranged, whenever practicable, when the treatment is likely to be painful or frightening. With children temporarily in public care this solution is nearly always ruled out, because the mother's unavailability is the reason for their being there. With ordinary hospital cases, if the mother can visit every afternoon or at any rate three to four times a week, this should largely overcome any bad effects. Alternatively, if the mother cannot visit, the other members of the family should do so as frequently as possible.

Another measure indicated by the cases quoted is that we should attend to the manner in which the separated child is reunited to its family. If it has been away a long time and has been kindly looked after it will naturally have taken to some extent to the staff of the hospital or institution, and its mother will be a bit of a stranger. This, then is the period of maximum sensitivity, when harm can be done if the child does not receive a warm and unpreoccupied welcome from the mother. It is not good enough to notify a mother that her child is ready for her to collect on a certain day; we should ascertain that she is available, in good health, and emotionally prepared to welcome it. It is also our duty to help mothers understand the emotional readjustment which a child has to make upon its return home, and to see that she is not disappointed if the child does not take to her immediately.

Long Separation: Contact Retained

The second category consists of those children who are more or less permanently in an institution but remain in touch with their families. A child is probably affected more fundamentally by his feelings about his family than he is by his day-to-day life in the institution. We should therefore regard the guidance of child-family relations as an important point of our work. This means doing our best to ensure that the parent or other relative visits frequently, does not fail to turn up or lightly postpone visits, and brings in whatever little luxuries can be afforded. If the parents are at a distance we should try to prevail upon them to write frequently. Incidentally many children are known to have relatives but these never think of contacting the child, or do so once in a while; in many cases we ought to persuade them to become active "aunties" and "uncles." Any reputable relative is of tremendous value to a child in giving it a sense of having a family.

One of the difficulties is that mothers or relatives left with orphaned children want to keep the girl but not her brother. If the latter only is placed in an institution he is very likely indeed to resent it bitterly and become the hostile-anxious sort of maladjusted child. Perhaps we should insist where possible upon both or neither of the children being taken into care.

Contact Lost

With the third category—those children out of touch with their relatives—we have to provide the nearest thing we can to a feeling of belonging to a family. I do not think this so hopeless as it may sound, but it will probably entail big changes in the organisation of some homes. We need not necessarily try to imitate the special type of self-contained small European family. The traditional Indian household and the African family are larger units. But all families, even though numerous, have their own structure of human relationships; each individual has his special place according to sex and seniority, and there are other members who are specially near him or her. A home of some 20 boys or girls, more or less of the same age, with house parents and one or two assistants, is not structured in this sense and so none of the children can feel that they are the special concern of any of the senior members of the group. The family-group basis into which some homes have been so successfully broken up is going a long way in the right direction. To carry the idea to its logical conclusion, the family group should be a mixture of ages and sexes, so that boys and girls from babyhood to leaving age would be in the same "family." This would enable us to dispense with the nursery institutions, and the presence of a baby in the group has been found to have a settling effect upon the older boys and girls. To follow this idea of the structured, diverse group further, we should so far as possible avoid communal eating, daily assemblies, or daily outings *en troupe*. This of course would not bar the occasional corporate gathering or excursion, which might be compared to the tribal assembly which gives a sense of being part of a powerful parent-body. That, by the way, is one of the things that a voluntary home can offer which a local authorities' home cannot.

A further difficulty we have to face is that of staff leaving; and the more family-like we make a group observations in that case were—subject to the effect of the Rules of Procedure—applicable to such a case as the present where the conviction, not having taken place in the United Kingdom or the Republic of Ireland, was only prima facie evidence of the infamous conduct alleged In so holding their Lordships had not lost sight of the changes produced by the Medical Act, 1950, in the position of the Medical Disciplinary Committee, as compared with the General Medical Council under the Act of 1858 The committee, however, were not *a court of law but a domestic forum charged in certain* cases, of which the present was one, with the peculiar duty of making "due inquiry" into the circumstances attending the conviction in a distant country of a medical practitioner with a view to deciding—of which they alone were the judges—whether he had been guilty of infamous conduct in a professional respect That duty they could not adequately perform unless they were in possession of the whole of the proceedings in the criminal court in which the conviction occurred It would be unfortunate if they had precluded themselves from so functioning by the rules, and in particular by rule 63 The record of proceedings was, in their Lordships' opinion, a "document" within the meaning of the second limb of rule 63 The admissibility of such documents was, however, limited to the statements of fact contained therein, and such a restriction might render the task of the committee and legal assessor extremely difficult in dealing with the record of proceedings in the criminal court and would exclude the judge's charge to the jury and other parts of the record which it was clearly desirable the committee should see

In the present case the record, with certain excisions, was put in by consent as soon as the committee had quite properly decided that the attendance of the witnesses from Malaya was not practicable and that their absence did not vitiate the proceedings The consent to the admission of the record was fatal to any objection on that score now being put forward, nor did their Lordships consider that there was any substance in the contention that the whole of the evidence was not read out in court Their Lordships desired, however, to draw *the attention of those concerned to the desirability* of an alteration in the Rules of Procedure whereby the committee could be empowered beyond all question to receive in evidence and examine the whole of the officially authenticated proceedings of the convicting court in this class of case

There had been no miscarriage of justice in this case and their Lordships had accordingly humbly advised Her Majesty that the appeal should be dismissed

Ong Bak Hin v General Medical Council—*Judicial Committee of the Privy Council* March 19 April 24, 1956 *Counsel and Solicitors* J R Cumming Bruce and R Barr (Hempsons) J G S Hobson (Waterhouse & Co)

CHARLES CLAYTON
Barrister at Law

Appointments

HOLBERTON, A S W, F R C P E, S H M O in venereology, Liverpool Royal Infirmary

HARTLEY, MARY J, M B Leeds, F F A R C S, D A, part time consultant anæsthetist, City General Hospital Sheffield

PATTINSON, J N, M B Camb, F F R, D M R D, consultant radiologist The Middlesex Hospital London

TOBIN, J, M R C S, D A, whole time anæsthetist, Kirkcaldy General Hospital

WHITESIDE, C G, B M Oxfd, F F R, D M R D, consultant radiologist The Middlesex Hospital London

Birmingham Regional Hospital Board

ASTLEY, W F C, M B Camb, D M R D, whole time consultant radiologist, Stoke on Trent group

LITCHFIELD, J A, M B Birm, M R C P, part time consultant physician Walsall group

PARKER, R B, M B Edin, M R C O G, part time consultant obstetrician/gynæcologist, Birmingham (Central B) and Walsall groups

SCRASE, W H, M B Birm, F R C S E, part time consultant orthopædic surgeon, Birmingham R H B

Diary of the Week

MAY 6 TO 12

Monday, 7th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
2 P M *Experimental Medicine and Therapeutics* Dr W D Prof A Haddow Dr G B Brown, Dr Aaron Bend Dr D A G Galton Antitumour Agents

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W
4 P M Dr Aubrey Leatham Systolic Murmurs

Tuesday, 8th

UNIVERSITY OF LONDON
5 30 P M (University College, Gower Street, W C 1) Dr S Kuffler (Johns Hopkins University) Factors in Control of Movement

ROYAL SOCIETY OF MEDICINE
8 P M *Psychiatry* Dr J Pollitt, Dr T Pippard Obses Compulsive States

INSTITUTE OF DERMATOLOGY, Lisle Street W C 2
5 30 P M Dr H Haber Cutaneous Manifestations of Syphi

WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, St Ma Hospital, W 2
5 P M Prof L Pillemer (Cleveland, Ohio) The Nature of Properdin System

ROYAL COLLEGE OF PHYSICIANS, Edinburgh, 2
5 30 P M Prof F H Smirk Treatment of Hyperten (George Alexander Gibson lecture)

Wednesday, 9th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fie W C 2
3 45 P M Dr B E Heard *Cortisone and Inflammati* (Erasmus Wilson demonstration)

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Prof C F Barwell Laboratory Diagnosis of V Infections

INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell The Rôle of Fungi in Skin Dise

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S W 3
5 P M Mr Vernon Thompson Surgical Treatment of Bronchi Carcinoma

UNIVERSITY OF OXFORD
5 P M (Radcliffe Infirmary) Prof M A van Bouwdijk Bastiaans (Amsterdam) Toxæmia of Pregnancy (Litchfield lecture

MANCHESTER MEDICAL SOCIETY
4 30 P M (University Medical School) *Pathology* Dr A Holm Dr G M Komrower, Mr V Schwarz Galactosæmia

ROYAL COLLEGE OF SURGEONS, Edinburgh, 8
3 30 P M Prof C F W Illingworth Inborn and Extraneo Factors in the Ætiology of Peptic Ulcer

Thursday, 10th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Mr C W D Lewis Melanomas and Melano (Hunterian lecture)

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr Sheila Sherlock Portal Hypertension

INSTITUTE OF DERMATOLOGY
5 30 P M Dr I O Oliver Laboratory Diagnosis of Syphilis

ALFRED ADLER MEDICAL SOCIETY
8 P M (11, Chandos Street, W 1) Prof H Baruk (Charenton Thirty Years of Research into the Problem of Psych physiology of the Will

NUFFIELD ORTHOPÆDIC CENTRE, Oxford
8 30 P M Mr R G Taylor Extra articular Calcification T Joints Following Trauma Mr J Agerholm Zig zag Osteotomy

HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place Edinbur Prof E J Wayne Clinical Surveys and Clinical Trials

UNIVERSITY OF ST ANDREWS
5 P M (Queen's College, Small's Wynd, Dundee) Prof A Walsh, PH D Chemistry and Cancer

UNIVERSITY OF DUBLIN
5 P M (Trinity College) Dr Moacyr L Alvaro Ætiology a Pathogeny of Uveitis

Friday, 11th

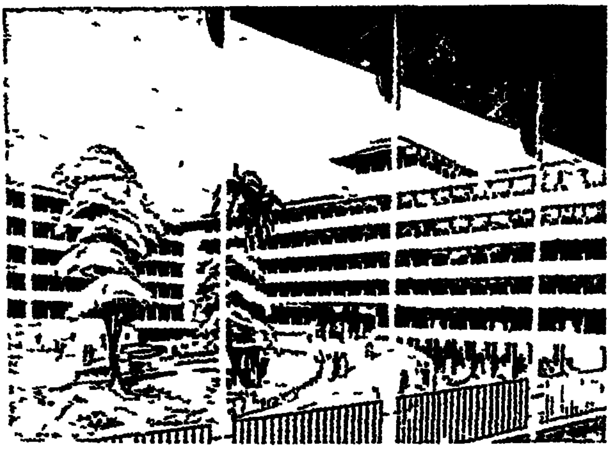
POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A M Prof B W Windeyer The Reticuloses
4 P M Dr John Shillingford Tricuspid Incompetence

ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington, W 2
5 P M Prof A St G Huggett Chronology of the Placenta

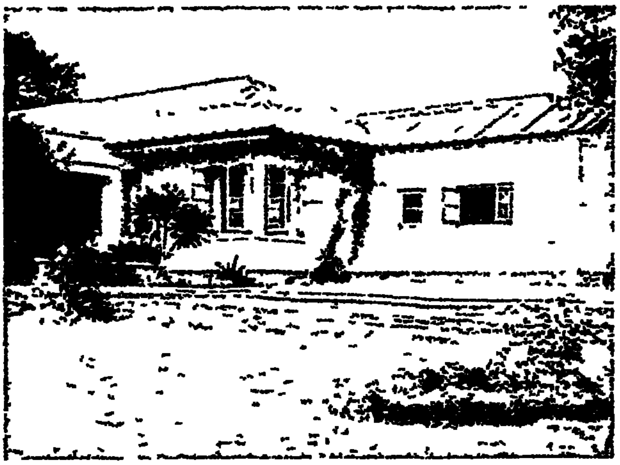
INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330, Gray's Inn Road, W C 1
3 30 P M Mr Kenneth Rotter Diagnosis of Cancer in the Nose and Nasopharynx

INSTITUTE OF CHILD HEALTH
5 P M (The Hospital for Sick Children, Gt Ormond Street, W C 1) Prof Robert Debré (Paris) Primary Tuberculosis in the Infant and Child

UNIVERSITY OF OXFORD
9 15 A M (Radcliffe Infirmary) Prof C Bruce Perry Ætiology and Prophylaxis of Acute Rheumatism



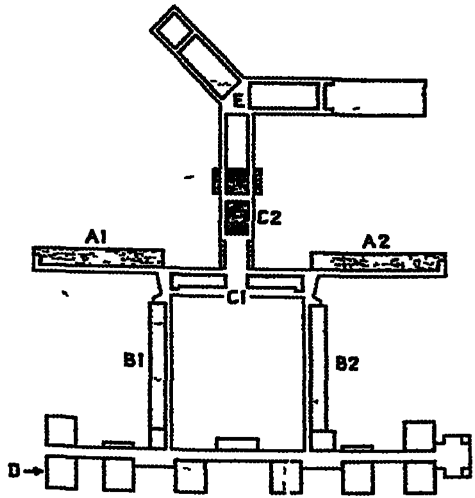
The courtyard of the future hospital



Part of one of the staff houses

those for clinical training in the two existing hospitals of Ibadan were not of the requisite level. Accordingly the government of Nigeria decided in 1951 to press forward with plans for the building of a separate teaching hospital, associated with but administered independently of the University College. Meanwhile the University of London, as an interim measure, agreed to make room for Nigerian students for clinical study in British medical schools until it should be completed.

In Nigeria, of course, there are fewer difficulties about space than would have to be faced in planning a great new teaching hospital in this country; and the board of management, in acquiring a site not far from that of the University College, were able to plan with reasonable freedom. When the hospital is finished, it may well be the envy of clinical teachers in some of our own medical schools.



Plan of the hospital

Building began in 1952 and progress has been such that at the time of the visit of the Queen on Feb. 14, the hospital was assuming something like its final shape. Its occupation is expected to begin this year and clinical teaching in October, 1957. Besides the teaching of students, the hospital is also to provide research facilities for the medical faculty; a school for the training of nurses up to the standard prescribed by the General Nursing Council has already been established and the first group of students has qualified.

No expense is being spared to make the hospital, both in standards and equipment, fully comparable with teaching hospitals in the United Kingdom. Grouped around the main building—each a notable example of modern design—are the ancillary departments. These include the medical school and hostel for clinical students, a school of nursing, a nurses' home, a school of hygiene, a resident medical officers' hostel, sisters' quarters, and housing for medical, administrative, and technical staff.

As shown in the plan which we reproduce, the hospital itself consists of eight blocks. Blocks A1 and A2 have five floors, while blocks B1, B2, and C1 have six floors, including a lower ground floor. Block C2 has eight floors, including a lower ground floor, whilst blocks D and E consist of ground floor and lower ground floor only.

On the ground floor, the board room and administrative offices are housed in blocks C1 and A2, the casualty department in B2, an X-ray department in C2, and laboratories in A1 and B1.

The wards for inpatients are on the upper floors of blocks A1, A2, B1, and B2, and the professorial units on the upper floors of C1, while the air-conditioned operating-theatres, the cardiographic department, and the central sterilising department are in C2. A hall with provision for eight lifts is also included in these latter blocks.

A spacious outpatient department is located on the ground floor of block D. This floor also contains the pharmacy, almoners' offices, and patients' record department; a physiotherapy department and an antenatal clinic are on the lower ground floor. Block E houses the kitchens, laundry, boiler-house, and staff dining-rooms.

When complete, the hospital will have 490 beds. Of these, 116 will be medical (including 28 for dermatological and neurological cases); 144 surgical and orthopædic (including 28 for septic surgical cases and 28 for ear, nose, and throat and ophthalmic patients); 109 obstetric and gynæcological; 68 pædiatric; and 28 for tuberculosis and thoracic surgical cases. There will also be 23 cots for sick babies and 2 observation (metabolic) beds; in addition 14 recovery beds adjoining the operating-theatres and 6 labour beds are envisaged.

The new hospital, besides providing for the training of students, will more than double the number of beds available for inpatient treatment in Ibadan. But University College Hospital will, it is hoped, do more than serve the local needs; as the centre of the country's medical life, it will provide a consultant service for the treatment of difficult cases throughout Nigeria, stimulate research, and play a vitalising part in the hospital services as a whole.

Naturally the cost of this great undertaking has been high, and according to current estimates a total capital outlay of £4½ million will ultimately be required. But it is a remarkable tribute to the determination and foresight with which the federal government are facing their responsibilities that the whole of this sum is being provided exclusively from Nigerian resources. At the moment the number of students entering the medical school is small, numbering only 30–40 a year. The new hospital is a sound investment in that it will both

Royal College of Physicians of London

At a comitia held on April 26, with Sir Russell Brain, the president, in the chair, it was announced that the Wellcome Trustees had given £40,000 as an endowment for research into the history of medicine, and £6000 towards the extension of the college building, as well as a grant towards a new edition of the Harvey film in colour which will be made by the Foundation's film unit

Dr E R Boland, Dr T C Hunt, and Dr J B Harman were reappointed as representatives on the Central Medical Recruitment Committee

The following were elected to the fellowship

T P Rees, Warlingham, Surrey, A D Porter Dunmow, Essex, J K Maddox, Sydney, Samuel Berman Cape Town H W E Jones Wolverhampton, J V Dacie London, H S Davis, London, J W Graham, Toronto, T E Jones Davies, Carmarthen, S D M Court Newcastle upon Tyne, C R B Blackburn, Sydney I B Sneddon Sheffield, R I S Bayliss, London, Raymond Daley London D W Pugh, Bath R H Girdwood, Edinburgh, J C Houston, London, Gerald Garmany, London, J D N Nabarro London Deryck Taverner, Leeds J E Cates, Bristol A J S McFadzean, Hong Kong, W S M Craig, Leeds G M Wilson, Sheffield, S Monteiro Singapore, H A Magnus London, W P Stamm, Aylesbury, F S Cooksey, London I G W Hill Dundee Sir David Campbell, Aberdeen, Sir Charles Hercus, Dunedin, C G McDonald, Sydney

The following, having satisfied the censors' board, were elected to the membership

Mohamed El Hassan Abu Bakr Diploma Kitchener Sch of Med, Khartoum, J S Bearcroft, M B Durh G M Berlyne, M B Manc, R A Carter, M B Camb, T P Casey, M B N Z, G W Cooper, M B Melb, A C Crooke, M D Camb, James Crooks, M B Glasg, M S Dunnill, M B Brist, J H Edwards M B Camb A G Fisher, M D Melb, R H Fox, M B Lond I K Fry, B M Oxfd, P A L Horsfall, M B Witw'srand, J P Hughes, M B Lond, R S Jones, M B Lpool, B J Lake M B Sydney, A L Latner M D Lpool Patricia J Lindop, M B Lond, A V Livingstone L R C P B L Mallett, M B Lond, S C Melnick, M B Lond, H S Moore, M B I, M B Lond captain R A M C, David Mymin M B Witw'srand, Donough O Brien M D Camb, Elizabeth A F Priest, M B Aberd, H M N Rees, M B Wales, L Z Resnekov, M B Cape Town, J G Richards, M B Sydney, G G Scott Brown M B Camb, I R T Stevens, M D Melb, J E P Thomas, M B Cape Town, H J Weston, M B N Z, E H Williams, M B Camb, L G Young M B N Z, surgeon lieut commander R N Z N

Licences to practise were conferred upon the following 157 candidates who have passed the final examination of the conjoint board

Peter Adlington, Hilary Allin Babatunde Oladipo Amure, M J Andrews Solomon Bacchus Armaity Bamboat R T Barber, J S Beales M F J Board I D L Bell Phyllis J A Bell P J Bennison A C S Bloomer V A W Blunt D J Bowen, J F Brooks, A G Bryer, I F M Buchanan D R Burcombe, A L Bussey R P Callaghan, D I Campbell J W Carter Joseph Connolly Neville Conway P L Cook, A H Crisp, Nickel Crombie, H G Davies, J E Davies, J J De Jode G T Dunger, A G Edwards S T Eng R H Evans, T G Evans D J Fairclough, J O O Fajemisin Parviz Faridian Aragh, I W J Fearne D M C Forster, M J N Frohn, Margaret Fuest, D A Furniss, I R M Gibson A D R Goodliffe, Fiona M Graham Rodney Grahame, Aubrey Greenbaum Ajeet Bans Lall Gulati, Teresa M Gurrin, C L G Hale, D M Harris P R Hawley, R B Hayden, Jennifer Hill J R Hobbs C V Horn E A Horniman Pauline M Hughes, C J B Hundleby G M Hunter, H E Inniss Palmer, G W Jenkins Trefor Jenkins, Jane G Jenkinson, G J Jewell Pauline M Jones W G G L Jones W R B Jones Winifred M Jones, A J Jordan S F Josse Amirali Kanji, J J Kelly J M Kennedy, J C Kent M G Kielty D G Law S C Lennox, Patricia E Linnell, W A Lishman, V St C D Logan J N Lunn, P D Marsden Faith L Maurice Williams Ann P Melville, C W Millar F J C Millard R B Miller, R L Mills D A Montgomery B B Mook Sang Janice H Mount D H Murphy, P H Nankivell M A Nelson John O Brien Bell P C Ofili, P F B Owen Hosep Pambakian Amelia W H Parker G T Parker, G W Pennington, Harel M Phillips, G E Pickup, P W Pitt C J Powel Smith D A H Pratt John Price Valerie J Prior John Quantrill, Kathleen M Rich, J D M Richards, A R Robertson I G Ross, Stanley Rowlands Mary G Russell, M P Y Scott B S Smith, D G Smith Jean M B Smith K G R Somer M J Sparrow Elizabeth A Spence P A J Starr, R E Steel G M Steiner, Henriette R P Sutherland, G R Swift S W Tarlton I A Theobald D A Thomas G D Thomas C B Thomson A C Ticehurst J E Tindle J W Turner W H C Walker Margaret M Walshe Eileen Waring D A Weatherhead, Harry Westbury C T Western P I K Will D O Williams D P Williams E J Williams J G P Williams M G Williams Donald Winstock T K W Woolacott Douglas Wright P R Wykes Barbara K Zamoyska Klaus Zobel J S M Zorab

The following diplomas and those mentioned in our issue of April 21 (p 519) were conferred jointly with the Royal College of Surgeons

D C H—Mary K M. Lindsay

D A—R P Holmes

D I H—Doreen P Allan

D T M & H—Douglas Buchanan, A M Rankin

Royal College of Obstetricians and Gynæcologists

The following were successful in a recent examination f the diploma in obstetrics

R M Adam, M D Adams, Colina C Adeniyi Jones W K Aitchison, Patricia M Alexander, L J H Arthur, J F P Asbury Mehroo Dinshah Aziz, P B Bailey Jean L Baker, Patricia Baker Jacqueline E Banbury J G Banton R C Begg, P J Bell Geoffrey Berry, J R Birkett D B Bower, Patricia M Boyd James Bradshaw, Cynthia A R Bray, R A Briggs, Gordon Bri J A Browne, C J Buckingham, H M Buckland, M J V Bull R A Butler, D S Carroll, Robert Chalmers G V P Chamberlain Elizabeth P Cloake, J B Coldrey, J A Collings Wells Diana J Collins, L J Conway, M B S Cooper, Anne M Cormack M L Cox G R Cubitt, Maria W Dabrowska L R Dalton Alice L Dav L R Dennis, A E L de Thierry R T Donald, G D Downe R G Dryden, G T Dunger, Robert Edmond, J P English, J A L F Espitalier Noel R S K Essame Hilary J Evans, J L Evan Andrew Fairley J K Fanning, M V J Fitzgerald D L Flu Sheila M Forbes, W T Frame R T Gaukroger William Gauk R H S Gibbs, J R Gillespie P R Gittins, G T Goodey, H M Gough, Rosemary A Grange, Peter Greaves Ruth J Gree Irene C Hain, E B D Hamilton, I G Hamilton J M G Hark W B Hepburn, Fred Hewitt, I A Hill, C P Hindley, A H T Hodgkinson, Joyce Honey, T J G Howie, T O Hughes A B Hugo, J G P Hunt, Elizabeth M Innes, Edna M Irwin P D C Jarman Wendy J Jefferson, Ruth W Jolson W M Jordan M A Kalina, Terence Kavanagh, G B Kelly, Lilias Kilpatrick J W Kirkbride, D A Lamont P F P Lansdown, W G R M Laurie, Ann B Lewin, E S Linton, W C Logan Helen D Macfarlane E J Mackay, Tormod Macleod, W I Martin Gillian G Matthews, John McIntosh, J T McLeod, D C S Millar, J F Moo Alan Moore, Kamalini Narayan J G Nicholson G K Nixon Sheelagh M O Grady P J Olney A M Orcharton L W Padgett Joyce E Page, R B Pardoe, D W Paterson, Iris O Peachey P L Pelmear, Gordon Penny, Ruth E L Pocock, P A P Pompa, W St M Prendiville, M G Price, W W Ramsay H W S Rankin M J Roe, J A Reynolds, A D Richardson, J G Rigby, J B Rose C A Rushmer, Attiya Sabir, A H Saddler Lino Sammut R E M Sanders, J G Sanderson, I P Q Scott, E J Sheppard, Beryl M Shipton, E M Shuttleworth, D L Sladden, J J Slome, A M Smith, Alison Smithies, Ismat Ibrahim Snobar, Brijendra Kumar Sood E I Stacey, Betty Standeven T D Steigne, Owen Thomas Ma Ma Tin, A I Tulloch, D E Tunnadine, L P D Tunnadine I C S Turner G R Veitch Elizabeth H M Walker M R B Wallice, Mahinder Chand Watsa P A Watt, Joyce D Waye, James Weatherup, Joy E West D C Williamson, James Wilson, P M Wine, H J Wood, R F Wright

Royal Medical Benevolent Fund

The annual general meeting of this Fund is to be held on Tuesday, June 5, at 5 P M, at 11, Chandos Street, London, W 1

Institute of Dermatology

A semi permanent exhibition by Dr I Friedmann on diseases of the nose and ear in relation to dermatology will be held at the Institute, Lisle Street, W C 2, from May 7 to 25

Heroin Banned in Italy

By a decree, entered in the official gazette of the Italian government (March 24, 1956), the manufacture and importation of heroin has been prohibited in Italy

Royal Society of Arts

On Mondays, May 7, 14, and 28 at 6 P M, at the society's house, John Adam Street, London, W C 2 three Cantor lectures will be given on Recent Studies of Sociology On May 7, Prof T S Simey, M A, will speak on Class Conflict and Social Mobility On May 14, Prof D V Glass, PH D, will speak on the Development of Demography The last lecture will be given on May 28 by Dr R F Tredgold, whose subject will be Changes in Social Responsibilities

Industrial Medicine Unit

The North West Metropolitan Regional Hospital Board have agreed that an industrial medicine unit shall be set up at the Central Middlesex Hospital It is proposed to appoint a consultant physician who will have beds at the hospital and will study the prevention of conditions in factories which contribute to the hospital load in the casualty and out patient departments as well as the wards" The Nuffield Trust will meet the cost of the unit for the first three years

Settlement of Dispute in Malta

In Malta the dispute between the government and the Medical Officers' Union (see *Lancet*, April 21, 1956, p 519) has been settled (*Times*, April 26, 1956) Doctors, after withdrawing their letters of resignation, are to be reinstated A commission, comprising a legal chairman and two members nominated by the Royal College of Physicians and the Royal College of Surgeons, will be appointed to review the medical service and the terms of employment Meanwhile no action will be taken to fill posts in Gozo or similar posts

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The honorary fellowship of the American College of Physicians has been conferred on Dr Macdonald Critchley

TABLE I—SPORADIC CASES AND OUTBREAKS OF *S enteritidis* INFECTION IN MAN IN THIS COUNTRY

Jena							Danysz					
No affected	Fatal cases	Sporadic	History unknown	Outbreaks		Year	No affected	Fatal cases	Sporadic	History unknown	Outbreaks	
				No	Cases						No	Cases
56	1	31	14	2	11	1944	4		2	2		
184	7	17	22	3	145	1945	1		1			
28	1	22	6			1946						
38	1	20	10	1	8	1947	5		3	2		
29		22	7			1948	3		3			
109	1	29	6	2	74	1949	3	1	2			
289	3	66	6	3	217	1950	7		2		1	5
134	2	50	25	4	59	1951	351		4	1	1	346
141	3	67	60	2	14	1952	4		3	1		
170	1	74	37	5	59	1953	21		9	4	1	8
58		30	28	1	7	1954	8		5	3		
31	1	22	9			1955 to June	6	1	6			

this period this variety was isolated from 80 patients and 2 healthy persons 2 of the patients had meningitis, from which they died, and 78 had acute gastro enteritis Kristensen states that 17 of the patients had either eaten or been in contact with 'Ratin' shortly before the onset of symptoms, in 31 of 38 cases ratin had previously been laid out in places frequented by the patients He also found that ratin bread stored for 88 months still yielded *S enteritidis* var *danysz*

Many human infections due to *S enteritidis* occur in this country each year, it can be seen in reports on food-poisoning that this species has been the second commonest cause of salmonella food-poisoning in each of the years 1951, 1952, and 1953 (Ministry of Health 1954, 1955) *S enteritidis* can be subdivided by biochemical reactions into four varieties, of which *S enteritidis* var *jena* is the most common and *S enteritidis* var *danysz* the second commonest in this country

Table I has been compiled from information received with cultures which have been identified in this laboratory It shows that both the jena and the danysz varieties may cause sporadic infections or outbreaks Some infections were fatal, but, as with salmonella infections due to other species, some of the deaths were in patients with another disease in which the superadded *S enteritidis* infection merely accelerated the fatal issue Of 21 deaths due to *S enteritidis* var *jena* 7 were associated with one of the following diseases leukæmia, fractured femur, severe hypertension, early carcinoma of stomach, cardiac failure, pneumonia, and severe mental illness In the remaining 14 cases death was directly attributable to infection with *S enteritidis* var *jena* The danysz variety gave rise to a fatal meningitis in a patient with anæmia In another case, recorded in 1955, infection with the danysz variety caused the death of an otherwise healthy man aged 57 The clinical symptoms due to the two varieties were much the same In 1954 the history of 16 cases of the jena type showed that the duration of the illness was 2–28 days (average 10); in 4 patients with danysz infection the illness lasted 5–10 days (average 7) The symptoms in both infections were those usually associated with food-poisoning pyrexia, diarrhœa, vomiting, occasionally blood and mucus in the stools, and some abdominal discomfort or pain Although the clinical symptoms were not usually severe, in some instances there was cause for alarm A patient with jena infection was suspected of having infective endocarditis due to this organism, a patient with danysz infection had rigors, and another collapsed Though these serious symptoms are unusual they may occur, and individual patients may show any degree of severity, even to a fatal outcome, both in jena and in danysz infections

Outbreaks

Table I shows the number of outbreaks from which information and cultures were received Both the jena and the danysz varieties can cause large outbreaks In this survey an outbreak has been defined as affecting 5 or more persons and therefore has not included some smaller outbreaks Descriptions of some outbreaks are given below from reports received here and from other sources

Outbreak due to S enteritidis *var* danysz

This report was made by Dr M Avent, medical officer of health for Basingstoke, and is published with his kind permission

REPORT ON OUTBREAK OF FOOD-POISONING CONNECTED WITH BASINGSTOKE SCHOOL MEALS DEPOT

On Friday afternoon, June 8 1951, a message was received that children at Silchester, Monk Sherborne, and Ramsdell schools had been taken ill with diarrhœa and vomiting

Inquiries suggested that the illness was connected with the midday meal at school on the previous day, June 7 Reports were later received of similar illness among children at Herriard Steventon, and in the Kingsclere and Whitchurch Rural District (Hannington, Overton) and the Alton Rural District (Wield, Medstead)

Specimens from patients were examined in the Public Health Laboratories at Reading and Winchester, both of which reported the presence of *S enteritidis*, an organism commonly associated with outbreaks of this type

Head teachers in the schools give the following figures

(*a*) Schools supplied by Cooking Depot	25
(*b*) Schools reporting cases of illness	12
(*c*) Children at (*b*) taking meal	939
(*d*) Children affected with illness	346

The staff at the depot ate the same meal, and about half were taken ill 4 of them so seriously that they were off duty for several days and 3 are still away (June 20) Examination of specimens from all 4 of them showed salmonella present in 2 and they have been excluded from work at the depot till clear

Unfortunately the only material used in the preparation of the meal in question which could be obtained was some custard and a few bread crumbs, examination of which gave negative results It was impossible to obtain any of the meat which had been used in the "savoury mince" supplied that day, because it had all been disposed of

TABLE II—*S enteritidis* INFECTIONS IN ANIMALS 1944–54

Source	Jena isolations	Danysz isolations
Sheep	1	
Duck	2	
Guineapigs	65	4
Cow or calf	2	2
Pony	1	
Mice	43	4
Dog	1	
Duck eggs	2	
Hamster	2	
Chick	1	
Porcupine	1	
Pig glands	8	1
Rats	3	85
Horse	1	
Rabbit		1

TABLE II—EFFECT OF FAMILY SIZE ON AVERAGE WEEKLY CONSUMPTION OF SOME FOODS *

	No of children				
	0	1	2	3	3+
Milk (pints)	5 7	5 6	5 4	4 9	4 9
Meat (oz)	44	33	27	24	22
Eggs	5 5	4 3	3 8	3 3	2 7
Vegetables except potatoes (oz)	43	35	29	24	22

* From Domestic Food Consumption and Expenditure, 1953 (1955)

rationing, though these may have political as well as economic bases Effective rationing ensures a more even distribution of specified foods both by restricting the highest levels of consumption and by increasing the lowest levels This was achieved in Britain by the triple system of ration-books, price control, and subsidies As a result of these factors, the variation of consumption with income was much reduced for commodities such as meat, cheese, eggs, and milk I also include here the schemes for the distribution of milk to nursing mothers, young children, and school children A large part of the present high consumption of milk—nearly 40% more than before the war—is undoubtedly due to these schemes

Other Factors

Before leaving physical factors, let me refer to two others—food technology and fuel Food technology has, as we have seen, made available foods far from their origin, and far from the time of harvesting or slaughtering It has also made available new foods, some of considerable importance, like margarine

The shortage of fuel in this country two hundred years ago, and in countries like India up to the present, necessarily restricts the sorts of foods which will be eaten Thus, it will be useless to provide India today with foods, however palatable and however nutritionally desirable, if their preparation is beyond the resources of the stone hearth and cow dung fuel

Social Factors

Religion and Social Custom

The effect of religion on food choice is best known through its prohibition of the eating of pork by Jews and Moslems and of beef by the Hindu, and of meat eating on Fridays and throughout Lent by the Roman Church Vegetarianism is met with in many religions—examples include again the strict Hindu Brahmin, as well as the Jains of Indian and the Kikuyu of East Africa The origins of these religious taboos are not always clear, though early ideas of hygiene played a part, economic factors were probably in many peoples more potent causes The nutritional effects may be enormous, Orr and Gilks (1931) have shown how the vegetarian Kikuyu are nutritionally far inferior to the neighbouring meat eating Masai

Social custom may dictate a variety of strange food habits In many countries common foods may be prohibited at certain times, such as pregnancy or lactation, or during illness or mourning, or other unusual foods may be eaten at these times Insects are an acceptable food in Mexico, Nigeria, and Siam and to the aboriginals of Australia (Bristowe 1953) In Latin America, foods are divided into "hot" and "cold" (Wellin 1953) The former may be consumed at any time, the latter only by healthy adults, but not in the mornings and only if their cold effects are neutralised by hot tea Foods are also divided into "heavy" or indigestible (for example, rice, milk, dates, figs) and "light" or easily digestible (mutton, chicken, bananas, carrots) Apart from milk, young children are not given heavy foods Natural sweet foods—that is, fruits—are not compatible with prepared sweet foods containing sugar, and must not be eaten together

Such customs usually are very strong and resistant to change Jews from the Arab countries who have recently migrated to Israel greatly resented the new foods which were imposed on them by the strenuous system of rationing there Even after several years they seek every means to revert to their original food habits—to use many spices, to take rice rather than wheat, and to use vegetable oil rather than other fats (W Straus, personal communication)

Social Class

There is commonly an appreciable difference in food habits between different social classes In this countr it shows itself in a preference by the so called upp classes for brown bread rather than white, for bitt marmalade rather than sweet, for coffee instead of te for coffee without rather than with milk, for savour rather than sweet puddings, and for the avoidance such foods as kippers and tripe These preferences, however, are not static since they occur or are cultivated al in those who are ambitious to move upwards in the soci scale The reverse is seen in the Hampstead and Chelse intellectual who cultivates a preference for tea an kippers—a form of inverted food snobbery The chi difference between social classes is the increasing rang of foods eaten as the social scale is ascended It i difficult to get working class peoples to try new foods on the other hand, trying new foods is almost a prerequisite of the socially superior The origin of thes customs is clearly economic

Education in Nutrition and Hygiene

Here I include those ideas of food values and food hygiene, whether sensible or nonsensical, which a group, a school, a society, or even an individual actively propagates As examples of hygiene propaganda, I may quote the acceptance by most people of pasteurisation of milk as a sensible hygienic measure (which it is) or of leaving foods in tins as hygienically dangerous (which it is not) Sometimes, sensible nutritional propaganda is effective, and it is possible that some part of the present high consumption of milk is due to the acceptance of propaganda that milk is a nutritionally desirable food We have seen, however, that probably a greater part o this high consumption is due to imposed State policy Somehow, it seems easier for people to accept foo nonsense than food sense It may be quite difficult t persuade people to drink milk and eat vegetables and fruit, but much easier to persuade them to take yogurt molasses, brewers' yeast, and wheat germ, or to eat their meat and their potato at separate meals Fortunately it is often true that the vogue of these fashions i usually amongst the wealthy members of the community who are likely, almost without wishing it, to take wha eventually adds up to a reasonably adequate diet Bu there have been examples where restrictions of foo choice imposed by one or other of these fads have prove harmful to those who have been duped

It would be interesting to speculate on some of th underlying reasons which make people susceptible to th sort of propaganda Let me mention only one—th hankering after naturalism Probably as a reaction t some of the less pleasant manifestations of civilised life it is easy to persuade people that natural foods are likel to be superior to sophisticated foods Hence the conviction amongst many that fresh vegetables are nutritionally superior to canned vegetables, or that butter i nutritionally superior to margarine, neither of thes statements is true

In general, however, food habits as we have seen ar established so early in life and so firmly that they ar little affected by propaganda When new knowledge i accepted at all, it tends to become moulded so as to fi the existing culture Thus, villages in Peru to whic something about vitamins has percolated have kept t agriculture, made certain recommendations about using bacterial rodenticides (Toxic Chemicals Working Party 1953) These recommendations were the least which could be accepted, and, in my opinion the use of bacterial rodenticides is unjustified because they may infect man and animals they may constitute an uncontrollable source and chain of infection of long duration, and they are said to be not so effective as other methods of controlling rodents

The use of bacterial rodenticides is banned in the U S A

Summary

In this country between 1944 and June, 1955, *S enteritidis* var *jena* accounted for 1267 known cases of infection in man of which 21 were fatal, and *S enteritidis* var *danysz* for 413 cases, of which 2 were fatal

In animals *S enteritidis* var *jena* was isolated most commonly from guineapigs, mice, and pig glands, and *S enteritidis* var *danysz* from rats, guineapigs, and mice

The use of bacterial rodenticides containing either of these organisms is no longer necessary and should be stopped

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Air Pollution

Logan[1] has estimated that about 1000 people died in the Greater London area as a result of the fog of Jan 4–6 this year The fog of Dec 5–8, 1952, was responsible for some 4000 deaths in London[2], and as Logan reminds us this January's episode is the third major fog incident in London since 1948 Unhappily, further incidents can be expected so long as air pollution continues at the present rate. Indeed, we may expect things to get worse as more people, houses, industries, and petrol and diesel vehicles are gathered together

London fogs have no exact parallel elsewhere Previous episodes (such as those at Donora and in the Meuse Valley, or the eye-smarting annoyances of Los Angeles) are very different from the wet thick smog of London Drinker,[3] in an arresting article, remarks that Londoners have looked upon "pea-soupers' with a sort of friendly familiarity not shared by strangers He recalls the two gentlemen who collided in Hyde Park during the 1952 fog 'With the formal politeness characteristic of the English, one said 'I beg your pardon. Can you please tell me where I am going?' The other replied, 'Yes, I can—into the Serpentine I have just come out'"

The Clean Air Bill which is based on the Beaver report, is now over some parliamentary hurdles Its far-reaching provisions show that Parliament, and we hope the public mean business now as well as in the near future The cure for our ills is not easy, and much money and trouble must be expended We must face the fact that we just do not know exactly what it is that makes smog lethal Amdur's valuable work on sulphur dioxide has been criticised and further research is a matter of the first importance Drinker draws attention to interesting observations by Clayton[4] and others on the use of radioactive isotopes to 'tag" fuels like coal and motor fuels and thus enable their presence to be detected in the air This method might help us to decide whether sulphur dioxide and smoke in this country come mainly from domestic fires from power-stations or other industrial sources or from motor exhausts

Electricity power-stations have been accused of pouring out huge quantities of oxides of sulphur But in a paper read in New York Rees,[5] of the British Electricity Authority discusses the effects of the ban put on "scrubbers' (for removing sulphur dioxide) during the late war because the effluent streams were steamy and made good beacons for enemy aircraft and claims that there is insufficient evidence to justify a return to the pre-war practice of scrubbing and that nobody can measure the difference chemically or by health surveys whether or not the sulphur dioxide is scrubbed out Since the process is very costly, those in charge of the power plants are opposed to its use

In many ways, London is far behind some other large cities which have recently 'cleaned' their air Pittsburgh for example handles enormous quantities of raw materials in its steel mills and blast-furnaces, whose activities caused much pollution by ash, grit and carbon particles It can certainly be proud of its anti-pollution drive and can point with satisfaction to the fact that a transatlantic plane was recently unable to land anywhere near New York or Boston because of poor visibility but was accommodated easily at Pittsburgh Some less effective preventive measures have been taken in this country Last winter the Government supplied masks to those with bronchitis asthma, and cardiovascular disease and these helped many patients to breathe less polluted air Elderly persons were advised to remain indoors and if possible to rest But little has so far been done to get rid of the cause or causes

The scientist, the combustion engineer and the local authority must get together to change our traditional methods of heating Compulsion may have to be used for Government reports and exhortations have proved to be largely ineffective At least one line of research must be pursued further Wilkins, of the Fuel Research Station, has devised an adjustable wick dipped into a bottle of ammonia as a means of neutralising both the sulphur-dioxide gas and sulphuric-acid mist This method may protect humans in the same way as the pigs and sheep at Smithfield Show were protected during the 1952 fog The scrupulously clean (and therefore non-ammoniacal) animals were seriously affected whereas those less meticulously cared for were unharmed.

Vaccination against Poliomyelitis

The initial batches of the British poliomyelitis vaccine have now passed their safety tests and will be used for first injections to about 200 000 children in Great Britain These will be children born in November of each of the years 1947–54 and in March of the years 1951–54 These children will receive first injections shortly, and after about three weeks second injections Any vaccine left over from this first distribution will be used for children born in August of the years 1947–54.

In the first phase of the vaccination programme, in May and June, it is hoped to vaccinate over 300,000 children in England and Wales and 40 000–50,000 in Scotland The remainder of those registered will be given priority when vaccination is resumed in the autumn

Children registered for vaccination number 1 610,899 in England and Wales and 299,144 in Scotland—29% and 42% of those eligible Returns were received from 144 of the 146 local health authorities in England and Wales and from each of the 55 authorities in Scotland choose his diet wisely Since observations on man have not given us any completely satisfactory explanation of this, let us turn to the experiments on animals

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[1] Logan W P D *Brit med J* March 31 1956 p 722

[2] Mortality and Morbidity During the London Fog of December 1952 H.M. Stationery Office 1954

[3] Drinker P *New Engl J Med* 1956 254 421

[4] Clayton G D Arnold, J R. Patty, F A *Science*, 1955 122, 751

[5] Rees R L Proceedings of 1st International Congress on Air Pollution, New York, March 1955 p 143

The most important and by now classical experiments in this field were those reported by Harris and his collaborators from Cambridge (Harris et al 1933) They found that rats depleted of vitamin B_1 will choose a diet containing it in preference to one that does not An animal may be sufficiently confused by a wide array of possible choices that it cannot select, but it can be taught to recognise the correct diet Again, it may be deceived by giving it a deficient food with a flavour which it has previously learnt to associate with the vitamin-containing food, but once more it can be re educated to the correct food

Harris explained these findings on the basis of learning The condition of the deficient animal is so rapidly improved when he eats the right diet that he soon learns to associate this with the resulting feeling of well-being

Since that time, many examples have been reported by other workers of the ability or otherwise of animals to choose a correct diet (see Lepkovsky 1948, Scott and Verney 1948) Adult rats, offered a diet of pure nutrients in separate containers—for example, five containers with protein, fat, carbohydrate, mineral elements, and vitamins—can select an adequate diet, they do not do so, however, when they are very young or during pregnancy or lactation Rats rendered deficient in vitamin B_1 or riboflavine or pyridoxine or calcium select an adequate diet, but rats rendered deficient in protein or vitamin A or vitamin D do not do so If deprived of the adrenal glands, an operation whose effects are relieved by taking salt, they would choose a salt-containing diet If deprived of their pancreas, a condition relieved by avoidance of carbohydrates, they reduce their intake of carbohydrates And finally, we have recently shown that rats deprived of vitamin B_1 reduce their intake of sugar, some avoiding it entirely and surviving for long periods

All of these results support the view of Harris that a deficient animal learns to choose the correct diet when by so doing he rapidly feels better Where the deficiency is of a nutrient like vitamin A, or vitamin D, which does not lead to a correct choice, the explanation is that the correction of the deficiency does not produce improvement rapidly enough for the animal to learn to associate the improvement with the food which gave rise to it Even one apparent exception to this supports the learning theory Animals rendered deficient in magnesium *avoid* diets containing this element, it seems that magnesium deficiency results in a sort of intoxication which the animals find pleasurable, and that they learn to avoid eating magnesium in order to preserve this sensation

It has been suggested that nutritional choice is brought about by some inner drive or instinct by which the animal is made to seek out a food containing the appropriate nutrient (Richter 1947) My own reading of the evidence at present available is that the theory of learning, as developed by Harris, is much the more likely explanation

One more animal experiment is worth quoting If animals from whom the adrenal glands have been removed are offered a choice between water and a salt solution, they choose the salt and so live much longer If, however, they are offered a choice between sugar solution and salt solution, they tend to take the sugar, and die sooner (Harriman 1952) We can therefore modify Harris's theory to the extent of saying that a wise nutritional choice may be prevented if a sufficiently palatable but nutritionally unsuitable food is offered too

What then are the general conclusions we may draw from such animal experiments ? First, animals presented with individual nutrients are sometimes able to select these in such a way as to satisfy their nutritional needs Their ability to do so depends on age, physiological state—e g, whether or not they are pregnant—and heredity, and some do it better than others

Secondly, a deficient animal will select the missing nutrients, and perhaps also avoid harmful ones, if the beneficial or harmful effect is fairly considerable and occurs fairly quickly

Thirdly, it seems to follow from this that the correct choice of individual dietary items is not due to an instinctive urge but to learning that animals learn to associate the consumption of the right food with the feeling of well-being induced by it This would also explain why people have come to like alcohol or tea or coffee or cola

Fourthly, a nutritionally wide choice may be diverted to one which is unwise or even fatal by offering a palatable but, in the circumstances, worthless food

These conclusions, interesting as they are, still do not provide the whole answer They do not explain why man, with quite different foods at his disposal in different parts of the world, is usually capable of showing nutritional wisdom in his choice of food, provided he is not limited, by, for example, economic circumstance or by nutritionally unsound social pressure

A possible explanation might be that it is a result of experience By experience, translated into and transmitted by social custom, man has learned what foods to select to maintain reasonable if not perfect health That is to say, the food habits of a people, which begin to be formed from the moment of birth, have been built up on the experience of previous generations who themselves have learnt by trial and error

But to my mind this is still an inadequate explanation I believe that the key to the understanding of food selection according to physiological need is something which might be called the hypothesis of satiety If to this is added an extension of Harris's theory of learning, and the possibility of cultural transmission of patterns of food selection, then I think we can explain the phenomenon completely

I derive the hypothesis of satiety from the observation —common to all the experiments on food choice with human beings and animals—that no person or animal will consume only one article of diet but always takes some from all or at least several of the sources available Consider the experiment of an animal offered an array of pure nutrients He eats a little protein, then some carbohydrate, then perhaps some fat, then more protein, in due course he consumes—or at least *often* he consumes —a nutritionally sound mixture of all the essential nutrients The question why he will choose to eat vitamin B_1 if he is short of this vitamin we have already answered But there are two further questions which are not answered by the learning theory First, why does the deficient animal *stop* eating the missing nutrient after a time, and move on to another ? Second, and even more important, what determines food choice in the non deficient animal ? We must accept that, with a reasonably wide variety of nutrients or foods from which to choose, the animal often makes a good enough choice to avoid deficiency altogether He does not, as it were, wait until he is deficient in vitamin B_1 before taking this nutrient The constant choice of an adequate diet, by man or animal, clearly therefore cannot depend on a sequence of specific nutrient deficiencies and the subsequent learning to eat the foods which correct them

I suggest that these questions may be answered somewhat along these lines The increase in consumption of a particular food, or of a pure nutrient, leads first to the pleasant sensation of satiety, but beyond this to an unpleasant sensation which makes the animal stop eating this food This unpleasant sensation, such as we might get by eating too much sweet or fatty food, might perhaps be a feeling of nausea by direct action on the stomach wall, or arise from a change of taste sensation

In England Now

A Running Commentary by Peripatetic Correspondents

ONCE upon a time there was a very poor country, where nobody had enough to eat and the average expectation of life was 24 years There was also a very rich country, where everybody had plenty to eat and the average expectation of life was 64 years In the very rich country people used to save up milk and butter and cream and eggs and send them to the very poor country, where they were distributed, especially to the children, who would otherwise have had none In this way the expectation of life in the very poor country was raised from 24 to 27 years Meanwhile the expectation of life in the very rich country was rising too, and went up from 64 to 67 years, and everyone who didn't die of cancer of the lung from smoking too many cigarettes died of coronary thrombosis Then someone discovered that coronary thrombosis was due to eating and drinking too much milk and butter and cream and eggs So people stopped eating and drinking milk and butter and cream and eggs in the very rich country, and sent it all to the very poor country, so that the expectation of life in the very poor country might be raised high enough for them to start dying of coronary thrombosis so that they, too, could stop eating and drinking milk and butter and cream and eggs

* * *

Attendance at a symposium in the spring, if not too slavish, is an effective tonic for those who live and work at the periphery If the meetings are held in London a country-dweller is also subject to the extra stimuli of continued partial asphyxia and other unaccustomed features of the bustling, abrasive way of life in the capital This year's deliberations on bacterial anatomy seemed to call for a lot of microbial vivisection of a violent kind Here were descriptions of germs with their limbs torn away in disintegrators, whilst others had their outer walls eroded by enzymes to lay bare the naked protoplast or else thickly coated with a clinging layer of antibody Some spoke of the behaviour of germs exposed to severe cold Some had tried the effects of over-heating or immersion in strong brine One experimenter confined his subjects to the airless end of a sealed capillary tube, there to swim "till the last, *nastiest amino-acid* was consumed" We were delightfully reminded here that a bat may nourish its wing-muscles on the same residue In the chamber of the micromanipulator any plump bacillus may be subjected to acupuncture, though techniques for inflicting moxibustion are still lacking If Blake had sat among the audience he might have heard the molecular screams of dismembered viruses, but the company would surely have requested the evidence of tape-recordings and an electron micrograph of the microbial mouth-parts

A non-microbiological wife (taken to reading the journals since the rising tides of inflation cut off the evening paper) was as much diverted by the appearance of the microbiologists as by the morphology of the microbes The feminine eye can at once distinguish on sight between the reliable and the untrustworthy During the respectful silence that greeted a cine-film on motility came the whispered observation that the ones with tails were clearly males, while the sleek, stationary ones must be female

The dictionary affirms that a symposium is a convivial meeting for drinking, conversation, and intellectual entertainment Considering that most of the communications can well be read in print in the comfort of a fireside-chair, is it not worth arranging such a meeting, without the set speakers, to take place in a large tent lined with barrels? Back at the periphery now, we are working on this idea whilst coping once more with the vagaries of children, pets, gardens, clinical colleagues, and the local plagues

* * *

Before he can arrive at a diagnosis, the Young Doctor must arrive at his patient (cf Mrs Glasse and her jugged hare) A major obstacle in the Practitioner's Progress is the patient's garden gate As your correspondent lately sucked his lacerated fingers, it occurred to him that this is another topic on which postgraduate education is of no help

The Englishman in this part of the Island surrounds his castle with such fortifications that it resembles the lair of an immured robber baron Concealed craftily among the defence works and composed of cutting edges fastened together by barbed wire, is the garden-gate These devices fall into two groups

1 Those that won't shut
2 Those that won't open

Group 1, very rare, is a godsend to the Y D unless he is fighting a delaying action with one of the household's paranoic dumb chums

Group 2 includes almost all gates not included in group 1 The Y D confronted with a gate *in group* 2 should not waste time attempting a parley with the garrison Inevitably the Y D will have to "go it alone" Two lines of strategy are open to him If he weighs-in at ten stone or under, let him produce his screw-driver and heavy wire-cutters and dismantle the gate The Y D in the heavier weight-classes is advised "to retire in order to jump the better," and with (or without) a hoarse shout of "A Nye! A Nye!", to hurl himself at the gate He will then either descend into the garden in a cloud of disintegrating wood and metal, or find himself rushing up the garden path carrying the entire gate before him, with a bow-wave of prams, milk-bottles, toys, and juvenile delinquents

It should now be obvious why the assault direct is contra-indicated for the light-weight Y D The gate may be so resilient that he rebounds violently across the pavement If lucky, he will merely drive his occiput through the side-window of his car, and the resulting scalp-wound should heal nicely in about ten days If unlucky he will disappear under a passing bus In either event, there will be Delay in Seeing the Patient

* * *

The Ganglion has been promoted at about the same rate as I have In those bad old days when I started as a casualty dresser *we students were set to work dissecting* them out in the outpatients' theatre during the afternoons By the time I was a house-surgeon it was recognised, and how rightly, that this was not good enough, and I was again set to work during slack afternoons dissecting out ganglia, this time in the main theatres Now that I have struggled into the ranks of the senior registrars I find that the ganglion is considered too strong meat for the house-surgeon and it appears once more on my list Among the consultants the waiting-lists grow short The heroics of the operating-theatre recede, and their places will soon be taken by humbler activities that once would have been thrown as crumbs to the registrars I see *no escape Ganglion, you are my fate*

* * *

About five years ago I was digging in my garden on a very warm spring day when a little elf appeared He offered to finish my digging for me, and I was only too glad to sit in the sun in a deck-chair on the lawn Well, he soon finished that off *and started clipping the hedge* To cut a long story short, he offered to look after the whole garden; and from that day on I never had to do a stroke I used to sit out under a tree with a glass of beer and the newspaper, and the industrious little elf used to dig and delve from crack of dawn till dewy eve He was a real glutton for work The garden had never looked so neat and well stocked, I was the envy of my neighbours for miles around

Then two years ago he suddenly stopped coming Didn't say a word, just didn't turn up I was lost The garden went to wrack and ruin It was a wilderness Yesterday he turned up as though nothing had happened and started working No *apology or anything* I was livid "Look here," I said, "where do you think you've been all this time?" "I been for me National Service," he said "And what sort of National Service do you do, my little man?" "What? Ain't you never '*eard* of the National Elf Service?" he replied

* * *

A patient's comment on the exhibition of the Medical Art Society—Never before have so many doctors done me so much good at one visit

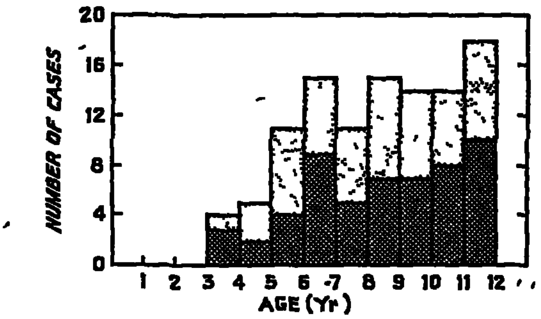

Fig 1—Age at onset of rheumatic fever and sex-distribution (*thatched*, boys, *stippled*, girls) of 107 cases surveyed

The distribution of cases by years of age at onset is shown in fig 1 The number of cases in children under the age of 5 is small—a usual finding

The frequency of antistreptolysin-O titres of 200 units or more per ml for the nine age-groups is shown in table I together with the geometric mean A S O, the frequency with which group A β hæmolytic streptococci were recovered at admission or within one week, and the frequency of preceding upper respiratory-tract infection within a month of onset of rheumatic symptoms (median period of 13 days)

Because the numbers in each of these nine age groups are small consecutive age-groups have been amalgamated into four groups for statistical analysis (table II) The four summed age-groups shown in table II show no significant differences in the frequency of upper respiratory infection and group A β-hæmolytic streptococcal isolations, but both the frequency of elevated A S O titres and the mean A S O titre is less in the younger children, particularly in the under-6 age group This is shown clearly in figs 2 and 3 This difference between the youngest age-group and the remainder is statistically significant ($\chi^2 = 12.6$, $n = 1$, $p < 0.001$)

TABLE II—DATA IN TABLE I REARRANGED UNDER FOUR SUMMED AGE GROUPS

—	Age (yr)				Total
	Under 6	6 to under 8	8 to under 10	10 to under 12	
No of cases	20	26	29	32	107
A S O titres No raised	9 (*45*%)	20 (*77*%)	25 (*86*%)	27 (*84*%)	81 (*76*%)
Mean (units per ml)	144	288	345	380	288
Upper resp infection (no of cases)	10 (*50*%)	16 (*61*%)	12 (*41*%)	18 (*56*%)	56 (*52*%)
Infection with group A β hæmolytic streptococci (no of cases)	9 (*45*%)	10 (*39*%)	15 (*52*%)	13 (*41*%)	47 (*44*%)

Discussion

We have not been able to detect any selection bias in the youngest age group, such as a more frequent administration of penicillin in the treatment of the preceding upper respiratory tract infection It would be desirable to examine a larger series in order to avoid summation in the younger age groups, but the frequency of attacks of acute rheumatic fever among children under 6 years of age is low, in the present seven year survey, only 20 such children were admitted to this unit who fulfilled the necessary criteria of diagnosis, activity, and age These children differed essentially from those in older age groups only in their lower antistreptolysin O level (fig 4) This is contrary to the earlier findings of Coburn and Pauli (1935), according to which A S O levels in rheumatic children showed, if anything, a tendency to lower levels with *increasing* age

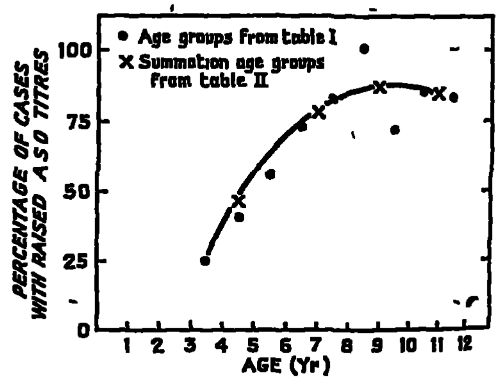

Fig 2—Age and percentage of cases with raised A S O titre (200 units or more per ml)

The present results show, then, that both the mean A S O level and the proportion of cases with raised titres are significantly lower in very young rheumatic children than in children over 5 years old These differences are also found, though not to a significant degree, in the 6–7 age group

We have also compared the levels with those in a small group of 40 children under the age of 12 years admitted to this unit with conditions unrelated to rheumatism (including 13 children under 6 years) In this group the mean A S O titre for those under 6 years was 49 units per ml (15% raised) and for those aged 6 years and more 105 units per ml (41% raised) It is therefore clear that in the youngest rheumatic group, although the titres are relatively diminished, the mean level of these titres and the frequency of raised titres are considerably higher than in non-rheumatic cases of a similar age in hospital We have not, however, had an opportunity of making a comparison with healthy children of various ages after β hæmolytic streptococcal infection

Powers and Boisvert (1944) have demonstrated an alteration in the natural history of streptococcal respiratory disease during the early years of life, the ill

TABLE I—RELATION OF AGE TO A S O LEVELS, PRECEDING UPPER-RESPIRATORY-TRACT INFECTION, AND RECOVERY OF GROUP-A β-HÆMOLYTIC STREPTOCOCCI

—	Age (yr)									Total
	3–	4–	5–	6–	7–	8–	9–	10–	11–	
No of cases	4	5	11	15	11	15	14	14	18	107
A S O titres No raised	1 (*25*%)	2 (*40*%)	6 (*55*%)	11 (*73*%)	9 (*82*%)	15 (*100*%)	10 (*71*%)	12 (*85*%)	15 (*83*%)	81 (*76*%)
Mean (units per ml)	89	112	199	282	295	380	300	372	380	288
Upper resp infection (no of cases)	2 (*50*%)	3 (*60*%)	5 (*45*%)	8 (*53*%)	8 (*73*%)	6 (*40*%)	6 (*43*%)	6 (*43*%)	12 (*66*%)	56 (*52*%)
Isolation of group A β hæmolytic streptococci (no of cases)	2 (*50*%)	2 (*40*%)	5 (*45*%)	5 (*33*%)	5 (*45*%)	9 (*60*%)	6 (*43*%)	6 (*43*%)	7 (*39*%)	47 (*44*%)

Dumbfounded, I was unable to detect—even on repeated re reading—the reverential awe usually accorded to pronouncements of the Royal College of Physicians—in the present instance unassisted, it seems, by any other earthly body

Since large sums of public money are involved I hope the publication of Professor Wyburn's letter may assist those who are attempting the heartbreaking task of opposing specialised interests in order to render the training of medical students "economic," and thus to produce a doctor confidently consulted when one is ill

Sheffield JOHN L EDWARDS

WHOLE-TIME SPECIALISTS

SIR,—I should like to say how much I approved of Dr Gilchrist's masterly résumé (April 14) of the situation that now confronts full time specialists—consultant and S H M O alike

The inequalities and injustices which he lists are unlikely ever to be righted until *adequate* representation for the non teaching full-time specialists is obtained on the Joint Consultants Committee (which is also in practice the staff side of Whitley B)

This committee is the only body that negotiates with the Ministry and the management side of Whitley B on behalf of the specialist services It is an autonomous body, and in particular it is not responsible to the Central Consultants and Specialists Committee There have been, in fact, occasions when the Joint Consultants Committee have altered documents or policies which have previously received approval in the regional and central consultants organisation (the Strachan report on hospital staffing is an outstanding example)

It is extremely difficult for the full-time consultant and S H M O to see why their reasonable request for adequate representation on the Joint Consultants Commiteee is resisted The reasons given are usually three.

(*a*) That it is a mistake to introduce sectional interests on to this committee

(*b*) That the full time specialists have opportunity through the regional machinery that finally produces 6 members of the Central Consultants and Specialists Committee on the Joint Consultants Committee to get their representatives elected

(*c*) That alteration of the present machinery would result in "splitting" of the profession

None of these "reasons" seems to me valid or even true The first, about sectional interests, begs the question entirely It is difficult to see what particular quality part-timers have that make them less likely to be partisan than the *full* timer The results of the past eight years' negotiations have been much to the advantage of one section—and that is the section that practically monopolises the representation

It is true that the full timers could obtain representatives by the regional machinery Their numbers are nearly equal to the part timers' and they would have the support of 1200 part-time S.H M O s whose interests march with theirs But this would mean a deliberate electoral campaign in the regions the displacing of many valuable men who are now representatives and ill feeling between the two sections At the end they would obtain a share of the 6 seats on the Central Consultants and Specialists Committee and would still be out numbered by the 11 representatives of the colleges This solution would indeed mean "splitting"

As to the third reason, I submit that the exact opposite is true It is the consistent discouragement and the refusal of his reasonable requests that will drive the full-timer to a split This seems more and more likely to happen

The solution would be to enlarge the Joint Consultants Commitee to 23 and give the 6 extra places to the full time specialists This would ensure that their viewpoint was adequately heard and at the same time correct the present overbearing representation of the colleges Such a committee would present a united front to the Ministry and represent the whole specialist services

As this graceful gesture by the Joint Consultants Committee seems highly unlikely, I support Dr Gilchrist's suggestion of a full-time specialist group We must get our representation the hard way

Derby G HOWELLS

ADRENALECTOMY FOR VASCULAR DISEASE OF DIABETES

SIR,—While I agree with much that Dr Malins says in his article last week, there are two points which, I think, require modification

In the first place he quotes me as saying, in a personal communication, that hypophysectomy may produce intractable hypoglycæmia My experience of this operation is limited to one case in which severe hypoglycæmia occurred after operation, but the fact that the patient is still alive and well one year later makes the word "intractable" inappropriate

Secondly, I cannot agree that there is sufficient justification for the statement that "it seems certain that retinopathy will develop in every diabetic who lives long enough, and that the final stage of blindness will arrive in those who do not succumb to renal failure before their sight fails" Both Dr R D Lawrence and I have seen a number of patients who have had diabetes for thirty years or more and are completely free from complications, I see no reason why these patients should develop either retinopathy or nephropathy Dr Joslin, of Boston, also has many such patients and indeed gives them a victory medal

There would seem to be a group of long-standing diabetics in whom such complications are absent or minimal, and, until more is known of the ætiology of the complications of diabetes, such a dogmatic statement as that made by Dr Malins seems to me to be unduly pessimistic

London W 1 WILFRID OAKLEY

PERFORATED ACUTE AND CHRONIC PEPTIC ULCER

SIR,—I read with interest the latest results of conservative therapy published by Mr Hermon Taylor and Mr R P Warren (April 14) and note that they confirm the fundamental difference in the prognosis of perforations in acute and in chronic ulcers to which I drew attention in presenting the results of primary suture in 1953[1]

In discussing the immediate-mortality rates they argue that there is little to choose between the two methods of treatment I must, however, correct their statement that my series of 206 perforations was "a selected group of operable cases," for this is a misconception My cases were the consecutive admissions of all the perforations which came into my wards on my receiving days during the period under review There was no selection, and although some were very ill none was refused the chance which operation offered The mortality of that series—6 3%—must therefore stand The records' officer at the Royal Victoria Infirmary tells me that during the past five years 942 patients with perforated peptic ulcers were admitted to the hospital of these, 41 died after operation (4 4%) and 20 were moribund on admission and died without operation (2 1%), giving a total mortality of 6 5% In 1955 the figures were even better there were 156 perforations, none of these patients was admitted moribund and 6 died, giving a total mortality of 3 8% for this series

Results of this kind amply justify the continued employment of laparotomy and primary suture as the local effect as well as to inhibition of the anterior lobe of the pituitary gland

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[1] *Lancet*, 1953, i 870

Material

This paper is an analysis of 106 cases of breast cancer treated with either œstrogen or androgen in women who died in a period of seven years, and the following data relate to the patients' state when accepted for hormone therapy

All the patients had advanced stage IV cancer of the breast and had already received all possible benefit from either X-irradiation or surgery or both, or else the lesion was too far advanced for anything except palliative hormone therapy

Previous treatment—Of the 106 women 3 had had surgery alone, 10 X-irradiation alone, 82 surgery and irradiation, and 11 no treatment

Histology—78 patients had histologically proved carcinoma, but Broders's grading was not stated in many of the pathological reports Records of histology were missing in 7 There were no pathological reports in 21 cases which were much too advanced for surgery and in which the diagnosis was obvious on clinical findings

The *duration of disease* before the start of hormone treatment was as follows 94 5% of the women had had the cancer for 6 months, 86 0% for 1 year, 68 0% for 2 years, 48 0% for 3 years, 34 0% for 4 years, 21 0% for 5 years, 10 4% for 7 years, and 4 0% for 10–15 years

Connubiality—24 6% of the patients were single and 75 4% married

Age distribution—9 patients (8 5%) were aged less than 40, 61 (57 5%) were aged 41–60, and 36 (34%) were aged 61 or more

The menopause had occurred in 81%, and of these it had followed either irradiation or oophorectomy in 12 6%

Pregnancy or miscarriage was recorded in 55 6%

Distribution of metastases was as follows

Axillary, supraclavicular, or other lymph-nodes	74 5%
Skin nodules, ulceration, or infiltration	70 0%
Bones	52 8%
Lungs or pleura	33 0%
Other breast	21 7%
Other sites	14 3%

Some patients had metastases in several or all of these sites

General condition—Advanced cardiovascular disease was found in 8 5% The general nutrition was good in 37 8%, but 56 5% had lost weight up to 2 st and 5 7% more than that

Methods

All the patients were interviewed and examined monthly or every two months according to their condition and response to treatment Serial records of weight, hæmoglobin, erythrocyte sedimentation rate (E S R) (Westergren), and blood alkaline and acid phosphatase were kept Changes in lesions were recorded photographically or followed on serial radiographs

Œstrogen Therapy

Originally the British Empire Cancer Campaign wished to compare the effect of low dosage (0 3 mg q i d) with that of high dosage (5 mg q i d) of stilbœstrol Printed forms were received, and patients were allocated at random to the dosage printed on these, by this means no individual selection of high or low dosage was made by each investigator Patients were, if possible, kept on their allotted dosage until death A change to high dosage was made only if it was obvious that no effect was being obtained from low dosage Similarly, on occasions the dosage had to be lowered if symptoms of toxicity were intolerable

Much individual variation was noted in tolerance within the dosage range 0 3–5 0 mg q i d After preliminary nausea, anorexia, flatulence, or giddiness most patients became gradually tolerant, but a few remained unable to take stilbœstrol In my experience small doses of this hormone are practically valueless, hence early doses of 5 mg q i d are advocated, with increase of this amount to as much as 50 mg q i d if required

Although the œstrogen was usually stilbœstrol, occasionally ethinyl œstradiol was substituted because of intolerance or sometimes when large dosage was required

Androgen Therapy

57 patients were treated with androgens—of these, 6 were aged less than 40, 38 were aged 41–60, and 13 were aged 61 or more, 35 of these (61 4%) had bone secondaries when first seen

To determine whether androgen therapy was of benefit or not, it was decided to give the largest possible tolerated dosage and to maintain this until there was some clinical or radiographic improvement, or until it was obvious that the patient was rapidly deteriorating When this trial started, it was necessary to collect as many cases as possible for inclusion in the British Empire Cancer Campaign trial of low and high dosages of œstrogen, and some of the early cases were so treated although bone secondaries were present, when better judgment would have indicated treatment with androgens However, after some experience, the younger patients and those with osseous metastases were given only androgens

The high dosage chosen, 300 mg daily, was not limited at first by expense, because adequate material was freely available through the generosity of several firms

Most patients treated with androgens were given daily injections, but some, too thin to tolerate repeated treatment by this route, or to give them a brief rest, were given oral therapy with either methyl androstenediol or methyltestosterone A few were also treated with implants of testosterone or of testosterone propionate for various reasons—e g, difficulty of regular attendance and supervision

Large dosages of androgens were usually continued indefinitely, even when patients were in a quiescent stage in reasonable health, though often the frequency of dosage was lessened, only to be restored with signs of further deterioration or spread

For example, in a patient who survived for 260 weeks, the following enormous doses were given 60 7 g of testosterone propionate, 84 0 g of testosterone isobutyrate, 10·5 g of methyl androstenediol by injection and 8 4 g by mouth, and 6 72 g of methyltestosterone by mouth up to about a month before death

In the patients who had been menstruating until the start of treatment amenorrhœa persisted

Toxic Effects

Œstrogens

The well recognised toxic effects of stilbœstrol and ethinyl œstradiol are common even with minimal dosage for endocrine dyscrasias, but (as already stated) a much bigger dosage was believed to be necessary and was given Hence it is not surprising that 40 3% of the patients so treated complained of toxic effects It was necessary to encourage these patients to persevere with the prescribed dosage, and usually tolerance improved Some patients assimilated 160–200 mg of stilbœstrol daily

Toxic symptoms noted were anorexia, flatulence, nausea, retching, sometimes vomiting, dizziness, and general malaise These symptoms developed either early or late in treatment, in the latter case they were possibly due to hepatic metastases impairing detoxication Often these patients were lethargic, dehydrated, and wasted, with dry inelastic sallow skin

Androgens

Only 29 8% of the patients treated with androgen complained of nausea or vomiting Sometimes it was necessary to reduce the daily dosage, and potassium citrate and a powder of magnesium trisilicate and bismuth carbonate were of value In view of the suggestion that the toxic effect in the earlier cases in this series treated with massive therapy was due to hypercalcæmia, the ontribute as much to their therapeutic action as their nown effects on the thalamic structures It must be emembered that severe somatic pain may frequently be elieved by cortisone, and that the emotional upsets of he climacteric sometimes respond to œstrogens and/or ndrogens

Again, we have found that administration of meprobamate causes changes in fecal flora from a proteolytic to a saccharolytic type—a change to which the humoral effects of antibiotics have been ascribed [4, 5] and which have also been invoked to explain the dry-weight gain of domesticated non-ruminant animals ingesting them This explanation must be re examined in the light of a study at the Loblund Institute showing acceleration of growth-rate in germ free poultry fed antibiotics [6] Meanwhile an interesting common denominator underlying hormones, antibiotics, and tranquillisers seems to be emerging Patients on rauwolfia or meprobamate frequently show the voracious appetite and weight gain found in patients under treatment with antibiotics The mental effects of isoniazid [7] are now well known, and insomnia and enhanced psychomotor activity has been observed in some patients on long-term treatment with streptomyces derived antibiotics [8] It was in fact this complication of sustained antibiotic administration that led to routine administration of meprobamate in a series of patients with inoperable neoplastic disease to whom antibiotics were being administered [9], and this therapy has commonly modified the humoral effect of the antibiotic,[3] sometimes in the direction of enhancement

In acute experiments on unanæsthetised dogs, reserpine has been shown to augment hydrocortisone output of the adrenals [10], this effect is more intense and rapid on chlorpromazine administration (D M Hume personal communication) While the investigators who report this stipulate that no conclusions can necessarily be drawn regarding similar effects from clinical administration, we believe these to be forthcoming

Laurelton Long Island
New York U S A.

ROBERT D BARNARD
ELIZABETH H BARNARD

MENOPAUSAL PANNICULOSIS

SIR,—Referring to your valuable annotation (April 21) on menopausal panniculosis, which as Dr Baker says is a much better name than panniculitis, the practical problem has always been to decide on the most suitable diet whether in fact the increased weight is partly due to water retention, or is entirely fatty The problem can be solved by recording the weight for several days, then making the patient drink an appropriate amount of an exchange resin A drop in weight indicates whether water retention is a factor and to what extent The exchange resins are, however, very unpleasant to take in water, and I am not satisfied that eating biscuits made of the stuff, though helpful in treatment, would give a clear cut indication of the trouble

Recently I have used acetazolamide ('Diamox'), giving 250–500 mg (according to the weight) to thirty patients, all with possible water retention As with the exchange resin, the weight is recorded daily for several days, on one of which the drug is taken first thing in the morning Patients with severe water retention will have lost as much as 4 lb by the next day, though 2–3 lb is the most usual On the other hand, no drop in weight denotes that retention of water in the tissues does not play a part in the panniculosis syndrome and the low-sodium diet usually prescribed is needless

Of the thirty cases, seventeen were positive to the test and were put on the Foldes [1] diet with acetazolamide 250 mg once a week

My thanks are due to Messrs Lederle for a supply of 'Diamox' tablets

London W 1

H WARREN CROWE

TRANSPORTING PATIENTS WITH BULBAR OR RESPIRATORY PARALYSIS

SIR,—Dr Scott and Dr Knox (April 21) perform a valuable service in emphasising that patients with paralysis of swallowing or of respiration, or both, should be under medical supervision when they are transported to the hospital where they are to be treated They suggest, however, that patients with established paralysis of swallowing and slight respiratory involvement should have a tracheotomy before they are moved In our experience such patients can be moved easily and safely if a cuffed endotracheal tube is first passed under local anæsthesia The tracheotomy can then be done under good conditions on arrival at the final hospital, and the difficulties and danger of an emergency tracheotomy in a small hospital or in the patient's home are avoided

Department of Neurology and
Nuffield Department of Anæsthetics,
Radcliffe Infirmary
Oxford

J M K SPALDING
A CRAMPTON SMITH

Parliament

Unemployed Doctors

ON April 24 Dr DONALD JOHNSON reminded the House of Commons that 35 doctors are drawing unemployment benefit This figure he believed represented a much larger number who, for obvious professional reasons, were not attending the employment exchange, but were hanging about, either unemployed or under-employed, hoping for something to turn up It represented, too, a still larger number of doctors working as assistants in jobs without prospects It was not correct to say that these unemployed doctors were down-and-out and good-for-nothing Young men were qualifying and older men were returning from overseas, and they were unable to find places in the National Health Service It might be that more doctors were qualifying at present than were needed, but he suggested that the difficulty was really due to the falling-in of practices In the old days in every purchase and sale there was an agreement for goodwill to be handed on, and there was an incentive for the vendor, or the widow of a deceased doctor, to keep the practice together Now there was no incentive to do so A vendor gave notice and left, and the widow of a doctor who died suddenly had no particular interest in the practice and might create difficulties by holding on to the house It was left to executive councils to select a successor It was equally difficult for a doctor to establish himself in an under-doctored area He still needed money for a house, and with uncertain prospects he was not a good risk for anyone to advance money on mortgage In view of the ever-expanding need for medical attention in the country something should be done to make the fullest possible use of the medical man-power available

Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, felt that Dr Johnson had painted too gloomy a picture Medicine was an entirely independent profession and the Minister of Health was not responsible for ensuring that every doctor was employed. The profession would certainly fight to retain the liberty of choice as to the type of practice doctors might enter or the places where they should practise In the general-practitioner service most doctors were appointed by other doctors in partnerships A few

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These figures indicate that the prognosis in women aged more than 60 at onset was worse than in younger women 97 3% of the patients were still alive after 6 months from the onset of symptoms, 87 8% after 1 year, 62 2% after 2 years, 46 0% after 3 years, 34 0% after 4 years, 26 4% after 5 years, 5 6% after 10 years, and 2 8% after 15 years

Improvement was observed in 31 patients (29%) 1 aged less than 40, 19 aged 41–60, and 11 aged 61 or more In 13 of the 14 women treated with œstrogen the first symptom had started after the menopause Œstrogen therapy was started 4–27 years (mean 15 years) after the onset of the menopause 7 of these patients had not undergone operation, because the cancer was too advanced when they were first seen The average age of the 14 women was 63, and their average survival was 32 months a woman on 0 3 mg q i d survived 59 months with quiescent bone metastases, another on 0 3 mg q i d survived 29½ months with temporary regression of soft tissue metastases, a woman on 5 0 mg q i d or more survived 17 months with quiescent bone metastases, and 11 women on 5 0 mg q i d or more survived 31 7 months (mean) with good regression of soft-tissue metastases

Only 17 patients (30%) of those treated with androgens showed some improvement, their average age was 49 and average survival 17 25 months Of these 17 women 14 (82%) had their first symptom before the menopause (1 underwent hysterectomy 11 years before the first symptom), and 4 had had neither surgery nor radiotherapy The results of treatment were as follows

	No of patients
Skin deposits regressed	7
Lymph nodes regressed	6
Bone healing and recalcification	4
Abdominal secondaries regressed	2
Lung metastases regressed	2
Loss of pain and subjective improvement but no change in secondaries	3

The different types of metastases responded as follows

Type	*No of patients*	*No improved*	*With œstrogen*	*With androgen*
Skin	74	17	10	7
Lymph glands	79	13	7	6
Bone	55	4		4
Lungs and pleura	35	3	1	2

Of the 55 patients with bone metastases 35 were treated with androgens, and of 31 complaining of severe pain 11 were relieved, including the 4 showing improvement radiographically 6 patients had pathological fractures (4 during treatment) in which there had been no clinical improvement In one the fractures were present on starting androgen treatment and subsequently healed in another a fracture occurred during the early phase of treatment but later healed, together with radiographic improvement in the other bone metastases After œstrogen treatment none of the remaining 20 patients who had bone metastases showed clinical or radiographic improvement, and pathological fractures occurred in 4 during the course of therapy

In addition, less objective evidence of improvement was obtained by assessing the effect of treatment on the following

(1) Pain or distress, which occurred in 80 patients, 20 of whom obtained relief

(2) Serial hæmoglobin levels Before the start of treatment anæmia was found in 49 patients, 24 of whom had radiographically proved bone metastases There was virtually no improvement with treatment

(3) The E S R was raised initially in 68 patients and fell during treatment in 17

(4) The body weight increased in 23 (13 given androgen, 10 given œstrogen), decreased in 53, and did not change in 30

(5) Blood alkaline phosphatase no definite correlation was found between clinical improvement or extension or regression of bone metastases judged by radiographic appearances In one or two cases with bone secondaries which improved with testosterone where the initial pre treatment levels were high, subsequent values were much reduced On the other hand, some cases treated with œstrogen showed similar changes in phosphatase with progressive deterioration in osseous metastases

Discussion

A therapeutic trial of this kind can only help to assess the effect of alteration of the steroid hormone balance of the host and makes no allowance for the specific malignancy of the cancer Unfortunately the complete Broders's grading of each case was unknown In a few cases no details of the histology were available and many years had elapsed since the original operation

In the preliminary trials it soon became apparent that only the old postmenopausal women with soft tissue metastases might benefit

The survival of any one patient with breast cancer of this advanced stage of severity must obviously depend on numerous factors—the patient's age, the distribution and type of metastases, the grade of malignancy, the hormone dependence (whether of œstrogens or possibly of pituitary hormone), and other general health factors

Spontaneous regression has been reported by Gordon Taylor, but malignancy may lie dormant for years In the present series, however, the 106 patients had very advanced stage IV metastases Even so, some patients were in reasonable general condition, whereas others were almost moribund No cases were selected except that those with clinical evidence of considerable liver metastases were excluded

Comparison is necessary with the survival of patients with untreated advanced mammary cancer

Wade (1946) reported 27 untreated patients with breast cancer of whom 24 were in stage III The average duration of life was 8 months from first being seen, and all were dead in 2 years

Greenwood (1926) found a mean survival of 38 3 months from the onset of symptoms in 651 cases, Wyard (1925) found the mean duration of life to be 37 months in 311 cases, and Daland (1927) quotes 40 5 months in 100 cases Wade has collected these numbers together and found that the average duration of life in untreated cases was 38 55 months in 777 patients, and that the duration of life increased from the age group 25–34 to that of 65–74 and then decreased again

According to Wade (1946) X irradiation alone or together with surgery raised the survival time by 21 5% at one year, 22 5% at 2 years, 10% at 3 years, 10 5% at 4 years, and 9 5% at 5 years over the survival rates of untreated cases In her series the mean survival of 27 patients with advanced stage III untreated cancer when first seen was only 8 months, hence 12 months' survival in the present series of advanced stage IV cancer after treatment with hormones is possibly significant All her patients had died in 2 years, whereas 11 6% of the present series were alive at 2 years and 4 7% at 4 years

As regards surgical treatment alone, Lewison et al (1953) claim a 5-year survival rate of 43 2%, regardless of the type of operation These were presumably selected cases, inoperable stage IV cancer being almost certainly excluded

In the present series most of the patients had received standard surgical and X ray treatment in addition to hormones, and the mean duration of life was 58 5 months from the first symptom There was a 5 year survival rate of 26 4% from onset Although superficially this compares unfavourably, it must be remembered that my series consists solely of stage IV advanced cancer

The age at onset seems to influence duration of life In patients who developed cancer of the breast when over 60 the percentage expected survival in 5 years was 20% less than in patients aged less than 40, and 30% less than in patients aged 41–60 A similar prognosis was reported by Burdick and Chamatry (1954)

In the present series of advanced stage IV cancer the percentage expectancy of life in 5 years was significantly greater after hormone treatment in the patients aged

Obituary

ALAN SEYMOUR PHILPS

F R C S

Mr Seymour Philps, surgeon in charge of the eye department of St Bartholomew's Hospital, died at his home in London on April 26, at the age of 50

He was the son of John Philps, a former editor of the *Financial Times*, and he was educated at Aldenham School and St Bartholomew's Hospital After qualifying in 1929 he became house-surgeon at Barts to the late George Gask He took the F R C S in 1931 For a time he worked on the staff of London Passenger Transport Board, but he was already interested in ophthalmology and after holding house-appointments at the Royal Westminster Eye Hospital he became in 1932 out-patient officer at Moorfields Later he returned to Barts as registrar in the eye department and he also joined the staffs of the Victoria Hospital for Children, the Miller General Hospital, and the Royal Westminster Eye Hospital In 1934 he became chief assistant in the eye department at Barts and in 1940 a full surgeon at Moorfields

[Lafayette

During the late war he was an adviser in ophthalmology to the War Office and as an ophthalmic specialist in the R A M C he took part in the Normandy landings "My chief impression of that time (he later wrote in our peripatetic columns[1]) is feeling 'This is none of I,' as one did things no middle-aged oculist ought to do, such as wade through the French surf at dawn in charge of a section of 12 men"

In a D+3 battle dress, in which stains of blood, oil, and flavine fought for the upper hand, he paid a flying visit to liberated Paris before setting off to convoy 20 trucks across France to Belgium "This ignorant oculist (he relates), more used to removing fragments from the cornea than convoying three ton trucks, had imagined that anything as big as a lorry would be difficult to lose, but the trouble was to find any of them We made bad time, and still had 100 miles to go on the last day, but when we started at dawn someone had chalked on the front truck, BRUSSELS OR BUST, and that was how we all felt"

Back in the quieter atmosphere of Harley Street and Charterhouse Square, he settled down to the more orthodox aspects of ophthalmology, and in 1948 he was appointed surgeon in charge of the eye department at Barts In 1949 he also renewed an early interest when he became adviser in ophthalmology to the Ministry of Transport In 1950 he published his *Ophthalmic Operations*, beautifully illustrated with his own drawings and photographs

G B writes "Ophthalmology's attraction for Philps was a logical result of his personality He was fascinated by the delicate, the intricate, and the precise He was a first-rate cabinet-maker, and a magnificent draughtsman of tiny and delicate subjects The accuracy and beauty of his water-colour drawings of the fundus of the eye were only equalled by the precision and neatness of his surgery on that organ A brilliant operator and careful clinician, he was also a clear and good teacher, and his organising powers equalled his other talents

"As a medical student he was called 'Streak,' and this name stuck to him He was always thin in build, but in the nickname there was also an appropriate connotation of speed and lightning brilliance of mind, speech, and body His death at the age of 50 is cruelly premature He had potentially so rich a store of personal and professional qualities as yet unexpended His reputation was already international, and friends in Australia, the United States, and the European countries will lament the passing of a sparkling friend and a fine colleague His book on *Ophthalmic Operations* stands as a record of his achievement, but the memory of his personality, so richly endowed with flashing humour and with great gifts of sympathy and kindness will live in the hearts of his friends when operative techniques have been modified or superseded

"Not the least is Philps's memory linked with the virtue of great courage Two years before he died he knew that he suffered from a mortal illness But this caused neither weakening of his purpose, nor the reaction of bravado He remained his poised, sincere, cheerful self until his last hour He leaves a wife, to whom he owed much, and five children"

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[1] *Lancet* 1944 ii, 514

Medicine and the Law

Procedure of the Medical Disciplinary Committee

Dr Ong Bak Hin, of Malaya, appealed to Her Majesty in Council from a determination of the Medical Disciplinary Committee on Nov 25, 1955[1] The formal charge before the committee alleged that in 1953 he had been convicted in the High Court of Malacca of having unlawfully performed an operation of abortion which caused the death of the patient The committee adjudged the appellant guilty of infamous conduct in a professional respect and directed the registrar to erase his name from the Register

Lord TUCKER, giving the judgment of the Judicial Committee of the Privy Council (Lord Oaksey, Lord Tucker, Lord Cohen, Lord Keith of Avonholm, and Mr L M D de Silva), said that at the inquiry the appellant's solicitor submitted at the outset that justice could not be done to his client unless the witnesses who had given evidence at his trial were called to give oral evidence before the committee The legal assessor pointed out that the committee had no power to compel the attendance of witnesses from Malaya and advised the committee to proceed on the documentary evidence The solicitors on each side drew the attention of the committee to such portions of the evidence as they considered relevant, but it was agreed that the committee should be at liberty to look at any parts they wished It was contended before their Lordships by counsel for the appellant that the proceedings at the inquiry were defective and not strictly in accordance with the rules of procedure which governed the committee and that the determination should be set aside He further submitted that if the notes of evidence were received they should all have been read out before the committee and that failing that the committee should have read the entire evidence themselves which, he said, they could not have done in the time available having regard to the length of the hearing

His Lordship then referred to relevant sections of the Medical Acts of 1858 and 1950 and to the Medical Disciplinary Committee (Procedure) Rules, 1951, made under the latter Act, and to rule 63 thereof which provided

> 'The Committee may receive any such oral or other evidence as would be receivable in a Court of law, and in addition may after consultation with the Assessor to the Committee, treat any statement of fact contained in any document as evidence of that fact"

The position of the General Medical Council in relation to its disciplinary powers under the Medical Act of 1858 was considered by the House of Lords in General Medical Council *v* Spackman ([1943] A C 627) The

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[1] See *Lancet* 1955 ii 1187

SERUM-CHOLINESTERASE LEVELS IN DIABETES MELLITUS

R H S THOMPSON
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PROFESSOR OF CHEMICAL PATHOLOGY

J R TROUNCE
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In 1937 Antopol et al briefly reported that the plasma cholinesterase level was raised in diabetes mellitus—an observation which was confirmed by Faber (1943) and by Cristol et al (1946) Each of these reports, however, described only a small series of diabetic patients, and no details were given of the age of the patients, or the type or severity of the diabetes

Saviano et al (1948) reported raised plasma cholinesterase levels in dogs with alloxan diabetes Berry et al (1954), however, found a strong correlation between the amount of surface fat and the plasma cholinesterase level in a group of 345 men from three districts in England, and suggested that the high cholinesterase values found in diabetes mellitus might be related, not to the diabetic state per se, but to the obesity which often accompanies it

We therefore determined the serum cholinesterase levels in a series of diabetic patients and recorded whether these patients were "obese" or "non obese" The severity of the diabetes and the adequacy of the control by insulin were assessed Serum-cholinesterase levels were also determined in a series of obese non diabetic patients attending hospital for other reasons

Method

Blood was drawn from the antecubital veins of 50 adult patients with diabetes mellitus (25 of them obese and 25 non-obese), 25 adult obese non diabetic patients, and 33 non-obese healthy adults

In most cases, blood was taken in the afternoon , a study of 2 healthy subjects showed that there was no significant difference between the fasting serum cholinesterase level and the levels at one, two, three, and four hours after a meal containing 60 g of fat

The diabetics were all outpatients under treatment, and the diagnosis had been confirmed by blood sugar estimations The degree of control of the diabetes was assessed by the amount of glycosuria, determined by daily urine-testing (' Clinitest ') and interpreted as follows

Degree of control	*Results of urine tests*
Good	Never more than blue or green throughout the twenty four hours
Fair	Usually green, occasionally tan colour
Bad	Frequently tan colour

The severity of the diabetes was assessed by the dose of insulin required to establish control, but we realised that this was only a very limited method of assessment

The presence of obesity was established on clinical grounds, bearing in mind the patient's height, weight, build, and amount of subcutaneous fat

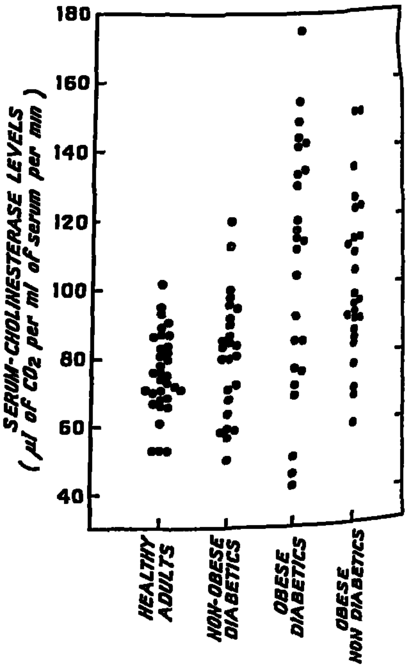
As it was not our aim to discover a precise correlation between plasma cholinesterase levels and small variations in the degree of obesity, we decided that this classification was adequate for the purpose of the investigation, and we did not attempt a more accurate assessment of the amount of subcutaneous fat, such as measuring the thickness of the subcutaneous tissue fold (Edwards 1950)

All but 4 of the obese non diabetic patients were attending hospital on account of their obesity In the remaining 4, the obesity was coincidental

Estimation of Cholinesterase

Cholinesterase activity was estimated manometrically on a sample of the separated serum by a modification of the method of Ammon (1933)

The free acid released from the choline ester by the action of the cholinesterase liberates carbon dioxide from the 0 025 *M* sodium bicarbonate medium, acetylcholine perchlorate (0 015 *M*) was used as substrate Measurements were done in duplicate and were corrected for non enzymic hydrolysis of the substrate These enzyme measurements were made by one of us (R H S T), who at the time was unaware of the patient's clinical state, but in every case serum either from a healthy person or from a non obese diabetic, and serum from an obese diabetic or an obese non diabetic patient, were assayed simultaneously Cholinesterase activity was expressed as µl of carbon dioxide per ml of serum per minute



Serum cholinesterase levels in four groups of adults

Results

The serum cholinesterase levels found in these 4 groups of subjects are shown in the accompanying figure, and the mean values and the standard errors of the mean are listed in the accompanying table The levels in the healthy adults varied from 53 to 102 µl of carbon dioxide per ml of serum per minute Of the 25 obese

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Notes and News

RESEARCH ON RHEUMATISM

On Tuesday, with the Duke of Gloucester presiding, the Empire Rheumatism Council received its 19th annual report from Dr W S C Copeman, who in 1953 succeeded Lord Horder as chairman

Describing the council as "pre eminently a research organisation although it in no wise neglects the subjects of teaching and treatment," Dr Copeman said that its laboratory, at the Hospital of St John and St Elizabeth, is being used by Miss H Muir, D PHIL, an E R C fellow working mainly on connective tissue polysaccharides at St Mary's Hospital Another E R C fellow, of long standing, is Mr J K Norymberski, D ING, director of medical research in the Sheffield centre, who is further investigating steroid hormones, and a third, Dr Madeline Keech, appointed last October, is studying denaturation of collagen and elastin with a view to analysing changes in connective tissue associated with disease A fund provided by the Geigy Pharmaceutical Company has enabled the council to send Dr Malcolm Thompson, Dr J Sharp, and Dr J Ball to work in the U S A, and a further Geigy travelling fellowship, for the same purpose, has been given to Dr E J Holborow The council is supporting steroid research by Dr J D Robertson and Dr L Chapman at the West London Hospital, a study of rheumatoid arthritis in two contrasting communities by Dr E Wittkower at McGill University, and investigations at Taplow by Mr H M Bassiouni, PH D, on the estimation of heparin like substances in blood tissues and by Dr S C Milazzo on antigenic substances in reticulin fibres and basement membranes A number of grants for apparatus have also been made

Turning to future plans, Dr Copeman spoke of a unit which is to undertake field research into rheumatic diseases Though probably based at first on Manchester University, it may eventually make investigations anywhere, including possibly the Dominions Dr J S Lawrence, the newly appointed medical director, will shortly be visiting other centres here and abroad where field studies of rheumatic diseases are in progress, and in due course a clinical, statistical, and radiological team will be assembled Dr E R Hargreaves, deputy M O H for Cornwall, has offered to do some additional preliminary survey work in that county, and Dr G R Fearnley's scheme for a parallel survey in Gloucestershire will be included Another survey conformative with the general one is to be made in Wensleydale by Prof C L Oakley, of Leeds

The Rheumatoid Arthritis Handbook prepared by the council for doctors to issue to their patients, has been "an unqualified success," nearly 20,000 copies having been distributed free of charge An Osteo arthritis Handbook is now in preparation

Supplements to this report are Dr Copeman's account of his official tour in Australia and New Zealand last autumn, and a description of the University of Manchester's rheumatism research centre directed by Prof J H Kellgren, whose chair was established by the council Also attached is a report from the finance committee expressing thanks but pointing earnestly to the need for new supporters The council's address is Tavistock House North, Tavistock Square, London, W C 1

B.M S A SYMPOSIUM ON MEDICAL EDUCATION

The British Medical Students' Association has been asked by the General Medical Council for its views on the medical curriculum An educational subcommittee is now investigating the 1st M B course and a report is being prepared To stimulate greater interest in the subject among students and to further the exchange of views between schools and between teachers and students, the London region of the association held, on April 21 at the London Hospital Medical College, a symposium on medical education Dr H B May, dean of the London, welcomed the participants, and the chairman, Dr R D Lawrence, of King's, opened the symposium The first speaker, Dr John Ellis, described medical education up to 1935 and the developments since that date Later, students from several London hospitals read papers on various aspects of present day medical teaching They all criticised the demands of examiners but most showed that their schools were doing the best that could be done for them under the present system

Dr G O Barber pleaded for the integration of the profession and asked that students, particularly the future consultants, should learn in their student days the importance of the general practitioner in the care of the community Prof Clifford Wilson emphasised that medical education should be a training in method not the acquisition of almost every available fact He outlined a medical course which seemed much better suited to fulfil this purpose

In a session on the teaching of specific subjects, Prof Ruth Bowden showed how, when teaching anatomy, she tried to persuade her students to study the body as a functioning whole, not as dissectable parts Prof G Payling Wright illustrated how the important diseases of one decade may not be the important ones of the next He thought that a full understanding of pathological processes was more useful than a vast knowledge of present histological appearances

In his closing remarks, Dr Lawrence drew attention to the problem continually facing medical students—what *can* they say and what *are* they to say when asked for information by patients? What had impressed him most during the symposium was the amount of thought which student speakers had given to their education and the way in which they had presented their views

BRITISH ASSOCIATION OF PHYSICAL MEDICINE

At this society's annual meeting, held in London on April 27 and 28, the following officers were elected president, Dr Philippe Bauwens, *vice president*, Dr Hugh Burt, hon secretary, Dr G O Storey, hon treasurer, Dr Donald Wilson, hon editor, Dr A C Boyle

At the annual dinner, on April 27, the toast of The Association was proposed by Dr W S Tegner, who remarked that this was the first meeting since the death of Lord Horder, the first president He forecast that the association would continue to flourish, citing as evidence the quality of the papers presented at the meeting Sir Harold Boldero replied for The Guests to a toast by Dr W A Fell, who likened the proposer of such a toast to a guide taking visitors round a zoo But his later remarks made it clear that those present had human interests

BRITISH STANDARD FOR SPECTACLE LENSES

A new standard for spectacle lenses (B S 2738) emphasises that "the criterion of success in a pair of spectacles is the comfort of the wearer" and points out that accuracy of lens preparation is essential to this end

> This standard includes requirements for definition of lens power tolerances on power of lenses cylinder axes centration of uncut lenses, optical centration of finished lenses, base apex direction, and powers of plano prisms, and the transmission characteristics of tinted lenses The standard calls for the glass or plastics used in lenses to be essentially free of such defects as bubbles, veins and other irregularities, and for lens surfaces to be well polished and free from waves, chips, and scratches Also specified are essential features relating to glazing and, for round spectacles, the marking of right and left lenses

Copies of this standard (price 3s) can be obtained from the British Standards Institution, Sales Branch, 2, Park Street, London, W 1

University of London

Dr A S Prophet, lecturer in dental surgery in the Queen's University, Belfast, has been appointed to the chair of dental surgery at University College Hospital Medical School

University of Bristol

On July 3 the hon degree of D SC will be conferred on Prof J Z Young, F R S, and the hon degree of M D on Dr J H Sheldon

University of Glasgow

On April 28 the following degrees were conferred

M D—M T D Braide J M White (with commendation)
Ph.D—S C Frazer

Royal College of Surgeons of England

On April 23 Sir Winston Churchill visited the college and signed the roll on his formal admission as an honorary fellow

Royal Society

At the invitation of the Academy of Sciences of the U S S.R this society is sending a delegation to Moscow, under the auspices of the *Soviet Relations Committee* of the British Council, to visit scientific institutions Lord Adrian, O.M, the immediate past president of the society will lead the delegation, and the other medical member is Prof J H Gaddum

to Dr C L Joiner for clinical help, and to Mr P G Hunt and Mr D E Jarvis for their skilled technical assistance

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PERIARTERITIS NODOSA

ITS RELATIONSHIP TO ENDOMYOCARDIAL SCLEROSIS

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IN periarteritis nodosa the heart is often involved, being second only to the kidney as the commonest organ affected Thus, Arkin (1930) states that it is affected in 70% of cases, and Harris et al (1939), from an analysis of the post mortem findings in 87 cases of periarteritis nodosa, give a figure of 84% In the varied clinical picture there are often symptoms and signs of cardiac disorder (tachycardia, dyspnœa, and œdema) and not uncommonly the end of the disease is congestive failure

Recently, cases presenting clinically as congestive cardiac failure of obscure origin have been described in which the principal finding at necropsy is a sclerosis of the endocardium and subjacent myocardium Several large series have been reported from Africa (Bedford and Konstam 1946, Ball et al 1954) Indeed, Davies and Ball (1955) state that endomyocardial fibrosis in their experience is the second commonest cause of heart failure in adult Africans The condition outside Africa is rare and, in the main, only isolated case reports have appeared A similar, though probably distinct, morphological picture is also seen in infancy First described as fœtal endocarditis, it is now most generally known as fibroelastosis of the endocardium (Weinberg and Himmelfarb 1943)

The interest of the following case lies in the occurrence of periarteritis nodosa in a boy aged 12 in whom endomyocardial sclerosis was a cardinal post mortem feature

Case-report

A boy aged 12 had mid abdominal pain on the evening of July 3 1955 He was seen by his general practitioner who prescribed a mild laxative On the following morning, his parents were shocked to find him dead

He was the fifth of ten children, and weighed 9^1 . lb at birth During the pregnancy, there had been no maternal illnesses and in particular no history of rubella, influenza or bronchitis At 1 year he was inoculated against diphtheria and re inoculated at the age of 9 but received no vaccination against smallpox During the first two years of life he h several attacks of bronchitis At 3 years he had pneumo and was treated in hospital with sulphonamides At 4 to years he had measles, whooping cough, and mumps, and one occasion was treated for threadworm infestation H development was normal until the age of 3, thereafter grow was retarded and at 12 years he was the same height as h 6 year old twin sisters—i e, 3 ft $9^1/_2$ in (average height 12 years is approximately 5 feet) He had a bright ale mentality, and led a normal active life, with full participati in games at school and never had any symptoms or signs *heart disease There was no history of rheumatic fev* asthma, or skin disease

On March 18, 1955, he was admitted to hospital becau he had had pain in the region of the left loin for 24 hou This was accompanied by dysuria He was toxic, the tong was heavily coated, and the temperature was 100 F Oth wise physical examination was negative In particular th was no swelling or tenderness in the left loin, and the kidne were not palpable Intravenous pyelography and cystograp showed no abnormality apart from bifid pelves A ch radiograph showed no evidence of any focal lung lesion b there was a doubtful increase in the transverse diameter of t heart The urine was normal A presumptive diagnosis of left perinephric abscess was made and he was treated wi penicillin 250,000 units and streptomycin 250 mg, both s hourly Progress was satisfactory, and he was discharg from hospital on April 12, 1955 Subsequently he led a norm life without further symptoms until his sudden death in Jul

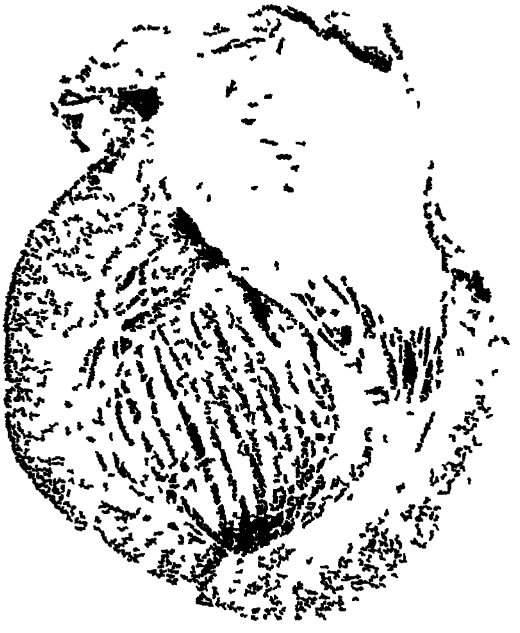

Fig 1—Left ventricle showing endomyocardial sclerosis (× 0 8)

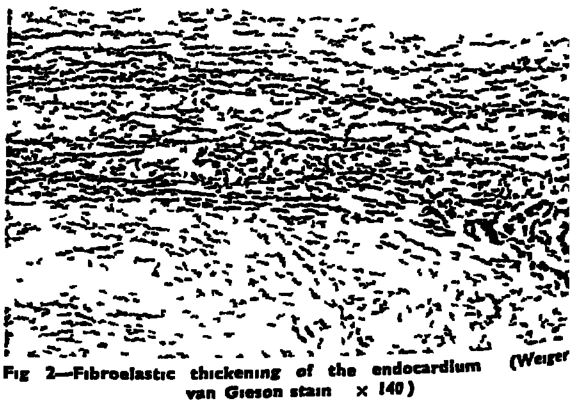

Fig 2—Fibroelastic thickening of the endocardium (Weiger van Gieson stain × 140)

MAN'S CHOICE OF FOOD *

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ANIMALS in their normal surroundings choose nutritionally adequate diets. Man too, in a wide variety of environments, often seems to do the same. We are usually content to assume that this demonstrates the existence of a food instinct. We can all think of apparent examples of this: the cattle that seek out salt licks containing mineral elements which their bodies need; the pregnant woman who demands fruit presumably because she would otherwise go short of vitamin C; the small child who eats plaster from the wall because he needs calcium. But when we look a little closer, we find that our interpretation of these events is very much coloured by our own emotions, by our tendency to evoke esoteric and mysterious reasons for matters which are not yet clearly understood. The pregnant woman may well demand not oranges but peaches out of season; the child may choose to eat boot-polish rather than the plaster, but it is not really likely that he now has a physiological demand for turpentine and wax rather than for calcium.

Looking still closer at the problem of food choice, we soon discover that it is determined by a great number of factors. Moreover, many of these are interrelated, so it is quite unrealistic to discuss in isolation the rôle of instinct in food selection.

We had better begin by realising that choice can be at quite different levels. At one level the choice may be between meat or vegetables, at another level between a cereal and a pulse or between meat and fish; at a third level between beef and mutton, or between rice and wheat; at a fourth level between Cheddar cheese and Cheshire cheese or between white bread and brown, or between fresh peas and canned. When we speak, therefore, of man's choice of food, we must make clear whether we are talking of a choice between, say, a meat diet and a vegetarian diet, or of a choice between ice cream made by one firm and that made by another.

The factors which determine choice may roughly be classified into three groups: physical, social, and physiological:

Factors of availability.—Geography. Season. Economics. Other factors: food technology, fuel.

Social factors.—Religion and social custom. Social class. Education in nutrition and hygiene. Advertising. Other social factors.

Physiological factors.—Heredity. Allergy. Therapeutic diets. Acceptability. Nutritional need.

Physical Factors

Geography

There is an understandable tendency to eat foods which are at hand. Geography has largely determined the very different diets of the Western European, of the Eskimo, and of the Chinese peasant. Even relatively small distances may make great differences to the diets consumed. In different parts of Nigeria, the staple food is either millet or cassava or rice. Nearer home, the Scots eat much more cakes, pastries, and biscuits, and much less fruit, green vegetables, and bacon, than the English (Domestic Food Consumption and Expenditure, 1953 [1955]).

The influence of geography has been greatly modified by the great improvements of transport during the last hundred to two hundred years. Before the 19th century there were great differences in diet even within England: in the south it consisted mostly of bread and cheese, with a little meat and bacon; in the north it was mostly oatmeal and milk. Only the large ports like London had access to the small amounts of imported foods.

This country in particular owes a great deal to modern communications for overcoming the dietary restriction imposed by geographical availability. Half of our food comes from overseas, both to supplement what we already grow (wheat, apples, cauliflower, potatoes, meat) and to give us foods we do not ourselves grow (vegetable fats, citrus fruits, tea, coffee, rice). Our choice of diet would indeed be restricted without modern means of transport.

Season

In many countries some foods are available only at certain seasons. Up to two or three centuries ago, this was also true to a large extent in this country. The winter diet of Britain was chiefly bread and salt pork; milk, cheese, and eggs were not easily available since it was not known how to maintain livestock adequately through the winter. It is often still true that the fruits of the earth are available only in their season. But in the industrially advanced countries the situation has now changed appreciably because of the improvement both in transport and in the methods of food preservation—canning, freezing, drying.

Economics

The rôle of economic factors is evident from study of the diets of different countries, or within one country from study of the diets of people of different degrees of wealth. Foods containing chiefly carbohydrate are on the whole cheaper than those containing chiefly protein or fat, and foods nutritionally less desirable cheaper than those nutritionally more desirable. With an increase in national income the intake of protein and fat increases, whilst that of carbohydrate stays fairly constant (table I).

TABLE I—RELATION BETWEEN NATIONAL INCOME AND DIET

Average annual income ($)	No. of countries	Average daily intake					
		Calories	Protein (g.)	Animal protein (g.)	Fat (g.)	Carbohydrate (g.)	Sugar (g.)
Less than 100	4	1860	48	11	34	345	42
100–200	9	2310	68	16	43	412	44
200–300	3	2590	77	27	68	416	63
300–400	4	2740	81	45	93	396	90
400–600	5	3070	92	46	112	424	84
Over 600	8	3210	95	58	129	416	122

Data compiled from Food Balance Sheets (Food and Agriculture Organisation, Rome, 1955) and from *Statistics of National Income and Expenditure* (Statistical Office, United Nations, New York, 1955).

There is also incidentally an increase in the consumption of sugar, implying a decrease in the consumption of other carbohydrate-rich foods like cereals and tubers—a fact to which I shall refer later. In any one country there is a similar dependence of the composition of the diet on income. In Britain these differences still exist, showing themselves chiefly as a decreased consumption of the more expensive and more nutritious foods with an increase in the size of family (table II). The amount of money available for food may be affected by a variety of factors. M'Gonigle and Kirby (1936) showed that the transference of people from slums to new houses, with higher rents, reduced the nutritive value of the diets. Tobacco and drinks may also be a prior call on income before food is bought. And in Peru and Bolivia the chewing of coca leaves by the chronically undernourished Indian, primarily to relieve hunger, leads to an even greater degree of malnutrition since the purchase of coca leaves reduces still further the amount of money left for food (Verzár 1955).

Under the heading of economic factors affecting food choice I include impositions by the State, such as first is the boy's age Most of those who have studied this subject think that congenital fibroelastosis is a disease of infancy and that it is a separate and distinct entity from the condition of adults which presents a similar macroscopic appearance Nevertheless, congenital fibroelastosis has been described in children at 6 and 11 years of age (Dennis et al 1953), and Thomas et al (1954), reporting cases at varying ages up to 70, thought that congenital fibroelastosis may persist into adult life The second discrepancy is the distribution of the endomyocardial sclerosis In particular, in this case the endomyocardium of the interventricular septum below the aortic valve was normal Thirdly, the degree of fibroelastosis of the endocardium was rather less than that is usually seen in the congenital type, and in contrast, the myocardial fibrosis was much more striking in the subendocardial region Therefore, despite the similarity of the morphological appearances, we do not consider this case to be one of congenital fibroelastosis persisting into late childhood

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* Inaugural lecture delivered on appointment to the new chair of nutrition in the University of London.

In endomyocardial fibrosis as described in adult Africans, the lesion is a gross one with the endocardium showing varying grades of thickening of 3 or 4 mm , or even more, in depth, with definite subjacent myocardial fibrosis Of particular interest are those cases in adults outside Africa which have been described by various authors, including Loeffler (1936), Comeau (1937), Becker et al (1953), and Thomas et al (1954) The degree of endomyocardial sclerosis in these cases was variable, but in general it was intermediate between the congenital and African groups The case we describe is in our opinion an early example of endomyocardial sclerosis of this type The age of the patient, and the lack of any symptoms or signs referable to a cardiac disorder would accord with an early lesion

Macroscopically the heart in periarteritis nodosa may show the characteristic picture of aneurysmal dilatations of the coronary arteries, often described as "beading" In the absence of this finding there are no specific naked-eye features either in the myocardium or in the mural endocardium There is commonly some hypertrophy of one or both ventricles, usually the left The appearances on section of the myocardium are usually normal, but varying degrees of myocardial damage from acute necrosis to fibrosis, diffuse or focal in distribution, may be seen We have not found, however, any macroscopic description corresponding to the picture in this boy, where the myocardial damage showed a striking localisation to the subendocardial zone Histologically, in periarteritis nodosa, the only characteristic findings are the typical vascular lesions, and in their absence the picture is a non-specific one, such as is found in "isolated myocarditis" whatever the cause The myocardium shows diffuse or circumscribed lesions mainly of the interstitial tissues but also affecting the muscle-fibres There is no characteristic predominant cell type, lymphocytes, polymorphonuclear leucocytes, and eosinophils being found on occasion All transitions from acute inflammatory cellular exudate and necrosis to scar tissue formation are found even in the same heart This variable appearance is exemplified in the case we record here

From the standpoint of pathogenesis, the case has some bearing upon the problem of endomyocardial fibrosis It is beyond the scope of this article to review the various hypotheses of ætiology in adult endomyocardial fibrosis—malnutrition (Gillanders 1951), vitamin-B deficiency (Smith and Furth 1943), an allergic phenomenon (Loeffler 1936), or a collagenosis (Hill and Reilly 1951, Becker et al 1953)

Loeffler (1936), under the title "endocarditis parietalis fibroplastica with eosinophilia," described a case in which sclerosis of the endocardium with overlying thrombus was the chief pathological finding in a patient who died in congestive cardiac failure Since then several authors have reported single cases (Mumme 1940, Büchler 1941 42, Egger 1944, and others) A possible early case, the first in the British literature, was described by Lennox (1948) What was considered to be the first case in the American literature was recently reported by Hoffman et al (1955) This syndrome of parietal endocarditis with eosinophilia is considered by Loeffler to have an allergic basis Lennox (1948) points out that in favour of this theory his case was one of status asthmaticus, Büchler's case had a severe urticarial skin rash, and Egger's rheumatoid arthritis, and all had an eosinophilia In a case of this syndrome described by Roulet (1944), there were lesions suggestive of an allergic polyarteritis in the splenic arterioles and venules

In current opinion, periarteritis nodosa is probably an allergic or hyperergic response to some infection or toxic agent The occurrence of early endomyocardial sclerosis in association with periarteritis nodosa of the splanchnic vessels is of interest, not only for its rarity, but also for the support it lends to Loeffler's hypothesis

Summary

The association of endomyocardial sclerosis and periarteritis nodosa is reported, and the pathogenic significance briefly discussed in relation to Loeffler's "endocarditis parietalis fibroplastica"

We thank Mr F Beckwith, of the Pathology Department University of Liverpool, for the photographs

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EPIDEMIOLOGY OF HYPEREMESIS GRAVIDARUM

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MANY obstetricians consider that hyperemesis gravidarum was less common and less severe during the years of the 1939–45 war, but this impression has not been confirmed statistically Such a change in incidence and severity might help to confirm the clinical impression that psychological factors are important in the ætiology of this condition, and I therefore studied hyperemesis gravidarum in North east Scotland in the years 1938–53

Material

Between 1938 and 1953 674 patients with vomiting were admitted to the Aberdeen Maternity Hospital as booked cases or emergencies 453 showed the characteristic picture of hyperemesis gravidarum, 91 had late vomiting of pregnancy of unknown origin, and in 130 the vomiting was associated with the conditions listed in table I urinary tract infections being the most common their original non-nutritional classification of good and bad foods, but now attribute these different qualities to the presence or absence of vitamins. They have also decided that there is a hierarchy of vitamins, the best being vitamin A, the next best vitamin B, and so on (Wellin 1953).

Advertising

In this country, something like twenty million pounds a year is spent on advertising foods—more than is spent on any other class of goods. Yet it appears that the result of advertising is far less to make people eat a particular food, than to make them eat brand A rather than brand B of that food. The sales of the different brands of breakfast cereals is in direct proportion to the money spent on advertising them; it is difficult to avoid the conclusion that if firm B were to spend as much as firm A on advertising, their sales would rise until they were equal to that of firm A.

Other Social Factors

Another social determinant is the status of a person or group. Thus, the head of a tribe or of a family may be considered to have a first claim on the more desirable foods. In many cultures this takes the form of the father being given most of the meat or eggs, irrespective of the nutritional needs of the mother or the children.

Finally, the choice of food may sometimes be determined by convenience. Consider a woman in a Western community who lives alone and goes out to work. She may consider it not worth while making herself a cooked breakfast; she may take sandwiches for lunch; for her evening meal it may be too troublesome to cook meat and vegetables, so she opens a tin of beans. Such people, even without undue economic pressure, are often found to be consuming diets which are nutritionally unsound. Scurvy is still most often found in this country in lonely people whose diet is conditioned chiefly by convenience of preparation.

Physiological Factors

Heredity

Experiments with animals have shown that, in conditions in which they show an ability to choose a sound diet, individual animals show this ability in different degrees, and that this ability may be inherited (Dove 1935). Whether man has a similar inheritable ability is quite unknown, but if it exists one might speculate quite interestingly on its effect on man's evolution.

Allergy

A surprisingly large number of people—probably as many as 1 in 20—are allergic to foods, even to such common foods as wheat, eggs, and milk; and allergy to shellfish or strawberries is well known. The identification of the offending food may be easy or difficult, but once identified or even suspected (perhaps wrongly) the pattern of food choice is modified.

Therapeutic Diets

The choice of food is modified by the prescription of a diet for a patient, but the extent of the modification will depend greatly on how closely the patient follows the doctor's instructions. The patient may sometimes be wise in not keeping too rigidly to a prescribed diet; iatrogenic scurvy is not unknown in dyspeptic patients whose diets have been constructed with great rigour but with less nutritional knowledge.

Acceptability

It may or may not be justifiable to call this factor physiological, but I do so because it depends very much upon the individual. I include in it the presentation of food, its palatability, and its possible pharmacological activity. A food of unpleasant appearance, badly served, of the wrong colour, even in an unattractive wrapping when offered for sale, will not be consumed so readily. That is why artificial colours are used in the food industry. That is why you will not get people to eat cakes covered with blue icing as readily as cakes covered with pink icing. That is why the housewife will often add soda to her peas when cooking them, whatever anyone says about it destroying vitamin C.

I need say little about the obvious effects of palatability on food choice. I would, however, point out that, with little or no propaganda, tomatoes and grapefruit have in very recent times become widely accepted foods in this country and that the main factor is undoubtedly their palatability. Similarly, I would refer to the consumption of sugar, which in this country is now some thirty times what it was two hundred years or so ago, and as we have seen depends in different countries on the national wealth. Nutritionally, sugar has the doubtful distinction of being the least desirable food since unlike every other food it contributes nothing whatever except calories to the diet.

Another reason for a food being acceptable is that it has a desirable pharmacological action. It is surely noteworthy that almost every community throughout the world has independently discovered the production of alcohol by fermentation. Similarly, many countries have discovered a plant from which a concoction may be prepared containing the stimulants caffeine or theobromine—tea, mate, coffee, cocoa, and cola.

Nutritional Need

We come finally to the choice of foods for the satisfaction of nutritional need. Whilst exact dietary analyses are rarely available, we may take it that from most varied foods in different parts of the world man often chooses a nutritionally adequate diet, provided he has not been limited by such factors as economic availability. Can we take it then that man and animals have an instinct in food choice which drives them to satisfy their nutritional needs? Let us see what sound evidence exists both for man and for animals, as distinct from unlikely anecdotes.

Some of the best-known experiments in human beings were made by Dr Clara Davis (1928, 1939). Her subjects were infants who were offered at weaning a selection of foods and who ate what foods and in what quantities they chose. Some of them were observed in this way for six years. All of them chose diets which were nutritionally absolutely sound. Now this would appear to prove that infants indeed possess an adequate food instinct. It has also been argued from this that the corollary is also true—that whatever food people do choose to eat must be nutritionally desirable. This is responsible, for example, for the widespread belief that sugar is desirable for children.

Yet there are many examples where man cannot at all be relied upon to make a wise nutritional selection of foods. I have already referred to the Kikuyu, where economic but chiefly social factors determine that they eat a poor diet. Another example is the Indian or Chinese who eats polished rice. How potent is the food instinct which does not teach him to avoid beriberi and imminent death by eating instead unpolished or parboiled rice? Moreover, the experiments of Dr Davis did not tell us what would happen if children were allowed to select from diets which included nutritionally less desirable, or even undesirable, foods instead of only good foods. What would have happened, for example, if sugar and sweet cake and jam had also been offered? Again, the children seemed to have spent some time deciding what foods they preferred; during the first few weeks they tasted most of the foods, but later they settled down to a more restricted diet. This suggests that learning rather than instinct guided their choice—a point to which I shall return.

Having said all this, we cannot overlook the fact that man does frequently and from so many different sources ten hours later Necropsy showed typical lesions in liver and kidneys

Case 2 —In 1942, a primigravida, aged 28, was admitted in a moribund condition after vomiting for 8 weeks She had neuritis, paralysis of the limbs, and pneumonia She died 13 hours later

In the whole of North east Scotland there were 14 maternal deaths due to hyperemesis between 1931 and 1940, 6 of them in residents of Aberdeen and 8 outside the city There has been only 1 such death since (case 2)

The elimination of deaths from hyperemesis is probably the result of improved treatment The records of the fatal cases before the 1939–45 war suggest that many patients with hyperemesis were very toxic when admitted to hospital, and that prolonged, inefficient treatment at home was largely responsible for this (cf the present case 1) Nevertheless, comparison of cases admitted to hospital in 1938–39 with those admitted in 1952–53 showed no difference in distribution by stage of gestation, duration of vomiting before admission, or length of hospital treatment no statistical evidence was found that in 1952–53 patients were sent to hospital sooner by their family doctors, nor did they require shorter treatment in hospital, than in 1938–39 Moreover, that serious forms of the disease still occurred in 1952–53 is shown by the fact that in that year many patients had to have their pregnancies terminated

RELATION OF PARITY TO HYPEREMESIS GRAVIDARUM

Hyperemesis tends to recur in subsequent pregnancies A third to a half of the multigravidæ admitted to hospital with hyperemesis in this series had been treated in hospital for the condition in previous pregnancies Of 106 patients treated for hyperemesis in their second pregnancy, 50 had been treated for this condition in their first Of 82 patients with hyperemesis in their third pregnancy 44 had had it in both, and 11 in 1 of the preceding pregnancies

Of the 159 primigravidæ admitted to hospital, details of subsequent pregnancies are known in 56 cases, of these, 27 were affected in their second pregnancy, and 7 out of 19 had hyperemesis in a third pregnancy

Discussion

It is reasonable to suppose that the relatively low incidence and diminished severity of hyperemesis in Aberdeen and North east Scotland in 1940–48 was experienced in other areas of Britain Robertson (1946) cited Dieckmann as noting that hyperemesis was relatively rare in Germany in the 1914–18 war, and added “ The ætiology of this change in prevalence is complex, but it could be attributed to the different psychosocial environment prevailing in the war years contrasted with the post war years, notably the separation of husband and wife during the years of combat ”

The decrease in the incidence of hyperemesis is most unlikely to be related to food rationing, improvement began abruptly in 1940, before war time food policies had their greatest effect, and after the war the number of cases began to increase before there was any great mitigation of food rationing

Summary

In 1938–39 and in 1949–53 the incidence of hyperemesis gravidarum necessitating admission to hospital was 5–10 per 1000 births in the city of Aberdeen The incidence and the severity of the disease were lower in the war and immediate post war years

Booked hospital patients required less treatment and less time in hospital than patients admitted as emergencies The prognosis for the pregnancy was better in booked cases, and termination of pregnancy was required much less commonly in these than in emergency cases

There were no maternal deaths from hyperemesis gravidarum in North-east Scotland between 1942 and 1953

In many patients, the condition recurred in consecutive pregnancies

I wish to thank Prof Dugald Baird for his advice and criticism

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PRIMARY SKIN CANCER OF THE FINGERS SIMULATING CHRONIC INFECTION

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THE soft tissues of the fingers may be the site o *a large variety of tumours, but* malignant disease i somewhat rare When it arises, the true nature of th lesion is *frequently* missed, and diagnosis often depend on whether the possibility is considered at all (Mason 1937) There are many references in published report to the high proportion of false preoperative diagnose (Mason 1929, 1937, Bickel et al 1943, Clarke 1944) and published series often include cases where continued treatment as for a stubborn finger infection, including removal of pieces of nail and curettage of the nail bed, was applied before the diagnosis became obvious

Primary skin cancer of the fingers is usually a squamou cell carcinoma or a malignant melanoma, and basal cell carcinoma is relatively rare

Clarke (1944) found only 18 basal cell tumours on the hand and fingers in a series of 181 cancers of the extremities

Squamous cell carcinoma of the fingers, like carcinoma elsewhere on the hand, may arise in an area previously irritated chemically, by irradiation, or mechanically, or in a previously benign tumour Often, it takes the form of a mass of exuberant granulations, slowly enlarging and involving the surrounding skin and covered with a seropurulent or sanguinous secretion which rapidly becomes malodorous from necrosis or infection with saprophytic organisms The granulations bleed easily and hæmorrhage may be quite brisk Pain is sometimes severe Squamous carcinoma also manifests itself as an ulcer arising on the dorsum or lateral aspects of the digit or on the web between the fingers It resembles in every way the commoner ulcerated cancer of the dorsum of the hand with its rolled or everted edges and granulations in its floor Both types are not infrequently misdiagnosed as chronic infective lesions of the fingers

Melanoma of the fingers may arise in a *long standing* mole, but the subungual tumour commonly arises from *an apparently normal nail bed*, *Hutchinson* (1886) termed this “ melanotic whitlow,” and drew attention to the frequency with which it is confused with a chronic paronychia About 50% of patients with melanoma of the fingers have a history of injury six months or so before the appearance of the tumour In some the trauma is followed by rapid growth or ulceration of a pre existing mole In the nail bed the first sign is often a blue spot or small mass beneath the nail In contrast to the glomus tumour the discoloration is painless and does not disappear on pressure In its later stages a melanoma may be confused with a subungual hæmatoma, but the pigment in a melanoma extends beyond the nail bed and in time the tumour fungates through the nail, destroying it When the melanoma is unpigmented, it closely resembles due to overstimulation, or from an accumulation of metabolic products in the blood-stream. The animal will now stop eating that food and proceed to the next Possibly the eating of another food relieves this unpleasant feeling, or the animal's hunger may simply not yet be satisfied and it has learned that the eating of another sort of food will stay its hunger yet not increase its discomfort

Whatever the reason the animal will in this way choose a variety of foods from which it will eat its fill We must remember that by so doing it will, even from a fairly restricted choice of foods, obtain a wide variety of nutrients, for almost all foods contain several nutrients Should it by chance avoid some foods and so develop deficiency of one or more nutrients, it might be able to learn to eat them if the deficiency is of a nutrient whose consumption results in rapid improvement

We must add, too that the animal's experiences may not have to be repeated in their entirety by its offspring, especially if it is a human animal He will be able, in varying degrees to direct his progeny to nutritionally sound food selection by education

Whilst this brief discussion may not provide an entirely satisfactory explanation of the complex problem of food selection and food instinct, it will I hope provide a basis for a more complete understanding of the problem than has been possible hitherto However little ultimate value these speculations have, they will at least have done a useful service if they only delimit the area of determinants of food choice within which instinct may play its part. Remember the infant and the boot-polish

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ANTISTREPTOLYSIN RESPONSE IN ACUTE RHEUMATIC FEVER IN CHILDREN

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IMMUNOLOGICAL studies have established beyond reasonable doubt that most patients with acute rheumatic fever show evidence of recent infection with β-hæmolytic streptococci of Lancefield's group A The serological findings, summarised by McCarty (1952), include the repeated observation (Anderson et al 1948, Rantz et al 1948, Harris and Harris 1950) that patients in whom rheumatic fever develops after streptococcal infection show a significantly greater antibody response than do patients with uncomplicated infections This seems to hold not only for antistreptolysin O (A.S O) but also for antibodies to streptococcal hyaluronidase, streptokinase, and possibly other streptococcal antigens

Rantz et al (1951) also studied respiratory infections with group-A hæmolytic streptococci and the associated A S O response in infants and young children They found three patterns of antibody response roughly related to age (1) a feeble response in infants, (2) a vigorous but short-lived response in young children (mean age 36 7 months), and (3) a vigorous and sustained response in older children (mean age 57 9 months) They described evidence that this sequence of antibody-response patterns, although related to increasing age, was more closely related to *repeated* streptococcal infections and they attributed the enhanced response to conditioning of the antibody-forming organs by repeated exposure to streptococcal antigens Rantz et al (1951) have linked this conclusion with the finding, mentioned above that in rheumatic fever antibody response is further enhanced. and have suggested that these observations, together with the known rarity of rheumatic fever in very young children, support the idea that " sensitisation " to streptococci or their products is closely related to the pathogenesis of rheumatic fever If this concept were correct, the incidence of raised A S O titres in children with acute rheumatic fever should be independent of the age of onset We describe here a survey of A S O levels in rheumatic children aged 3–12 years

Material and Methods

We have surveyed all eligible cases of acute rheumatic fever with onset before the 12th birthday admitted to this hospital in the seven-year period from April, 1948 Cases were taken to be eligible only if they fulfilled the diagnostic criteria of Jones (1944) (excluding chorea as a significant feature) and were seen in their first rheumatic attack within four weeks of onset of symptoms The survey was directed particularly at the relation of age to the frequency of raised A S O titres, the geometric mean of the A S O levels the frequency of preceding upper-respiratory-tract infections (within a month of onset), and the frequency with which group-A β-hæmolytic streptococci were recovered from the patients

Throat and nose swabs were taken from each patient on admission and after one week and were plated respectively on horse-blood agar and on the same medium containing gentian-violet (1/500 000) Hæmolytic streptococci recovered were tested for group-A-specific polysaccharide by Lancefield's (1933) method

Venous blood samples were taken on admission and at weekly intervals for serum-A.S O estimations The highest titre found within four weeks of admission was recorded for this survey Antistreptolysin was estimated by a method (Johnson 1955) based on Hodge and Swift's (1933) modification of Todd's test This serological method was standardised with Todd's horse antiserum as a reference and gave consistent results throughout the seven years of the study except for the period October, 1952, to July, 1953 when the standard globulin solution underwent gradual and, at first, unnoticed deterioration When this was discovered a new standard globulin preparation was obtained and cases admitted during this nine month period have been excluded from the survey Were they included, the outcome of the analysis would not be materially affected Excluding this period, the mean A.S O levels did not vary significantly from year to year, either in the group included in this study or in all A S O estimations carried out in the laboratory We have taken the arbitrary value of 200 units or more per ml to indicate significant antibody response to streptococcal infection.

Results

The criteria for selection were fulfilled by 121 cases, of which 14 were excluded because they fell in the unreliable serological period. Of the 107 remaining cases, 55 were in boys and 52 in girls At each age the distribution between the sexes was approximately equal finger persists despite treatment and in the absence of an adequate local or general cause, such as retained dead nail or foreign body, osteitis, or vascular disease, biopsy must be done Any apparent chronic granulomatous lesion with bluish pigmentation must be viewed with suspicion until proved innocent Benign lesions of the nail bed, such as subungual fibroma, subungual exostosis, or glomus tumour, do not break through the nail, nor do they invade the skin The malignant lesions at this site, however, they begin, lift the skin and nail and eventually replace them with fungating tumour (Jaffe 1930)

Biopsy of the tumour is easy under ring block anæsthesia and can be carried out in the outpatient department If it does not at first show the true nature of the tumour, repeated biopsy of the finger or biopsy of glands will establish the diagnosis

Summary

Primary cancer of the fingers is uncommon and squamous cell carcinoma and malignant melanoma are the commonest forms

These neoplasms are often confused with septic lesions of the fingers 5 examples of this confusion of diagnosis are described

Any apparent chronic infection of the fingers which does not respond to treatment should be investigated by biopsy

I should like to thank Prof R S Pilcher for his help and encouragement in preparing this paper, Mrs Gwen Hilton for permission to report case 5, and Mr A Bligh for the photograph

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INFLUENCE OF THE ADRENAL CORTEX ON GASTRIC SECRETION IN MAN

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THE secretions of the anterior lobe of the pituitary gland and the adrenal cortex are known to influence gastric secretion When these glands are atrophied, as in Simmonds's disease (Escamilla and Lisser 1942) and Addison's disease (Rowntree and Snell 1931, Sorkin 1949), gastric secretion is depressed and treatment with cortisone may restore it (Stempien and Dagradi 1954, Kyle 1955) Conversely, the administration of corticotrophin or of cortisone increases the acidity of the gastric juice (Gray et al 1951) and the excretion of uropepsinogen (Gray et al 1954) and may aggravate or even cause peptic (especially duodenal) ulceration (Sandweiss 1954) Hydrocortisone increases the excretion of uropepsinogen, but corticosterone does not (Wolfson and Timmis 1955) In Cushing's syndrome, in which adrenocortical hormones are produced in excess, the gastric secretion might be expected to be increased, but few observations have been reported, the excretion of uropepsinogen may be increased (Gray et al 1952) and gastro-intestinal hæmorrhage may develop (Swan and Stephenson 1955, Knowlton 1953) In the adrenogenital syndrome the gastric juice is said to be normal (Broster 1934)

It is not clear, however, whether the pituitary and adrenal hormones influence gastric secretion in the absence of overt disease of endocrine glands Some patients with peptic ulcer have diminished pituitary and adrenal activity, judged by negative Thorn tests (Turner 1951, Fota 1954), and in some patients with duodenal ulcer the urinary excretion of formaldehydogenic steroids has been decreased during exacerbations and largely restored during remissions The excretion of 17 ketosteroids is normal (Sandweiss et al 1950)

The present investigation was undertaken to measure gastric secretion in patients with Cushing's syndrome before and after treatment by subtotal adrenalectomy, and to discover whether, in these or in other people, there was any correlation between the level of gastric secretion and the urinary excretion of adrenal cortical steroids

Material and Methods

Gastric secretion in Cushing's syndrome was studied in 11 patients, 8 before and 7 after surgical therapy The operation in 6 was subtotal adrenalectomy (removal of $^9/_{10}$ of one gland and all of the other) and in 1 (case 9) subtotal removal of one gland which contained a cortical adenoma A satisfactory remission was obtained in all

The urinary excretion of reducing corticoids was measured in 5 patients with hyperchlorhydria (more than 45 clinical units of free acid in a gruel fractional test meal) but without clinical evidence of endocrine disorder

The excretion of 17 hydroxycorticoids was measured in the 8 patients with Cushing's syndrome and in 8 healthy people with normal gastric secretion, 8 patients with duodenal ulcer, 5 patients with hyperchlorhydria but no peptic ulcer, and 5 patients with achlorhydria without other evidence of disease

Gruel fractional test meals lasting two and a half hours were studied in each person This method of gastric analysis has serious limitations but was the one most readily available Histamine was not given, because we thought it might be harmful to patients with adrenal disease In those with Cushing's syndrome the test was done shortly before adrenalectomy and some months after operation, when cortisone replacement had been

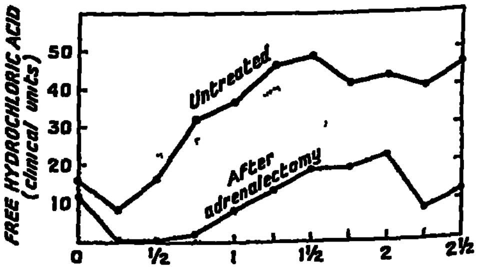

Fig 1—Free hydrochloric acid after fractional test meals in Cushing's syndrome (Figures derived from data in table I Normal range is derived from Bennett and Ryle (1921))

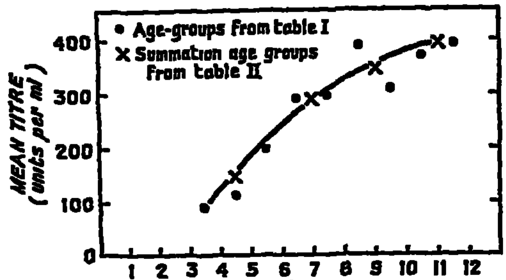

Fig 3—Age and mean A.S O titre.

localised indolent streptococcal infections of infants are gradually replaced (by about the age of 5) by a more acute, and clinically well defined, pharyngitis This altered response, they suggest, is related to sensitisation to streptococci through repeated infections Rantz et al (1951) have shown that such repeated streptococcal infections in young children lead to a striking enhancement of the antibody response their findings therefore support the idea that sensitisation (i e, increased antibody response) to streptococci tends to develop in childhood It is known that repeated infections with group-A hæmolytic streptococci commonly precede attacks and recurrences of rheumatic fever and this, together with the well established increase in antibody response which most rheumatic subjects show, has supported the concept that rheumatic fever itself is a phenomenon of sensitisation The results reported here suggest, on the contrary, that in young children with acute rheumatism this state of sensitisation is not uncommonly poorly developed and should therefore probably be regarded as dissociated from the mechanism by which streptococci induce rheumatic fever

Summary

107 children with acute rheumatic fever, aged 3–12 years, showed no age differences in the frequency of preceding upper respiratory-tract infection or of positive throat or nose swabs for group A β hæmolytic streptococci

20 children included in this study were under the age of 6 years, these showed a significantly lower frequency of raised antistreptolysin-O titres, and a significantly lower mean titre, than those over 6 years of age

This result suggests that, contrary to the current concept, the pathogenesis of rheumatic fever is not primarily related to the sensitisation to streptococci or their products that commonly occurs in childhood

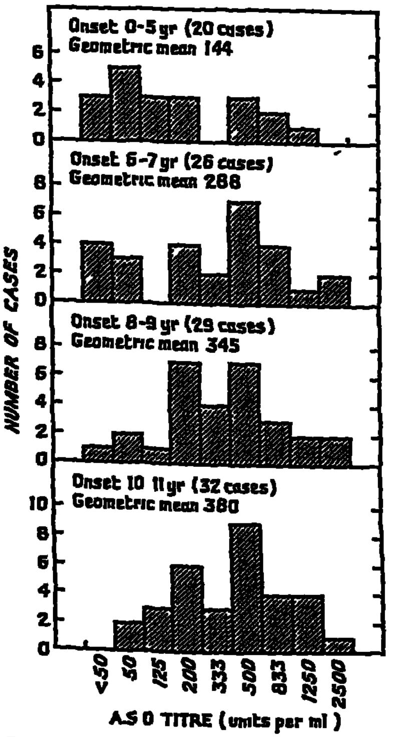

Fig 4—Distribution of actual A.S O titres in the four age-groups

The standard globulin preparation obtained in July, 1953, was kindly sent by Dr B F Massell, the House of the Good Samaritan, Boston, Mass, U S A

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PALLIATIVE HORMONE THERAPY OF ADVANCED MAMMARY CANCER

REVIEW OF 106 PATIENTS STUDIED IN SEVEN YEARS

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It has long been known that the ovaries influence the growth of the breasts, and that oophorectomy sometimes causes breast cancer to regress (Schinzinger 1889, Beatson 1896, Boyd 1900, Morris 1902, Thompson 1902, Lett 1905a and b)

Haddow (1935) found that certain carcinogenic hydrocarbons retarded experimental malignant growths in laboratory animals, and some of these substances had an œstrogenic effect This discovery led to a trial of synthetic œstrogens for carcinoma of the breast Most workers agreed on the value of œstrogens in postmenopausal women and that the best responses were obtained in soft-tissue metastases, with little benefit in skeletal metastases

Androgens were given to patients with breast cancer to inhibit œstrogens which might be stimulating the growth (Loeser 1938, 1939, 1940, McWhirter et al 1944, Adair and Herrmann 1946, Herrmann and Adair 1946, Cutler and Schlemenson 1948, Prudente 1948, Lowenhaupt and Steinbach 1949, Douglas 1952, Hallberg et al 1953)

It is now considered that some breast cancers are dependent on œstrogens, whose removal will improve the prognosis This view is emphasised by Cade (1955) and Dodds (1955)

The insufficiency of oophorectomy and/or androgen therapy gradually became evident Œstrogens secreted by the adrenal cortex are increased after oophorectomy because the adrenal glands then hypertrophy With the advent of cortisone to control patients during and after operation it was logical to remove the adrenal glands Since Huggins and Dao (1952) and Huggins and Bergenstal (1952) reported a series of cases so treated, adrenalectomy and oophorectomy have been widely practised for the young patient with advanced metastases If extirpation is complete, only those cases which presumably depend on œstrogens show a rapid and dramatic improvement and a recession of tumour growth which may last several months

All workers are agreed that there is no means of determining which case depends on œstrogens, and can then be expected to improve under treatment, except trial of hormone therapy This takes several weeks, but there is a dramatic response one *to six days* after adrenalectomy if the tumour is œstrogen-dependent

Old postmenopausal patients often show a spectacular temporary remission, particularly of soft tissue lesions, after large doses of œstrogens—possibly owing to a is evidence that some other adrenocortical hormones, besides the 17-hydroxycorticoids, may influence the gastric secretion In Cushing's syndrome, for instance, we have found the excretion of reducing corticoids to be increased more consistently than that of 17 hydroxycorticoids (D A D Montgomery and R B Welbourn, unpublished), and the patient (fig 2) who had 70 units of free acid and no 17-hydroxycorticoid in the urine excreted large amounts of reducing corticoids (8 2 mg in 24 hours) Of the 10 hyperchlorhydric patients who did not have Cushing's syndrome (fig 2) only 4 excreted more 17-hydroxycorticoids than normal On the other hand, 4 of 5 hyperchlorhydric patients (table II) excreted more reducing corticoids than normal This difference, though not significant, is suggestive

Our conclusions appear to conflict with those of others who found diminished pituitary and adrenocortical activity in patients with peptic ulcer Foti's (1954) series, however, included only patients with gastric ulcer, a condition in which gastric secretion tends to be diminished In Turner's (1951) series, in which the site of ulceration was not stated, it was suggested that the patients were studied during a phase of adrenocortical exhaustion following a period of overactivity which had induced an exacerbation of ulcer symptoms There seems no way of reconciling our results with those of Sandweiss et al (1950), who found diminished excretion of formaldehydogenic steroids in patients with duodenal ulcer

Gastric secretion is influenced by many factors, including vagal and gastrin stimulation, enterogastrone inhibition, and the number of parietal cells in the stomach It is not surprising, therefore, that no general correlation has been found between adrenocortical activity and gastric secretion Further investigation of their relationship is required by more precise methods of estimating adrenal and gastric function

Summary

Gastric secretion, measured by the gruel fractional test meal technique, is often increased in Cushing's syndrome and is restored to normal by adrenalectomy

The excretion of reducing corticoids is often high in hyperchlorhydric people who have no other signs of disease of the endocrine system

A high excretion of 17-hydroxycorticoids is usually accompanied by hyperchlorhydria

Adrenocortical hormones probably play a part normally in influencing gastric secretion

We wish to thank Prof H W Rodgers for his interest and help in this investigation

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PARAPLEGIA FOLLOWING SPINAL ANÆSTHESIA

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Many conflicting views have been expressed concerning the ætiology of paraplegia following spinal anæsthesia for, although in many cases the paralysis has been associated with adhesive arachnoiditis, the exact cause of the lesion has been difficult to determine There is, however, evidence suggesting that under certain conditions the anæsthetic itself may be incriminated The case reported here supports this view

Case-report

A housewife, aged 45, was admitted to hospital on Feb 24 1955, unable to walk She had difficulty with micturition, and her bowels were constipated In the autumn of 1953, a myoma of the uterus was removed under general anæsthesia, and a year later she was readmitted to hospital with symptoms and signs of small bowel obstruction Laparotomy was done under spinal anæsthesia and the obstruction was relieved The anæsthetic was given by the surgeon with the patient in the lateral position The spinal needle and syringes were autoclaved, and the skin was prepared with a 70% solution of ethyl alcohol 20 ml of a 1/500 " light " solution of cinchocaine hydrochloride ('Nupercaine') was used, and before the neck of the ampoule was opened it was sterilised with 70% ethyl alcohol, at no time was it immersed in antiseptic The postoperative course was uneventful until the seventh day, when the patient complained of slight weakness in her right leg Apparently little attention was paid to this complaint and she was discharged a few days later During the following weeks the weakness in her leg became more pronounced, and by the beginning of December, 1954, she was unable to walk unaided In January, 1955, there was progressive deterioration, with spread of the weakness to her left leg For three weeks before her admission to hospital she had been completely unable to walk, her bladder control had become more difficult, and constipation increasingly troublesome

Neurological examination on admission revealed absence of abdominal reflexes but very brisk knee and ankle jerks in both legs, with clonus, bilateral extensor plantar responses were elicited From the level of the 6th thoracic segment downwards sensibility to light touch, pinprick, and temperature, was impaired on both sides, position sense was absent There was muscle weakness in the abdominal wall, and wasting was obvious in both lower limbs

Cisternal puncture and diagnosis—Repeated attempts at lumbar puncture were unsuccessful and eventually cisternal puncture was done 45 ml of cerebrospinal fluid (C S F) was removed and was replaced by 100 ml of air There was a block at the level of the 4th thoracic vertebra Spinal tumour was provisionally diagnosed

Operation and postoperative course—On the basis of this diagnosis Dr Stig Lindgren did a laminectomy When the dura was exposed no pulsation was noted, and when it was opened extensive adhesions between the meninges and the spinal cord were found and divided As the ventral aspect of the cord was approached a cystic swelling extending upward at the level of the 6th thoracic vertebra was seen compressing the cord From this swelling 50 ml of clear colourless fluid was aspirated, and it was decided that the cyst was continuous with the subarachnoid space above After operation the patient's condition improved for two weeks, but this improvement was not maintained and her condition is now the same as before operation

Histological examination confirmed the operation finding of adhesive arachnoiditis There was no evidence to support the earlier diagnosis of spinal tumour erum-calcium level was investigated on many occasions ut was never found significantly raised

Side-effects

Œstrogens

Postmenopausal bleeding was not uncommon in patients taking a small ineffective dosage of 0 3–1 0 mg q i d for a month or so, treatment had then been stopped by either the patient or the doctor The correct procedure is to increase the dosage to 5 mg q i d and to impress on the patient the importance of not interrupting regular therapy With 5 mg q i d interval bleeding takes place only rarely, and then perhaps after the tablets have been omitted for a day, if patients were given continuous therapy with 20 mg q i d or more for many months, there was no bleeding Withdrawal of œstrogen caused bleeding in 31 2% of 61 menopausal cases 10 of them bled on a dosage of stilbœstrol from 0 3 mg q i d to 5 mg q i d, and 9 on one of 5 0 mg q i d, of the 42 remaining patients 2 on 0 3 mg q i d had not bled in seven and eleven weeks before death, and no report was available for 1 patient who discontinued attendance In 30 patients who received 5 0–50 mg q i d there was no bleeding during their treated lifetime—sometimes for as long as 125 weeks There was no bleeding in 3 patients while having ethinyl œstradiol 0 05 mg q i d or more, in 1 patient while having œstradiol benzoate 10 mg on alternate days, and in 5 patients while having stilbœstrol 1–5 mg q i d in addition to a daily dose of 100–300 mg of testosterone propionate by injection

Pigmentation was striking in some patients, particularly the older group and in those who were normally darkly pigmented, and in this series it developed in 32 8% It was very intense around the nipples and areolæ, the linea nigra, and the perineum, and in senile keratoses The colour varied from dark brown to almost black The nipple of an irradiated breast was often less pigmented than that of the other breast After months of therapy the pigmentation often disappeared, even though big doses were continued In association with this there was sometimes sufficient keratinisation of the nipples to give them a greyish black tinge which, like the pigmentation, ultimately disappeared, leaving a paler smooth nipple

Œdema of the ankles and lower legs was not unusual with continued large dosage, and sometimes the œdematous arm on the side of the radical mastectomy was still further enlarged Rarely in some of these old patients congestive failure was precipitated, but it was usually only necessary to restrict the intake of salt and to give an oral diuretic—e g, 'Mercloran' and acetazolamide

Androgens

Side effects with androgens naturally depend on the duration of treatment and the dosage, but there was also an individual susceptibility The most powerful known action of androgens is anabolic, with retention of nitrogen and sodium, increasing the weight of many patients, and making their muscles noticeably larger and firmer though the patients had advanced cancer Much of the benefit of androgen therapy is probably due to this effect, with subjective improvement of appetite and sometimes an increase in well being and energy, enabling patients to continue their work or their domestic duties There was often pronounced plethora

The unpleasant side effects are those of virilisation This varied from one patient to another some were rapidly affected, whereas others, who survived only a short time, showed very little virilisation The distribution of signs of virilisation, expressed as a percentage of patients treated with androgens, was as follows

Sign of virilisation	*No of patients*
Hirsutism	33 (*58 0%*)
Voice change	26 (*45 5%*)
Enlarged clitoris	15 (*26 3%*)
Acne	11 (*19 3%*)

Hirsutism was the most embarrassing and unpleasant side-effect for the patient and was often very considerable Not only was there an intense growth of long coarse hair on the cheeks, upper lip, chin, and general beard area but also the excess hair on the body, arms, and legs was considerable It is the former, however, to which the patient naturally objects Patients developing hypertrichosis were all recommended to shave daily, preferably with an electric razor, and not to resort to depilatory agents such as wax, pumice, emery paper, electrolysis, and plucking, all of which methods tend to cause infection of the skin follicles and unsightliness noticed by all, whereas, with a well kept shaven face, the fact that the patient shaves is known only to herself and her husband One patient with particularly heavy hirsuties controlled her appearance extremely well by rubbing off the hair from time to time with the pith side of lemon peel

Voice changes probably depend on the normal pitch of the patient's voice They developed early in some and very late in others The voice may be very deep and gruff or husky, or may crack and change like that of a pubescent boy Patients sometimes commented on their inability to sing in the same register, which may drop an octave or so This was rarely a source of dismay but is irreversible

Enlargement of the clitoris was sometimes considerable although not invariable The glans was often enlarged to 0 8–1 0 cm in diameter, appeared congested, and protruded from the enlarged prepuce, whose sulcus contained smegma The body of the clitoris was often 2–3 cm long Concomitant with this overgrowth of the clitoris there was increased vaginal secretion

Acne developed only occasionally The skin was more greasy in most of the patients in whom acne developed, and the acne then usually affected the face, chin, back, chest, and shoulders and probably depended partly on personal cleanliness

All the above mentioned virilising side effects were seen with all the androgens used, occurring almost as much with methyl androstenediol as with testosterone and its esters Although methyl androstenediol is said to be not so virilising, it certainly was so in the dosage of 100 mg daily for a long time

Increase of libido was an important side effect (cf Foss 1951), 14 patients (24 6%) admitted to a considerable increase of libido, but the actual incidence was probably higher It may be associated with hypertrophy of the clitoris Patients commented on constant irritability and sensitivity, but in some cases where examination revealed an enlarged clitoris an increase in libido was denied

Results

Survival—55 5% of the 106 patients were still alive 6 months after starting hormone treatment, 31 2% after 1 year, 11 6% after 2 years, 4 7% after 3 years and after 4 years, and 0 94% after 5 years The average age of these 106 women at the beginning of therapy was 55 years and the mean survival for the group 48 weeks The mean number of weeks lived in 5 years was 18 6% of the expected survival (Foss 1955) After the percentage expectancy of life in 5 years had been calculated for each case, statistical analysis gave the following results

Group	*Age (yr)*	*No of patients*	*% expectancy*	*S D*
1	40 or less	9	9 42	±3 6
2	41–60	61	16 3	±2 1
3	61 or more	36	24 5	±4 45

The differences between groups 1 and 2, and between groups 2 and 3 were not significant, but between groups 1 and 3 the expectancy of life was so increased as to be outside the range of random chance If the survival figures from the onset of symptoms are used instead of from the start of hormone treatment, we find that the average age at onset of symptoms was 51 2 (range 26–76), and the average survival 58 5 months (range 10 months–27 years Dividing the patients into age groups we get

Group	*Age (yr)*	*No of patients*	*Average age at onset (yr)*	*Survival (wk)*	*5 yr % expected survival*
1	Up to 40	18	35 5	230	88 8%
2	41–60	66	50 5	255	98 8%
3	61+	22	66 5	173	68 6%

was a gradually constricting arachnoiditis with subsequent interference with the blood supply to the cord

Williams (1954) described 9 cases in which adhesive arachnoiditis developed after spinal anæsthesia He drew attention to Horsley's observation (Horsley 1909) that the pathological changes in the cord and membranes in adhesive arachnoiditis were found most commonly in the mid dorsal region According to Williams there is a tendency for the anæsthetic solution to accumulate in this area (which in itself increases the risk of arachnoiditis) and he pointed out that the spinal cord is particularly vulnerable to injury in the region of the 6th dorsal vertebra because of a relatively poor blood-supply

Other anæsthetic techniques—Damage to the spinal cord and membranes may be caused by other anæsthetic techniques Koch (1947) described paraplegia in a patient who was inadvertently given an intrathecal injection of 5 ml of an 80% solution of ethyl alcohol, and Rosenbaum et al (1952) reported a series of 6 cases in which arachnoiditis developed after "heavy" cinchocaine had been used to induce "saddle" block anæsthesia in childbirth They suggested that the circulation through the vertebral vascular system is impaired by the high abdominal pressure during labour, and as a result a high concentration of anæsthetic solution may persist in the subarachnoid space longer than normal

pH of anæsthetic solution—One further factor to be considered in the causation of adhesive arachnoiditis is the hydrogen-ion concentration of the anæsthetic solution Normally the C S F is slightly alkaline, with a pH in the region of 7 6 The pH of anæsthetic solutions of cinchocaine is definitely acid (4 5 or less) Although a small volume of injected acid solution is probably neutralised at once, it seems likely that when larger volumes are injected neutralisation may be delayed and the membranes and spinal cord in contact with the solution damaged

Although much work remains to be done on adhesive arachnoiditis, there is sufficient evidence to justify abandoning techniques that require large volumes or continuous injection of anæsthetic solution Permanent paraplegia with its profound social and economic repercussions is too great a price to pay for any temporary advantage gained by the surgeon

Summary

A case of adhesive arachnoiditis following spinal anæsthesia with "light" cinchocaine is described

The ætiology of adhesive arachnoiditis, with particular reference to contamination and infection of the C S F, and anæsthetic drugs and techniques, is discussed

The use of "light" cinchocaine and continuous spinal anæsthesia should be abandoned

We are indebted to Dr Stig Lindgren and Prof Ian Aird for their advice and criticism

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DIAGNOSIS OF ISLET-CELL TUMOURS OF THE PANCREAS

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ISLET-CELL tumours of the pancreas have been known since Nicholls (1902) described them, but neither their physiology nor their clinical features were understood until after the discovery of insulin by Banting and Best in 1922 An islet-cell tumour was first successfully removed by Roscoe Graham (Howland et al 1929)

Despite the supposed rarity of this condition its prompt diagnosis is of great importance because these patients have often been labelled as neurotics, psychotics, or epileptics and have been treated as such

Until quite recently the diagnosis depended entirely on the fulfilment of the triad of criteria of Whipple and Frantz (1935) (1) a hypoglycæmic attack resulting from fasting or exertion, (2) a blood-sugar level below 50 mg per 100 ml during the attack, and (3) the prompt relief of an attack by glucose

Assay of serum for insulin content offers a possibility for differentiating hyperinsulinism from functional hypoglycæmia Willebrands and Groen (1954) obtained higher values than normal in 4 patients with an islet-cell adenoma confirmed by operation After removal of the tumour the insulin content of the serum returned to a normal level

Two main methods of plasma insulin assay have been investigated for practical application The first of these is an in-vivo method using alloxan diabetic, hypophysectomised, adrenalectomised rats (Bornstein 1950) These rats are difficult to prepare, and the mortality rate during the preparation is high, in addition many variable factors enter into the final calculations, increasing the possibility of experimental error

The in-vitro method, using the rat diaphragm, is technically easier and more satisfactory Gemmill (1941) demonstrated the uptake of glucose, by the isolated rat diaphragm, from a buffer solution and the deposition of glycogen in the muscle The process is accelerated by the addition of small quantities of insulin to the buffer solution, and a quantitative relationship between the amount of insulin present and the uptake of glucose by the muscle was established by Stadie and Zapp (1947) and Krahl and Park (1948)

As a result of experiments on young healthy men, Vallance Owen and Hurlock (1954), using the rat diaphragm, obtained fasting plasma-insulin levels of 31-82 micro units per ml in healthy people

With these figures indicating the range of normality a diagnostic assay was made on the patient whose case report appears below

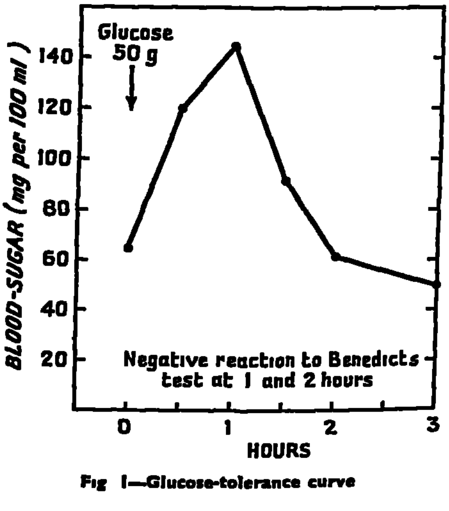

Fig 1—Glucose-tolerance curve

Case-report

A man, aged 33, was admitted semiconscious to St James' Hospital on April 3, 1955 His wife stated that he was subject to fits, the last one having occurred four hours previously more than 60 than in the younger patients Although breast cancer is more rapidly fatal if it begins at the age of more than 60, there is more chance of prolonging survival in this age group by hormone therapy when metastases are widespread

Assessment of improvement was made as objective as possible Temporary regression of metastases in glands, photographically recorded improvement in skin lesions and radiographic evidence of bone healing were accepted as beneficial effects of hormone therapy 5 cases were regarded as improved because pain of bone secondaries was diminished although no radiographic improvement was seen during long periods of survival in moderate health Only 4 of 35 patients with bone secondaries treated with androgen showed radiographic evidence of bone healing This figure of 11% compares unfavourably with 30% claimed by Hallberg et al (1953) who also claim improvement in general condition and palliation in 85% In the present series objective improvement was seen in 30% of those treated with androgen—a very similar figure to 27% found in a shorter observation period by Segaloff et al (1951) in 48 cases treated with *testosterone propionate 100 mg thrice weekly.*

Subjective improvement was noted in a few other patients in this series treated with androgens but it was doubtless partly due to the anabolic effect—increased appetite and temporary euphoria

For some old patients who present with fungating lesions too advanced for surgery or X-irradiation œstrogens are a useful means of palliation Healing of ulceration in some cases may last months

Huseby (1954), who treated with œstrogens 100 patients with advanced mammary cancer reported that those in whom the response was favourable had an average survival of 29 months from the start of therapy, and that 24 of these were more than 5 years past the menopause (natural or therapeutic) The response of those with bone lesions was poor Only 1 of his 5 patients who had not reached the menopause improved There was major regression of pulmonary metastases in 11. These figures are similar to my finding in 14 patients who improved with œstrogens Their average age was 63 (range 53–76) and average survival 32 months from the start of therapy

The considerable virilisation caused by big dosages of androgens is perhaps not so very important Shaving with an electric razor will maintain a presentable appearance Methyl androstenediol which is claimed to be less virilising has nothing to recommend it over testosterone Patients treated with 100 mg of methyl androstenediol daily for some months developed almost as much hirsutism as those given testosterone esters. moreover methyl androstenediol causes pain when it is given in crystalline suspension and in several cases it caused an abscess at the site of injection Segaloff et al (1952) observed similar results and achieved regression of the lesions in only 2 of 24 cases treated solely with methyl androstenediol

The choice of therapy was not dictated at first by a knowledge of œstrogen dependence of a particular cancer Usually old postmenopausal women with soft-tissue metastases were treated with œstrogens, and the younger patients or those with widespread bone metastases were given androgens Subsequent analysis of the 17 patients who responded to androgens, however, showed that 82% had had their first symptom of cancer before the menopause, whereas of the 14 who improved with œstrogens 93% had had their first symptom after the menopause This may possibly be a guide to selection for hormone therapy, and in the androgen-treated group with premenopausal onset this may indirectly indicate œstrogen dependence or conversely, the postmenopausal onset suggests that not even stroma-cell œstrogens were responsible stimulants to their cancer (Sommers et al 1953) In these old patients in whom pituitary activity is not inhibited by endogenous œstrogens, there may be excessive production of somatotrophin and prolactin as well as gonadotrophin, and the beneficial effect of œstrogen therapy may be due to inhibition of these hormones

It is quite clear that there is a type of patient with breast carcinoma which is temporarily responsive to treatment with androgens or by oöphorectomy or by adrenalectomy and that the essential common factor is œstrogen dependence (Pearson et al 1954) Unfortunately there is no way of detecting œstrogen dependence and only recently have chemical methods of estimating œstrogens in urine been elaborated but the method is laborious (Brown 1955) and is not yet readily adaptable to clinical use

In the present series the patients were so widely riddled with metastases that one could not hope for much benefit. hence an improvement-rate of about 30% for both œstrogens and androgens is possibly satisfactory

As Asher (1955) aptly remarked ' Prolongation of life is not the only aim of treatment. it should be a tolerable life It is better to be wholly alive for one month than half alive for two The latter part of his statement referred to cases after endocrine surgery, which like hormone therapy at present suffers from an inability to discriminate between cancer cases with and without hormone dependence

In the present series the side effects and possible upsets and the prolonged course of oft repeated intramuscular injections were a high price to pay by patients for no improvement perhaps it would have been better if they had been allowed to spend their remaining life under increasing doses of morphine So much however depends on each patient's temperament One can only remember the gratitude and faith of those who were fortunate in their response to treatment some of whom enjoyed many months' freedom from pain and freedom from odour, and lived reasonably normal lives Such results even though restricted to about a third of those treated, are worth while

Summary

106 women with stage IV mammary carcinoma were treated with either androgen or œstrogen and kept under observation until death

Improvement was observed in only 29% of cases Of the 17 women who improved with androgen 14 had had their first symptom before the menopause and of 14 patients who improved with œstrogen 13 had had their first symptom after the menopause

The average age of those patients who received benefit from œstrogen was 63 and from androgen 49 The prognosis was better for the older patients treated with œstrogen the average survival for these being 32 months compared with 17 25 months for those who improved with androgen

The possible significance of œstrogen dependence in the younger group and pituitary-hormone dependence in the older postmenopausal patients is discussed

My thanks are due to Sir Charles Dodds, who persuaded me to join in the British Empire Cancer Campaign œstrogen trial, the British Empire Cancer Campaign for a grant for three years for laboratory assistance, Prof Milnes Walker for permission to treat patients in the department of radiotherapy at the Bristol General Hospital the physicians and surgeons who allowed me to treat their patients, Miss G M. Jeffree, my technician, Dr C H. G Price and Dr. A L Taylor for advice and help and Miss J. E Nixon, of the records department of the department of radiotherapy, for much secretarial help The androgens were provided by Ciba Laboratories, Organon Laboratories Ltd, and British Drug Houses Ltd.

References overleaf

insulin assay is of most use in these cases, the other causes will usually be recognised during the course of clinical and laboratory investigations

Glucose metabolism in the body depends on the hormonal balance between the pancreas, pituitary, and adrenal glands, and an abnormal blood-sugar level only indicates hormonal imbalance and not dysfunction in one particular gland For this reason a low blood-sugar level may not reflect pancreatic hyperactivity

In some cases, as in the present one, because of compensatory mechanisms the blood sugar level may not drop below *50 mg per 100 ml*, and immediately one of the triad of criteria of Whipple and Frantz (1935) is not fulfilled, although a tumour is present

"Plasma-insulin" assay obviates the risk of these variable blood sugar levels and differentiates between organic hypoglycæmia (due to an islet cell tumour) and so called functional hypoglycæmia In the latter the fasting blood sugar is normal but becomes subnormal two to six hours after the ingestion of carbohydrate In contrast to this, organic hypoglycæmia always occurs after a period of fasting, and the fasting blood-sugar is persistently low

Summary

In a case of spontaneous hypoglycæmia due to an islet cell tumour of the pancreas, plasma insulin levels were assayed before and after operation

By means of plasma-insulin assay the diagnosis of islet cell tumour can be confirmed, and the causes of spontaneous hypoglycæmia differentiated

I am indebted to Dr Vallance Owen and his colleagues for the plasma insulin assays, Mr Norman Tanner, who operated, Dr G T Allen and Dr P W Kippax, who reported on the specimens, Miss E Mason, who prepared the graphs and photographed the specimen, Dr R J Harrison, without whose advice and encouragement this article would not have been written, and Dr M Bewlay, who originally diagnosed the case

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ARTIFICIAL INSEMINATION AFTER INTRATHECAL INJECTION OF NEOSTIGMINE IN A PARAPLEGIC

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In 1949 Guttmann reported that intrathecal injection of neostigmine in male patients with traumatic paraplegia induced erection of the penis and ejaculation of spermatic fluid Neostigmine administered by other routes has not been shown to have this effect

Guttmann injected neostigmine intrathecally in order to test the spermatic fluid and to control the progress of hormone treatment in paraplegics, and in 5 cases he used this method to obtain semen for artificial insemination, which, however, did not result in pregnancy

The technique of the neostigmine test is simple 0 2 mg of neostigmine in 1 1000 aqueous solution is injected intrathecally at L4–L5 vertebral interspace, the injection is made slowly after mixing the contents of the syringe several times with the cerebrospinal fluid After the injection the patient lies supine or on his side without a pillow About an hour after the injection erection followed by several ejaculations of spermatic fluid takes place Specimens are sent for examination

The injected neostigmine acts presumably on the undamaged spinal centres in the lumbar cord, below the level of the lesion, which control erection and ejaculation In addition the neostigmine temporarily diminishes the reflex activity of the isolated spinal cord, this effect manifests itself by diminished spasticity of the paralysed limbs In some cases there are other side effects, such as a decrease in the systolic and diastolic blood pressure, headache, nausea, and general weakness, all these *effects disappear after two to three hours*

I have injected neostigmine intrathecally for testing purposes, and in one case for the purpose of fertilisation Pregnancy resulted

Case-report

A man, aged 25, in 1948 sustained a fracture dislocation of T6 vertebra, resulting in a complete spinal syndrome at T6 segment He remained spastic with pronounced flexion and adductor spasticity In the early stages of his disability he had repeated attacks of severe bilateral orchitis, which responded to treatment He had from time to time had spontaneous erections without ejaculation The urine, routinely examined, sometimes contained a few spermatozoa

Neostigmine Tests —The first neostigmine test, before the patient's marriage in October, 1952, revealed only 500,000 spermatozoa per ml, with no motility A further test, in April, 1954, showed an improved count of 20 million spermatozoa per ml, 15% of the spermatozoa were motile, and there was considerable microspermia

Treatment —Testosterone 25 mg daily for fourteen days and gonadotrophin (Winthrop) 1000 units daily for four weeks were administered in order to improve the count sufficiently for an attempt at artificial insemination

Attempted Fertilisation —The first attempt at fertilisation was made in June, 1954 At the patient's request artificial insemination was not undertaken After intrathecal neostigmine he was left with his wife, and the induced erection was used for coitus This attempt did not result in fertilisation A specimen of semen recovered from one of the ejaculations showed a count of 10 million spermatozoa per ml, of which 10% were motile The decrease in the count, compared with that before hormone treatment, was apparently due to a "rebound phenomenon," associated with the administration of both testosterone and gonadotrophin From then onwards he was given 1000 units of gonadotrophin alone daily for four weeks A second unsuccessful attempt at impregnation was made under similar conditions in August, 1954

Artificial Insemination —The third attempt was made in November, 1954 This time artificial insemination was undertaken by a gynæcologist with a specimen obtained after intrathecal injection of neostigmine No spermatic count was taken This also proved unsuccessful The fourth attempt was made on Dec 4, 1954 This resulted in pregnancy, and the patient's wife was delivered of a healthy daughter on Sept 3 1955 When in March, 1955, it became obvious that his wife was pregnant, the patient's spermatic count was checked it amounted to 200 million per ml, of which 50% were motile

Confirmation of Paternity —Blood tests gave the following results

Father	Group A Rh′+, RhO+, RH″–, HR′+
Mother	Group A RH′+
Infant	Group A RH′+

Conclusions

So far as I know this is the first reported case of successful impregnation by the spermatozoa of a paraplegic after intrathecal injection of neostigmine In the present case impregnation would otherwise have been impossible, as there was no chance of spontaneous ejaculation There are of course well authenticated instances of fatherhood in spinal paraplegics without neostigmine having been administered (Freeman, unpublished and our own cases), but these cases have been in paraplegics with preserved faculties of coitus and ejaculation

This method opens an important new field in the physical and psychological rehabilitation of paraplegics

I thank Dr J Gordon chief medical officer, ministry of defence, for permission to publish this article, Dr C Rosen

MEAN SERUM CHOLINESTERASE LEVELS IN FOUR GROUPS OF ADULTS

Group	*No of* subjects	Mean activity (*µl of* CO₂ per ml *serum* per min)	Standard *error of* mean	Range
Healthy adults	33	76	±2	53–102
Non-obese diabetics	25	81	±3	51–120
Obese diabetics	25	107	±7	43–175
Obese non diabetics	25	102	±5	60–131

diabetics, 15 (60%) gave values above this range, varying from 108 to 175 µl , 9 of them (36% of the whole group) gave values over 120 µl The mean value obtained in the 25 obese non diabetic patients, as in the obese diabetics, was significantly higher than that found in the healthy adults, *11 of them (44%) having values ranging from* 105 to 151 µl On the other hand, of the 25 non-obese diabetics 23 (92%) had levels within the normal range, and no levels were above 120 µl

Statistical analysis of these results shows that, although 2 of the non obese diabetics gave values above the highest found in the present normal series, there was no statistical difference between the levels in the non obese diabetics and those in the healthy adults On the other hand, the difference between the levels in the non-obese and the obese diabetics is highly significant, *as is also the difference* between those in the obese non-diabetics and the healthy adults

No *significant correlation* was *found between the* serum-cholinesterase levels in the diabetic group and the severity or degree of control of the diabetes

Discussion

Although the serum-cholinesterase level in children is significantly higher *than in adults* (McArdle 1940), Callaway et al (1951) reported that age does not influence the level in adults Many workers have also shown that the plasma-cholinesterase level does not significantly differ between the two sexes The patients studied in the present series were all over the age of 18, and the mean *serum cholinesterase* level of 76 µl of carbon dioxide per ml of serum *per minute found in our healthy adults* agrees with the average normal values of 78, 65, and 79 µl found by McArdle (1940), Kunkel and Ward (1947), and Hutchinson et al (1951) respectively The results we obtained in diabetics indicate that high serum-cholinesterase levels are found only in patients who are also overweight, and they suggest that the high levels are associated with the accompanying obesity, rather than with the diabetic state itself , this accords with the finding by Berry et al (1954) of a positive correlation between the amount of surface fat and the plasma-cholinesterase level

The influence of diet on plasma-cholinesterase activity in man was first studied by McCance et al (1948), who reported a reduction in the serum-cholinesterase level in undernourished Germans (see also Hutchinson et al 1951) *Waterlow (1950)* found very low *plasma* cholinesterase levels in 20 malnourished African infants In 2 of them he measured liver cholinesterase *activity in* aspiration-biopsy specimens In both the initial liver-cholinesterase level was low compared with that in 4 *controls*, but it was more than doubled after the infants *were fed for* four to five weeks on a *high-milk* diet Hutchinson et al also found that a rise in the plasma-*cholinesterase* level was brought about by improvement of the diet

There is now good evidence that the plasma cholinesterase is, in the main, derived from the liver McArdle (1940) demonstrated that the serum cholinesterase level is lowered in patients with liver disease and that improvement in liver function was accompanied by *a rise* in the serum cholinesterase level

Brauer and Root (1946) further showed that, in rats with liver injury induced by intraperitoneal injections of carbon tetrachloride, both the plasma and liver cholinesterase levels were reduced , *after ten days' injections, the reduction was* more pronounced in the liver

The cholinesterase activity of human plasma is predominantly due to " pseudocholinesterase " (Mendel et al 1943), an enzyme differing in many respects from the " true " cholinesterase present in nerve and muscle tissue, whose physiological function is *presumed to be* the inactivation of acetylcholine released at certain nerve endings The function of pseudocholinesterase is at present obscure, but the above observations raise the question as to whether in plasma, and therefore also in the liver, *pseudocholinesterase may* not be concerned with some aspect of fat metabolism, rather than with inactivating acetylcholine It is known that the pseudocholinesterase level in the plasma can be reduced almost *to zero without signs of acetylcholine accumulation* developing (Mazur and Bodansky 1946, Hawkins and Gunter 1946) It is *also* known that pseudocholinesterase hydrolyses various non-choline esters, and Adams and Whittaker (1949) showed that it is responsible for about 90% of the hydrolysis of tributyrin by human *plasma*

Further *evidence suggesting a connection* between pseudo cholinesterase and fat metabolism was afforded by Hawkins and Nishikawara (1951), who showed that in male rats the *ingestion of a hypolipotropic diet led to a considerable rise* in pseudocholinesterase activity in both the plasma and the liver , the subsequent addition of lipotropic agents, such as *choline or methionine, to the deficient diet restored the elevated* plasma pseudocholinesterase level *to normal* In the rat, the *plasma contains, in addition* to pseudocholinesterase, an active true cholinesterase and also an eserine resistant tributyrin-hydrolysing enzyme , *neither of these enzymes* is affected by *giving hypolipotropic diets It* is also of interest that Kunkel and Ward (1947) found that the plasma pseudocholinesterase level is higher than normal in patients with the nephrotic syndrome, the *average in the 10* patients studied being 110 µl of carbon dioxide per ml of serum per *minute*

On the other hand, denervation experiments and the use of selective inhibitors tend to show that in certain other tissues, pseudocholinesterase, like true cholinesterase, may play some part in cell excitation *Supporting* evidence for this has been obtained from experiments on the central artery of the rabbit's ear (Armin et al 1953), cat ileum (Koelle et al 1950), cat skin (Hellmann 1952), cat iris (Burn and Philpot 1953), dog heart (Burn and Walker 1954), and cat brain (Desmedt and La Grutta 1955)

It is possible therefore, that, owing *to the overlapping* substrate specificity shown by *many of the* esterases, the term " pseudocholinesterase " is being used to denote *different* enzymes with fundamentally *different physiological* properties, and that the pseudocholinesterase in human plasma and liver *may* be very different from that in the nervous system, the myocardium, the *blood*-vessels, or the intestinal wall

Summary

The serum-cholinesterase level was determined in 50 *adult patients* with diabetes mellitus (25 obese and 25 non-obese), 25 adult *obese* non-diabetics, and 33 healthy non obese adults

High serum cholinesterase levels were found only in those *diabetic* patients who were also overweight, suggesting that elevation of the serum-cholinesterase level is associated with the accompanying obesity, rather than with the diabetes itself

The possibility is discussed that this pseudocholinesterase, *present in human* plasma and liver, may be concerned with some aspect of *fat metabolism*

We wish to thank the Medical *Research Council* for a grant towards the expenses of this work Our thanks are also due

A RAPID METHOD OF ESTIMATING FIBRINOGEN

ACUTE hypofibrinogenæmia occurring in pregnancy or after surgery is an emergency which requires rapid diagnosis and treatment The bleeding which then takes place can be rapidly fatal and is arrested only by intravenous injection of purified human fibrinogen, massive blood transfusion alone gives uncertain results Purified fibrinogen is scarce, and for economy it is essential to know the plasma-fibrinogen level before and during treatment Many methods for the quantitative estimation of fibrinogen have been described, but none of these combines accuracy with the simplicity and speed needed for such emergencies The method described below is accurate, simple, and quick, the result is obtained within 25 minutes of receiving the blood

Method

The coagulation temperature of fibrinogen is about 55°C in neutral solutions[1] Other plasma-proteins are coagulated at temperatures exceeding 60°C It was found that the turbidity produced by heating saline dilutions of plasma at 56°C is directly proportional to the fibrinogen concentration and that it remains constant for many hours, even after twenty-four hours the original turbidity can be restored by shaking The result has been expressed in terms of the barium-sulphate standard used by Kunkel[2] for his zinc sulphate turbidity test, so that this method can be adopted in any laboratory without further estimation of fibrinogen by Kjeldahl analysis

Procedure

Plasma is obtained from blood to which has been added 2 mg per ml of either the oxalate mixture of Heller and Paul or 'Disodium Sequestrene' 0 2 ml of plasma is thoroughly mixed with 3 ml of 1% sodium chloride in each of two half-inch diameter test-tubes One of the tubes is placed in a water-bath at 56°C for 15 minutes The extinction reading of the heated mixture is measured against the unheated blank in the 1 cm cell of a spectrophotometer set at 650 mµ At this dilution 1 Kunkel unit is equivalent to 42 8 mg of fibrinogen per 100 ml in the plasma sample

Comments on the Method

Measurements at timed intervals have shown that a constant turbidity is always obtained after 15 minutes at 56°C

Different dilutions of plasma are required if the fibrinogen content is much higher or lower than normal Serial dilutions of plasma were heated at 56°C, and it was found that, when the turbidity exceeded 20 Kunkel units, its relation to the fibrinogen content was no longer linear A plasma-fibrinogen level above 850 mg per 100 ml produces a turbidity greater than 20 Kunkel units when diluted 1 in 16 and requires further dilution—e g, 1 in 31—to obtain accurate results Fibrinopenic plasma gives a faint turbidity at a dilution of 1 in 16, therefore a less dilute mixture is desirable—e g, 1 in 11, or 1 in 7 The result is calculated from the formula given below

A 'Unicam SP 350' spectrophotometer was used for these experiments, but any photo-electric colorimeter or spectrophotometer may be used It should be calibrated at 650 mµ (or with 'Ilford filter No 608') with the barium-sulphate standard used by Kunkel[2] 1 Kunkel unit is equivalent to 26 8 µg per ml of fibrinogen in the diluted plasma The concentration of fibrinogen in the undiluted plasma can therefore be calculated from the formula

$$F = 2\,68 \times \frac{(Vs + Vp)}{Vp} \times \frac{(Et \times 20)}{Ek}$$

where Et = extinction reading of test, Ek = extinction reading of barium sulphate standard, F = fibrinogen content of plasma in mg per 100 ml, Vp = volume of plasma in mixture, and Vs = volume of saline solution in mixture

To find whether substances other than fibrinogen are precipitated at 56°C, many samples of serum were diluted and heated at this temperature These were from healthy people as well as from patients whose serum contained abnormal proteins or abnormal quantities of protein In none was there any turbidity The presence of dextran did not interfere with the result Dilutions of lipæmic sera which are clarified by heating to 56°C resume their original turbidity on cooling to room temperature, interference from this source is negligible if lipæmic samples are cooled under the tap before the turbidity is measured

Calibration of the Method

The fibrinogen content of 25 samples of plasma was estimated by micro-Kjeldahl distillation, the fibrinogen content of these samples was 197–534 mg per 100 ml Each sample was also tested by turbidity after heating at dilutions of 11, 16, and 31 For each of the 75 results a constant (K) was calculated by dividing the extinction reading by the concentration of fibrinogen in the diluted plasma From the mean value of K, which in these experiments was 597 × 10^{-3}, the conversion factor required to relate turbidity to fibrinogen content was calculated The standard deviation of K was 22 9 × 10^{-5} and the coefficient of variation 3 84% The greatest deviation from the mean for any result was 8%

I should like to thank Dr George Discombe for his advice and encouragement

Central Middlesex Hospital,
London

R M STIRLAND
B A, M B Camb

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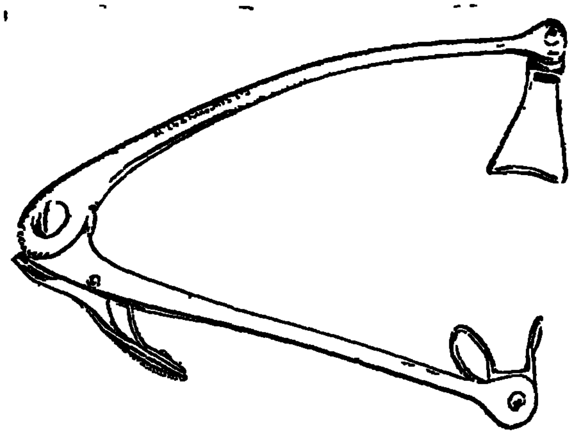
[1] Hawk P B Oser B L Summerson W H Practical Physiological Chemistry 13th ed London 1947 p 412

[2] Kunkel H G *Proc Soc exp Biol* N Y 1947 66 217

New Inventions

SELF-RETAINING RETRACTOR FOR VARICOSE-VEIN SURGERY

RETRACTION in the depths of a groin incision for juxtafemoral ligation has always been difficult The area is small, yet it is packed with thin-walled vessels which, if torn, can give rise to embarrassing moments The instrument shown in the accompanying figure has been designed to give an unimpeded field during the operation It renders tiring, and therefore unstable, hand retraction unnecessary in almost every case The shafts are curved in order to fit snugly to the upper thigh, while the wire-loop blades, which are gentle to the tissues, are pivoted at their point of suspension This ensures a consistently stable grip as the retractor opens along its very wide arc



I am grateful to Mr W J Cooper, of Messrs Allen & Hanburys, for his help

London, W 1

STANLEY RIVLIN
M.R.C.S

Necropsy Findings

The significant findings other than those in the heart were small stature, slight œdema of the lung, ante mortem thrombus filling the lumen of the splenic artery throughout its course, old infarctions of the spleen, thrombosis of the superior mesenteric artery with acute infarction of the lower half of the jejunum ileum, cæcum, and part of the ascending colon, accompanied by early peritonitis

The *heart* weighed 130 g All chambers were dilated and there was definite hypertrophy of the left ventricle The striking feature was the diffuse whitening of the endocardium and inner third of the myocardium of the left ventricle (fig 1) This was seen mainly on the anterior and lateral walls in the apical half of the ventricle, but it extended upwards on the posterior wall behind the mitral cusp The interventricular septum, except towards the apex, was unaffected There was no mural thrombus The aortic valve, the mitral cusps, and their chordæ tendineæ were normal, but the papillary muscles, both anterior and posterior, were fibrosed The endocardium lining the left auricle was distinctly thickened The foramen ovale was completely sealed off On the right side of the heart the endocardium and valves were normal but the right ventricle showed slight hypertrophy The coronary arteries showed no abnormality The pericardium and aorta were normal

Microscopy

Numerous sections of the heart showed focal fibrosis of the myocardium of the left ventricle The inner third was extensively involved, but the outer two thirds showed only slight damage Elastic tissue stains revealed fibroelastic thickening of the endocardium in the scarred area of the left ventricle (fig 2) In several places it was impossible to differentiate the endocardium clearly, owing to the fibroelastic change affecting both the endocardium and the subjacent myocardium The thickening, in general, was of mild degree The endocardium over the interventricular septum and in the right ventricle was normal In addition to the focal fibrous scars in the myocardium, there were numerous congested capillaries, occasional small areas of round cell infiltration, mainly lymphocytic, and also several foci of acute cellular infiltration including eosinophil polymorphonuclear leucocytes (fig 3) The myocardium in general was hypertrophied but there was some atrophy of the fibres immediately surrounding the scarred areas A few small foci of necrosis of the myocardium were present There was no evidence of rheumatic fever and in particular there were no Aschoff nodes The acute lesions of periarteritis nodosa were not seen in the coronary arteries or arterioles In a very occasional small artery in the subendocardial fibrous scars, however, a fairly marked fibroelastic thickening of the subintimal tissues was observed (fig 4) The pericardium showed a slight perivascular round cell infiltration

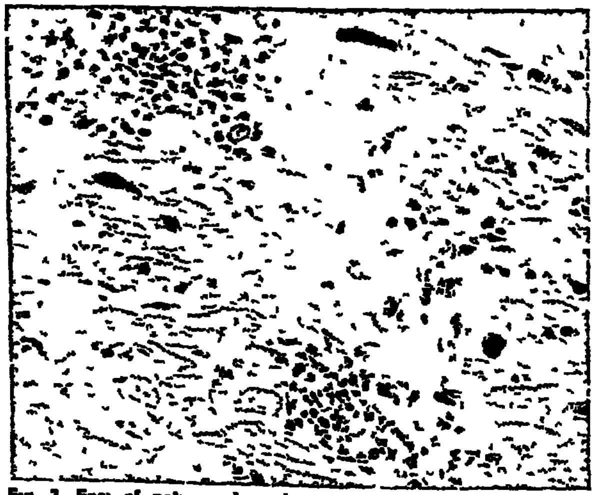


Fig 3—Foci of polymorphonuclear leucocytic infiltration of the myocardium (× 250)

The typical lesions of acute periarteritis nodosa were found in the superior mesenteric artery at the site of the thrombus formation Similar acute lesions were present in the vasa vasorum of the aorta, and in the vessels of the pancreas (fig 5) and testes Lesions in the healing phase with granulation tissue formation were seen in the wall of the splenic artery There was no evidence of periarteritis nodosa in the kidneys or in the liver The cellular infiltrate in relation to the acute vascular lesions was similar to that in the heart—i e, lymphocytes, plasma cells, and polymorphonuclear leucocytes, including eosinophils There were no other significant histological findings

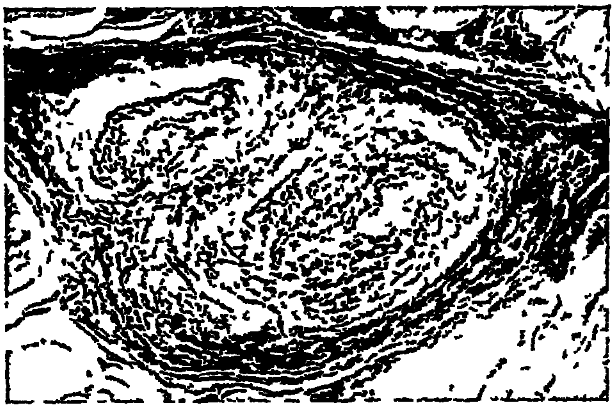


Fig 4—Two small subendocardial arteries showing fibroelastic thickening of the wall (× 140)

Comment

The sudden death was considered to be of cardiac origin and despite the age of the patient a tentative diagnosis of congenital fibroelastosis of the heart was made The clinical history of stunted growth since the age of 3 supported a congenital cardiac lesion The terminal illness with mid abdominal pain was explained by the superior mesenteric artery thrombosis with acute intestinal infarction The pre terminal illness with pain in the left abdomen was attributed to arterial thrombosis and infarction of the spleen These infarcts were several weeks old At the time of the necropsy the cause of the thrombosis in the superior mesenteric and splenic arteries was difficult to account for in the absence of any evident source of emboli Subsequent histological examination of these vessels disclosed the typical features of acute periarteritis nodosa The administration of sulphonamides, certainly on one occasion and possibly more than one, is of interest in view of these findings (Rich 1942)

Discussion

In congenital fibroelastosis of the endocardium, there is a typical macroscopic picture The endocardium is pearly white throughout one or both ventricles, usually the left, and this appearance was the striking post-mortem feature in this case But there are several findings not in accord with congenital fibroelastosis The

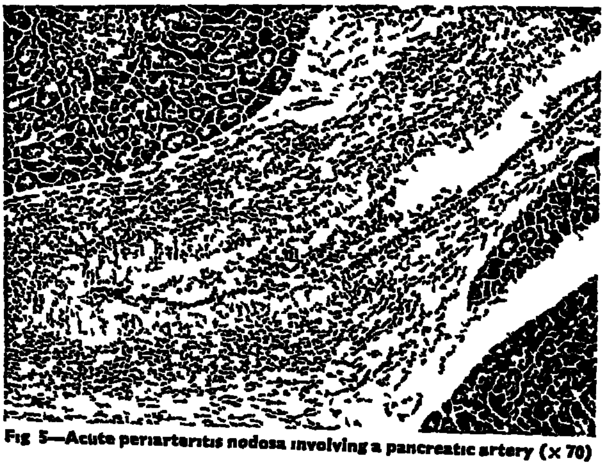


Fig 5—Acute periarteritis nodosa involving a pancreatic artery (× 70)

interested in the history of the theories by which men have endeavoured to explain disease or to heal their companions

Research Films in Biology, Anthropology, Psychology and Medicine

ANTHONY R MICHAELIS, PH D, technical director, Scientific, Industrial & Medical Photographic Laboratories Ltd, London New York Academic Press London Academic Books 1955 Pp 490 £4

BY describing in detail the film techniques available and by quoting many experiments in which they have been applied, Dr Michaelis hopes to encourage research workers to consider the use of film as a tool in their own work

He gives advice on cameras and camera stands for various tasks, types of illumination, the preparation of a film treatment and shooting script, and the use of time markers for obtaining quantitative results, of time lapse and high speed cinematography, of cinemicrography, and of X ray cinematography He even mentions the application of television as an image converter in certain circumstances

The section on the medical sciences occupies about a third of the text It is surprising to read, however, that in *1920* " not a single British surgical film could be named " in view of the fact that several surgeons, notably Alexander Don and Cecil Wakeley, had filmed operations before that date By 1929 films on such subjects as tuberculosis, venereal diseases, physiology, cytology, and health education were also available This section describes the techniques and equipment suitable for medical work, and their various applications in the investigation of locomotion, digestion, respiration, the genito urinary system, the circulation, the sense organs, neurology, pathology, and aviation medicine

There is perhaps too much detail in the book Descriptions of experiments are often accompanied by details of the scientific results derived from them, data that are surely readily available to the research workers for whom the book is intended And is Dr Michaelis right when he says that, in films other than those for personal analysis, no shot should exceed thirty seconds ? In the cinema and in television, Hitchcock and O'Donovan have shown that interest can be maintained in one shot for much longer, and the television interlude film of the potter's wheel is a well known proof to the contrary

If there is little in the book that is actually new, Dr Michaelis has collated information from most parts of the world where the cine camera is used for research, and his compilation of 1500 authors and references makes the volume the most valuable reference book now available in this field

Obstetrical Anesthesia

Its Principles and Practice B B HERSHENSON, M D, director of anesthesia, Boston Lying in Hospital Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 403 69*s*

THE administration of anæsthesia for obstetrics has in the past been largely left in the hands of obstetric residents or the more junior residents in anæsthesia This is an unsatisfactory state of affairs, and Dr Hershenson rightly places more faith in the competence and experience of a trained anæsthetist than in any special drug or method of anæsthesia Though he recognises that there is a real need for better drugs, he is forthright in his condemnation of the exaggerated emphasis often placed on a single agent as the safest or best method of anæsthesia in obstetrics

Dr Hershenson aims to help doctors in their selection of a technique for a particular case, and he presents a fairly full and well referenced account of the subject The accent is on general analgesia and anæsthesia but local methods are included The physiology of pain in labour, the pharmacology and selection of drugs used in obstetrics, diseases complicating pregnancy and labour, and asphyxia neonatorum are discussed in detail

The author is an anæsthetist, and his book will therefore be all the more welcome to those actively engaged in administering anæsthetics, since the literature of this subject has been written largely by obstetricians But *it is* a difficult book to read , there is much needless repetition and a great deal of elementary fact which one would like to assume every anæsthetist knows before he assumes responsibility for an obstetric patient It is also a pity that no recognition is given to the considerable amount of knowledge accumulated on this side of the Atlantic about the value and use of trichlorethylene as an analgesic in labour

Galen on Anatomical Procedures

Translated with introduction and notes by Prof CHARLES SINGER, F R S London Oxford University Press 1956 Pp 314 37*s* 6*d*

UNTIL recent years the works of the greatest and most prolific medical writer of antiquity were closed books to the modern reader Professor Singer has now added another to the few works of Galen which have been translated from the Greek into English

Galen's work entitled *De Anatomicis Administrationibus* is the text of lectures on anatomy delivered in Rome about A D 177 It thus preserves the very words of an ancient teacher The Greek text was translated into Latin in 1531, and in this form the work had a profound influence on Vesalius and *other great Renaissance anatomists Though Galen had* some knowledge of human anatomy, especially of the bones, most of his dissection was done on the rhesus monkey and the Barbary ape, in which many parts are greatly different from their counterparts in man Professor Singer has not only provided a scholarly translation of Galen's text, but he has also identified wherever possible the structures mentioned, and has given them their modern anatomical names

The book, which is illustrated, is a basis for the study of the sources available for the foundation of modern anatomy It has been published for the Wellcome Historical Medical Museum

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Surgery of the Ambulatory Patient (3rd ed Philadelphia J B Lippincott London Pitman Medical Publishing 1955 Pp 866 96*s*)—This book from the University of Pennsylvania is divided into five sections Hrant H Stone describes anæsthesia, with particular attention to local and regional infiltration E J Pulaski deals with antibiotics and sepsis, and gives a refreshingly common sense exposition of the relations between organism, antibiotic, and patient H M Burros discusses urological conditions, and *Louis* Kaplan fractures and dislocations The main author, *L K* Ferguson, coordinates and completes the work with descriptions of techniques and equipment, soft tissue trauma, tumours, and a variety of lesions arranged according to the regions in which they arise It is an impressive parade of the types of case treated in the outpatient departments of the Pennsylvania University hospitals

The emphasis is on conditions which *the author* and his contributors have treated as ambulatory, but they allow themselves to discuss those which can *sometimes* be treated in the ambulant, and also similar conditions, to be distinguished from them, which require bed rest and admission to hospital More and more conditions are now being treated with the patient out of bed, so that there may soon be no limits to a book with this title The surgical reader will draw his own line between what he treats in outpatients and what he admits to hospital, and in this country he will probably include such conditions as flexor tendon suture, thyroglossal cyst, and supraspinatus bursa in those he prefers to keep under his own observation The advantages of early ambulation have to be balanced against the fact that rest is essential to tissue healing as it is to the resolution of inflammation

Individual surgeons will disagree with some of the details in this book, but, read with discrimination, it will be very useful in those hospitals where outpatient surgery is highly developed and under experienced supervision It includes a number of conditions, some of them not uncommon, such as mucous cyst of the nail fold, which have not, so far as we know, been described elsewhere in surgical literature Illustrations are copious clear, and often beautiful Advice on treatment is detailed and practical The catalogue of pathological conditions is exhaustive Lippincott's continue their policy of printing each page in two columns, and have produced the whole work accurately, generously, and attractively Not only those concerned with outpatient and accident surgery, but all general and orthopædic surgeons, will find something of interest and value in it

TABLE I—PATIENTS WITH DISORDERS GIVING RISE TO VOMITING IN PREGNANCY REQUIRING ADMISSION TO HOSPITAL, 1938–53

Disorder	No of cases	Disorder	No of cases
Pyelitis and urinary tract infections	72	Breech presentation	2
Pre eclampsia	7	Subarachnoid hæmorrhage	1
Diaphragmatic hiatus hernia	7	Hypertensive encephalopathy	1
Peptic ulcer	5	Cerebral thrombosis	1
Gastritis	7	Otitis media	1
Gastro enteritis	1	Influenza	1
Appendicitis	2	Pneumonia	2
Cholecystitis	2	Bronchitis	2
Pylorospasm	1		
Intestinal obstruction	3	Total	130
Infective hepatitis	2		
Constipation	2		
Accidental antepartum hæmorrhage	5		
Degenerating fibroid	3		

Of the 453 patients with hyperemesis, 305 lived in Aberdeen, they were studied separately because it was possible to calculate the incidence of the condition in that city The figures, of course, relate only to cases sufficiently severe to warrant admission to hospital, although many relatively mild cases were admitted, many more of similar severity may have been treated successfully at home, especially in the earlier years

All maternal deaths from hyperemesis in North east Scotland between 1931 and 1953 were also studied

Results

INCIDENCE

Table II shows the average number of patients with hyperemesis admitted per year and the percentage of cases in which pregnancy was terminated

These figures suggest that the condition became less common and less severe between 1940 and 1948, and this is confirmed by the data for Aberdeen in table III In Aberdeen the rate of admissions fell sharply from 10 per 1000 births in 1938 to less than 3 per 1000 in 1940, and it remained low until 1949, when the pre war level was almost regained, since then the rate has fluctuated between 6 and 10 per 1000 births

Pregnancy was terminated in 7 cases (13 7%) in 1938–39, but in the five year period 1940–45 only 3 pregnancies were terminated (3 8%) Since 1949 the proportion of pregnancies terminated has risen again, but it is still a little lower than the pre war rate Over the whole period, the rate of admissions due to hyperemesis in booked cases was 7 7 per 1000 births in primigravidæ, and 9 9 in multigravidæ

TABLE II—PATIENTS ADMITTED TO HOSPITAL WITH HYPEREMESIS, BY YEARS

Years	Patients admitted with hyperemesis	
	Av no per year	Pregnancies terminated (%)
1938–39	33	12
1940–45	19	6
1946–48	25	8
1949–53	39	14

Age and parity did not appear to be important factors, but the condition was commonest in third to sixth pregnancies

RESPONSE TO TREATMENT

The results are summarised in table IV

Booked Cases—In 67% of primigravidæ and in 60% of multigravidæ, simple measures led to rapid recovery, the remainder required more active treatment, including fluid replacement per rectum or intravenously 2 of the 99 primigravidæ aborted spontaneously, and in 1 the pregnancy was terminated because of the persistence of severe vomiting Of the 144 multigravidæ 1 aborted and in 4 pregnancy was terminated

Emergency Cases—Only 43% of primigravidæ and 34% of multigravidæ responded to simple measures, as in the booked cases, the multigravidæ were more ill and difficult to cure than the primigravidæ

7 of the primigravidæ and 14 of the multigravidæ aborted spontaneously Termination of pregnancy was necessary in 10% of the primigravidæ, and in 20% of the multigravidæ

As table III shows, 11 out of 6221 pregnancies in Aberdeen in 1952–53 were terminated because of hyperemesis, 9 of these were in multiparæ

MATERNAL DEATHS

Of the 453 women admitted to the Aberdeen Maternity Hospital because of hyperemesis in 1938–53, 5 died, but only 2 of the deaths were attributed to hyperemesis, the other 3 being due to difficult labour, pulmonary tuberculosis, and eclampsia

TABLE III—DATA ON ABERDEEN PATIENTS ADMITTED TO HOSPITAL WITH HYPEREMESIS GRAVIDARUM, 1938–53

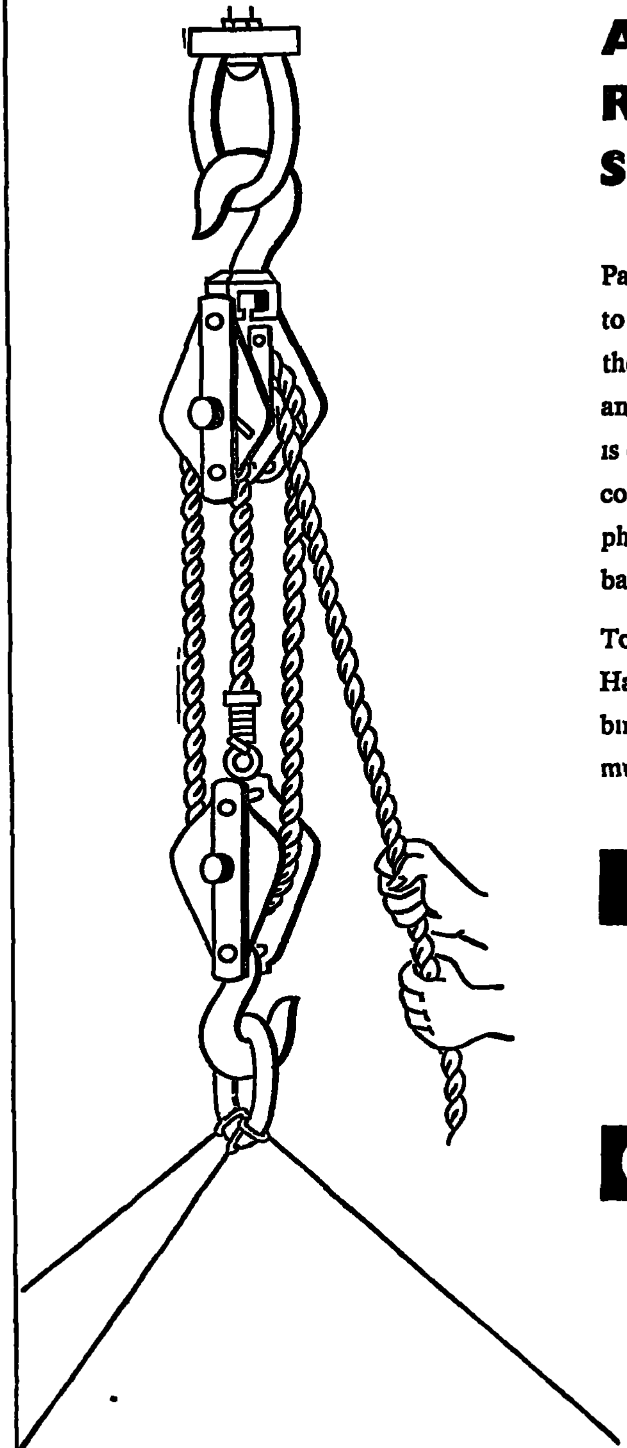
Year	Total no of deliveries in Aberdeen	Patients admitted with hyperemesis								
		Primigravidæ			Multigravidæ			Total	Rate per 1000 births	Percentage of pregnancies terminated
		No	Active treatment	Pregnancy terminated	No	Active treatment	Pregnancy terminated			
1938	3133	14	8	1	18	5	2	32	10 2	13 7
1939	3089	3	3	—	16	11	4	19	6 1	
1940	2918	2	—	—	6	2	—	8	2 7	3 8
1941	3003	6	1	1	8	3	—	14	4 6	
1942	2993	5	2	—	11	4	—	16	5 3	
1943	2972	4	—	—	12	2	1	16	5 3	
1944	3057	7	3	—	7	2	—	14	4 5	
1945	2901	5	1	—	6	5	1	11	3 7	
1946	3877	6	1	—	13	4	—	19	4 8	4 1
1947	4231	9	3	—	6	3	1	15	3 5	
1948	3096	7	4	—	7	3	1	14	3 8	
1949	3369	11	3	—	21	11	—	32	9 5	8 6
1950	3300	6	2	—	13	7	—	19	5 7	
1951	3094	9	1	—	13	3	—	22	7 1	
1952	3082	9	4	1	14	4	3	23	7 3	
1953	3139	10	3	1	21	10	6	31	9 8	
All years	51,854	113	39 (34 5%)	4	192	79 (40 1%)	19	305	5 8	7 7

The details of the 2 fatal cases of hyperemesis are as follows

Case 1—In 1938, a primigravida, aged 32, and 15 weeks pregnant, was admitted with a history of vomiting for 8 weeks She was wasted, jaundiced, and dehydrated, and she had tachycardia and was mentally confused Hysterotomy was performed after 7 days' treatment in hospital, but she died

TABLE IV—RESPONSE TO TREATMENT OF BOOKED AND EMERGENCY CASES ADMITTED WITH HYPEREMESIS GRAVIDARUM, 1938–53

Type of case	No of cases	No of patients recovered		No of abortions		Maternal deaths	Stillbirths and neonatal deaths	No data on outcome
		Without active treatment	With intravenous and rectal fluid	Spontaneous	Induced			
Booked								
Primigravidæ	99	67 (67 8%)	29	2	1	2	7	6
Multigravidæ	144	87 (60 4%)	50	1	4	1	7	3
Emergency								
Primigravidæ	60	26 (43 3%)	27	7	6	2	7	28
Multigravidæ	150	52 (34 6%)	46	14	34	—	5	64



Avoiding Resistant Strains...

Particular emphasis has been given to the use of combined chemotherapy in the treatment of infections, and it has been realised that there is considerable merit in the judicious combination of antibiotics and sulphonamides in the prevention of bacterial resistance

To aid the Practitioner, Allen & Hanburys have introduced two combinations of drugs known to exhibit mutual reinforcement

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a chronic infective granuloma, but on careful inspection a thin bluish line or area can often be seen at the periphery, either at the tip of the finger or at the lateral edge of the nail. This characteristic pigmentation is said to be pathognomonic of malignant melanoma (Pack 1952).

Case-records

The first 3 cases were seen at a clinic for infections of the hand.

Case 1.—A housewife, aged 60, first attended the hand clinic in June, 1955. She had suffered from acrosclerosis for many years, and she had had many infections around the nails. About a year ago she had noticed that the right thumb was sore around the tip of the nail, which bled and discharged some pus. This sequence had been repeated at intervals up to about six weeks previously. On this occasion the condition had not subsided, and the thumb had started to swell, bleed freely, and smell unpleasantly.

On examination in the hand clinic, the right thumb distal to the interphalangeal joint was almost replaced by necrotic granulation tissue, most noticeably over the site of the nail bed. Seropurulent fluid oozed from the granulations, which were covered with crusts. The other fingers showed trophic changes at their tips and the nails were stunted and blackened. There were some soft glands in the axilla. Carcinoma of the thumb was provisionally diagnosed and a biopsy specimen was taken. This was reported as showing hyperkeratinisation due to non-specific inflammation with no evidence of malignancy. A further more generous biopsy specimen, however, confirmed the clinical diagnosis of malignant disease, and was reported as a multicentric squamous cell carcinoma grade I–II. The thumb was amputated through the carpometacarpal joint as this was the most distal area free from growth on frozen section. Postoperatively the enlargement of the axillary glands rapidly subsided.

Case 2.—A housewife, aged 76, was seen in the hand clinic in 1948 with a history of a penetrating injury to the dorsum of the web of the first left space one year before; this had never completely healed. A few weeks before it had become painful and she had treated it herself with poultices.

On examination, there was a hard plaque on the dorsum of the first web on the left hand. It was ulcerated with a rolled edge and there was a scab overlying the ulcer; the surrounding tissues were inflamed. Biopsy showed a squamous-cell carcinoma and the lesion was widely excised. When last seen early this year, the patient was well with no sign of recurrence. When referred to the clinic this was an obvious tumour but its early evolution was like that of an infected wound and its chronicity would have suggested a retained foreign body.

Both these cases are typical examples of squamous carcinoma of the fingers. During most stages of the type exemplified by case 1 the lesion may be mistaken for a chronic infection with massive granulomatous changes, and it is important to realise that biopsy may not at first show the true nature of the lesion, partly because of changes due to the overlying chronic infection.

Case 3.—This patient, aged 30, nine months previously had sustained a minor injury to the interphalangeal joint of his right thumb. About a month later he had noticed a small dark blue line at the base of the thumb nail. The line had slowly extended to the distal end of the nail, and the nail had begun to thicken and split until a V-shaped cleft had formed in the nail through which "flesh" began to protrude. The thumb had become painful for the first time. Three months previously he had been referred to another hospital where chronic infection of the nail bed had been diagnosed and the nail removed.

On examination in the hand clinic the nail and nail bed of the right thumb were almost replaced by "granulation tissue" covered with pus and dried blood with the remains of deformed nail at the side of the mass (see figure). On close inspection there was a faint bluish discoloration at the distal end of the mass. Radiographic examination showed rarefaction of the distal phalanx but no signs of bone erosion, and biopsy confirmed the diagnosis of malignant melanoma. The thumb was disarticulated through the metacarpophalangeal joint. Gland biopsy showed no evidence of malignant deposits.

The next 2 cases were seen in other departments, and in both the initial diagnosis seems to have been chronic infection.

Case 4.—A motor mechanic, aged 53, attended with a history that about five months previously he had sustained an abrasion to his left forefinger which had failed to heal despite local applications.

On examination, there was an ulcer measuring 1 × 1/2 in on the radial side of the left index finger, involving the proximal phalanx. It had a raised edge with red granulations overlying a hard base. There was some slough overlying the granulations; it was mobile on the underlying tissues and painless. Biopsy showed a grade I–II squamous cell carcinoma. The index finger was amputated together with the head of the metacarpal.

Case 5.—This patient was initially treated elsewhere, but was referred to the department of radiotherapy at this hospital. He was a man, aged 62, who had been found to have "eczematous ulceration around the right thumb nail with blackish pigmented patches in the skin around." This had been treated with sulphonamides, penicillin, and immobilisation but it had failed to heal; and three months later the terminal phalanx and the head of the proximal phalanx had been removed; the wound had healed well. Nine months afterwards two small firm subcutaneous nodules had appeared in the skin of the forearm, and biopsy of this lesion had shown a malignant melanoma. Metastases developed rapidly in his axilla, and he died shortly afterwards with multiple secondary deposits.

Discussion

My purpose is to draw attention to primary malignant disease of the fingers presenting as a septic lesion.

The precise incidence of these tumours is difficult to assess. Mason (1937) estimated that 10% of all skin cancers affected the hand, but Clarke (1944) indicated that only 4% did so. Clarke suggested that 5% of all cancers of the upper extremities were on the fingers. Bickel et al. (1943), in a review of 155 melanomas of the extremities, found that 6.5% arose from the nail beds of the fingers; and Pack et al. (1952) found that 1.3% of his series of 1222 melanomas of all sites arose in this situation.

It is important that these tumours should be diagnosed as soon as possible, since the prognosis, particularly of malignant melanoma, depends directly on the extent of spread of the growth before treatment is begun. Driver and MacVicker (1943), discussing subungual melanoma, estimated that the five-year survival rate was only 2% if lymph nodes were involved at the time of treatment, whereas nearly half the patients with no lymphatic metastases survived longer. The prognosis in squamous cell carcinoma of the fingers is excellent if the lesion is treated by excision before metastases occur.

It is clear from published reports that, as in the cases reported here, neoplasms of the fingers are still commonly diagnosed and treated as chronic septic lesions for long periods before their true nature is recognised. It cannot be too strongly emphasised that if a chronic lesion of a

Hormones and Breast Cancer

ALTHOUGH the endocrine control of mammary cancer was attempted, with initial success, sixty years ago, this method of treatment has yet to be widely used Increasingly radical surgery and more intense radiation have been urgently pursued for decades, with little improvement in survival rates and often only questionable benefit to the patient Yet these measures are still the only relief offered to the great majority of women with breast cancer

Increasing knowledge of the factors affecting the growth of mammary tumours, and the evolution of endocrinology, have gone hand in hand, so that today the clinician has a large volume of experimental fact on which he can draw It has been shown that many breast tumours depend for their maintenance and continued growth on those hormonal factors which control the growth of normal breast epithelium The maturation and rupture of the ovarian follicle, with its waxing and waning secretion of the steroid hormones œstrogen and progesterone, follows a similar rhythmic rise and fall in the secretion of the pituitary gonadotrophins Thus, removal of the ovaries destroys the synergistic action of the pituitary and ovarian hormones responsible for the stimulation of breast growth and consequently causes regression of mammary tumours which are dependent on these mechanisms As the original work of Woolley [1] demonstrated, the adrenal cortex can secrete steroid ovarian hormones after ovariectomy and can thus make up for their deficiency in the stimulation of breast growth It was this work which prompted the courageous and effective technique, introduced by Huggins and Bergenstal,[2] of total adrenalectomy with or following ovariectomy, this operation once more removed the stimulus to malignant breast growth and produced rapid though temporary regression of symptoms in about half the patients with advanced metastases This treatment was successfully adopted in this country, notably by Cade [3] and Pyrah and Smiddy [4] But the operative mortality is appreciable, and by no means all patients are relieved of symptoms for long enough to justify the operation It remains to decide whether it should be reserved for patients in an advanced stage of the disease Despite the removal in this way of the only glands known to produce steroid hormones, œstrogens can still be excreted in the urine,[5] and this activity sometimes persists even after hypophysectomy There is as yet no adequate evidence to show whether or not adrenal rests, normally encountered on occasion along the line of the urogenital tract, are responsible for this activity, but failing such an explanation it seems that an additional source of steroid hormones must be sought

Another approach to abolition of circulating steroid hormones is hypophysectomy, which will deprive the target organs (the ovaries and adrenals) of the essential trophins secreted by the pituitary [6] This operation has the virtue of removing at the same time pituitary secretions such as mammatrophin (prolactin) and somatotrophin (growth hormone), which are important factors in breast development and secretion [7] According to Russell's [8] recent report, division of the pituitary stalk—a less severe operation than complete hypophysectomy—produces almost total loss of pituitary secretion by cutting off the blood supply and causing selective necrosis of the anterior pituitary This operation might well be substituted for the more severe one Another alternative is irradiation of the pituitary Forrest et al [9] implanted radon seeds into the pituitary fossa by means of a cannula passed through the nostril and sphenoidal sinus, but damage *to the optic tract was a serious complication in* 4 out of their 33 cases Other techniques of irradiation are being investigated which may reduce the risks of blindness In his communication on p 671 Mr Davies describes a method of injecting radioactive fluid into the pituitary fossa But irradiation does not with certainty destroy all the endocrine cells, and methods which achieve this aim will be more effective

Other hormonal factors are certainly of fundamental importance in the growth of breast cancer and it is possible that what are now regarded as autonomous tumours may in fact be dependent on secretions as yet unidentified One known hormone stimulating breast growth, however, is mammatrophin or prolactin Much less is known about it than about steroid hormones, but it is encouraging to know that a method has been developed for the estimation of this substance in urine,[5] and that it is being applied to the investigation of the hormonal status of cancer patients So much concerning these mechanisms is still unknown that we may be guilty of neglecting what we do know Certainly this seems *to be* the case so far as the relation of the thyroid gland to breast growth is concerned It has been suggested by Loeser [10 11] for many years that hypothyroidism is conducive to and aggravates breast cancer, and there *is some statistical evidence* to support this Experimentally, it is known that thyroid deficiency sometimes permits a more florid growth of the breast,[12] and there is fragmentary evidence [13] that pituitary adenomas consequent on thyroid deficiency can cause increased stimulation of breast growth It seems that the simple trial of thyroid administration to women with breast tumours would be easy, cheap, not obnoxious to the patient, and possibly beneficial

While the endocrinological approach offers hope that the fundamental mechanisms of mammary carcinogenesis may finally be unravelled, *it is* obvious from clinical experience and from the detailed observations of Foulds [14] that "progression" to an autonomous state takes place in breast cancer To interfere with hormonal mechanisms in the ways we are *doing today seems to halt tumour* growth and spread for a time only If treatment was advised before the patient's condition had seriously deteriorated and before the tumour had "progressed" to a considerable degree of autonomy, then the delay to further spread might at least be longer Before autonomy is completely established, however, the lot of the patient can be improved, and, as Dr Foss shows in his article

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[1] Woolley G W Recent Progress in Hormone Research New York 1950 p 383

[2] Huggins C Bergenstal D M *Cancer Res* 1952 12, 131

[3] Cade S *Proc R Soc Med* 1955 48 549

[4] Pyrah L N Smiddy F G *Lancet* 1954 i 1041

[5] 53rd Annual Report of the Imperial Cancer Research Fund 1956 p 13

[6] Luft R Olivecrona H *J Neurosurg* 1953 10 301

[7] Ciba Foundation Colloquia on Endocrinology, 1952 4, 381

[8] Russell D S *Lancet*, April 21 1956 p 466

[9] Forrest A P M, Peebles Brown D A Morris, S R, Illingworth C F W *Ibid* April 14 1956, p 399

[10] Loeser A A *Brit med J* 1954 ii 1380

[11] See *Lancet* 1955, i 491

[12] Trentin J J Hurst V Turner C W *Proc Soc exp Biol, N Y* 1948 67 461

[13] Furth J *Cancer Res* 1953 13 477

[14] Foulds L *Ibid* 1954 14 327

TABLE I—GRUEL FRACTIONAL TEST-MEALS IN CUSHING'S SYNDROME (FREE HCL IN CLINICAL UNITS)

Case no *	Untreated											After adrenalectomy										
	Pesting	Hours after giving gruel										Resting	Hours after giving gruel									
		¼	½	¾	1	1¼	1½	1¾	2	2¼	2½		¼	½	¾	1	1¼	1½	1¾	2	2¼	2½
2												0	0	0	0	5	10	15	20	20	0	25†
3	0	0	0	18	0	48	50†	30	40	40	35	0	0	0	0	0	10	20†	10	15	15	10
4												0	0	0	0	15	20	20	22†	22†	15	20
5	0	0	0	0	0	0	5	0	10	10	15†											
6	5	0	55	100	105†	95	90	80	75	75	75	55	0	0	0	0	5	5	10	25†	0	0
7	30	15	0	0	35	70	105	95	100	80	115†	15	0	0	5	25†	15	20	20	25†	0	10
8												0	0	0	5	8	12†	12†	8	5	0	0
9	0	5	15	20	25	40†	35	15	15	5	15	15	0	0	3	5	20	40	45†	40	28	22
10	30	15	35	60	70†	60	45	40	30	40	55											
11	55	20	25	30†	25	12	12	12	12	10	10											
12	8	8	9	25	32	39	41	60	61†	60	52											
Mean	16	8	17	32	36	46	48	41	43	40	46	12	0	0	2	8	13	19	19	22	8	12

* Numbers 2–6 are those used by Beck et al (1954)

† The highest concentration after giving gruel

discontinued In 4 only was the test done both before and after operation

The excretion of reducing corticoids (Broadbent et al 1953) and of 17-hydroxycorticoids (Reddy et al. 1952) was measured in twenty-four-hour specimens of urine without corticotrophin stimulation

Results

Fractional Test meals in Cushing's Syndrome (table I and fig 1)

Untreated —The average free-acid curve rose above the upper limits of normal after three quarters of an hour and remained high for the rest of the test In 2 cases it rose to over 100 clinical units In 1 (*case 5*), who was very ill and had a slightly raised blood-urea level (51 mg per 100 ml), a very low curve was obtained The mean highest concentration after giving gruel—i e excluding the resting juice—was 61 units None of the patients showed evidence of peptic ulcer

TABLE II—URINARY EXCRETION OF REDUCING CORTICOIDS IN FIVE HYPERCHLORHYDRIC PERSONS

Highest concentration of free acid in gruel fractional test meal (clinical units)	Reducing corticoids (mg per 24 hr) (normal range 1 1–2 1)
62	6 6
100	0
80	12 4
78	5 6
80	3 9

After adrenalectomy the average free acid curve remained near the lower limit of normal throughout the test The mean highest concentration after giving gruel was 25 units, which is significantly lower than that before operation (t = 2 32, D F = 13, P = <0 05) In the 4 cases in which preoperative and postoperative tests were made there was a considerable reduction in the concentration of acid after adrenalectomy The acidity of the resting juice was not altered significantly

Correlation between Gastric and Adrenocortical Secretions

Preliminary investigation showed that the urinary excretion of reducing corticoids was often increased in hyperchlorhydric patients (table II) For this reason a controlled investigation of the excretion of 17-hydroxycorticoids (which was thought to be a more specific measure of adrenocortical function) in relation to gastric secretion was undertaken The highest concentration of acid obtained after giving gruel was plotted against the twenty four hour excretion of 17-hydroxycorticoids (fig 2) Though no significant correlation was found between the two variables, most of the patients who had high 17 hydroxycorticoid excretion (including several without Cushing's syndrome) also had a high concentration of gastric acid On the other hand, a high acid concentration was often associated with normal or zero excretion of 17-hydroxycorticoids

Discussion

It seems clear that the gastric hypersecretion in Cushing's syndrome is caused by an excessive production of steroids by the adrenal cortex, for it is abolished by adrenalectomy, and similar hypersecretion is produced by administering corticotrophin or cortisone Although fatal bleeding from an acute gastric ulcer (Swan and Stephenson 1935) and from an unknown source (Knowlton 1953) has been reported, duodenal ulceration does not appear to have been observed in Cushing's syndrome, and it was not present in our cases This is surprising in view of the gastric hypersecretion and the frequency with which ulceration follows the therapeutic use of pituitary and adrenal hormones

The high level of excretion of reducing corticoid and 17-hydroxycorticoid excretion in some hyperchlorhydric patients suggests that the level of adrenocortical activity may be one factor influencing gastric secretion, even in the absence of overt disease of endocrine glands There

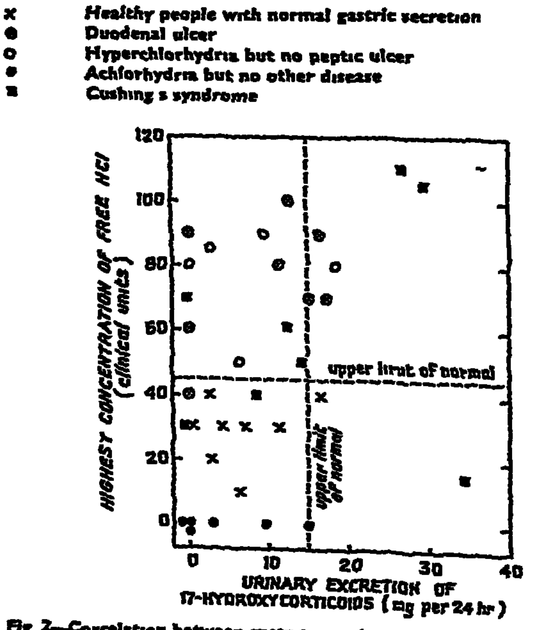

Fig 2—Correlation between gastric secretion and urinary excretion of 17 hydroxycorticoids

Though there is no correlation in general, most of those who had high 17-hydroxycorticoid excretion were hyperchlorhydric home nurses The very mention of these subjects makes it obvious that modern public-health practice cannot be successfully carried out in isolation it requires serious cooperation, not only between the branches of our profession but with a host of outside agencies as well The society's council includes a number of doctors who are not themselves in the public-health service, and its minutes show the great importance it attaches to representation on other bodies, lay and medical, and to joint meetings to discuss matters of common interest Similarly, many of the fellows themselves are making every effort to increase collaboration with their colleagues in the hospitals and in general practice The barriers, indeed, are breaking down at last, and this is one of the most hopeful aspects of post-war public health Let us trust that the years of disappointment are over, and that the Society will prove as adventurous at the beginning of its second century as it was at the beginning of its first

Annotations

SMOKING

ON Monday the Minister of Health was questioned in the House of Commons about the association between tobacco smoking and lung cancer The tenor of his replies (see p 696) was profoundly unsatisfactory He might have used the occasion to state the danger categorically and to undertake to bring this to the notice of the public by other means Instead he refused to initiate a publicity campaign and suggested that "the extent of the problem should be neither minimised nor exaggerated" *Within an hour the tobacco companies* had issued a smoke screen thick enough to obscure even a much plainer statement

If any other poison sold for public consumption were believed to be causing some thousands of deaths each year, its sale would be suppressed One reason why this step has not been taken in the case of tobacco is that any Government initiating such a measure would fall on the morrow as a nation we are tobacco addicted A second reason is that if the Treasury were denied the sum of £707 million a year now being yielded by the tobacco duty our fiscal policy would have to be radically re-shaped There is at present no chance—or, as the smokers among us would put it, no risk—that the sale of tobacco will be controlled

But this does not signify that we should accept the status quo In London nearly all those engaged in investigating the long-term effects of tobacco on health or specialising in the treatment of lung cancer gave up smoking some time ago We must not rest content until the whole community has understood the facts that have led this small group to change their habit Occasional statements in Parliament do not reach, or are not long remembered by, most people In 1954 the then Minister of Health issued a warning[1] which was hardly less explicit than that uttered this week Yet since then we have all often heard well educated people ask whether there "is anything in this tobacco scare" Their ignorance may be due partly to reluctance to learn, but partly without doubt it is due to the mortal unwillingness to accept anything which has not been said again and again

A decision to control the sale of tobacco would be administrative—in other words, political But a decision to impress the hazards on the public may properly be regarded as medical Such a campaign would yield no rapid results heavy smoking bears none of the stigma of heavy drinking, and an exchange of cigarettes is as *much part of the established social* order as an exchange of handclasps But a useful start has already been made For instance, in a recent B B C television programme a doctor set out the facts with admirable objectivity Beyond such individual efforts, the Central Council for Health Education might suitably issue pamphlets for distribution by general practitioners and the British Medical Association might again use the occasion of its annual representative meeting—always closely watched by the lay press—to rehearse the facts If such approaches prove ineffective doctors might band themselves together to bring home the risks to their patients This would be a fine exercise in preventive medicine—and incidentally in public spirit Few patients with bronchial carcinoma could then say they had not been told how this might have been averted

ILEOSTOMY

BETWEEN 1928 and 1952, 871 patients were treated for ulcerative colitis at the Lahey Clinic, 413 (47%) being submitted to surgery, during this period the mortality for the ileostomy fell from 18 to 5% Dr Neil Swinton gave these figures in a discussion by the proctology section of the Royal Society of Medicine on May 2 He dealt more fully with an analysis, by Colcock and Mathiesen, of their more recent cases between 1946 and 1954, 307 patients were submitted to ileostomy and colectomy, including operative and late deaths the mortality was 11% (34)—a figure which closely matched that given by Mr B N Brooke of 12% (15 deaths in 126 patients) Dr Swinton and Mr Brooke agreed that intestinal obstruction was a common sequel, this complication developed after discharge from hospital in 38 of 307 Lahey Clinic patients and in 9 of Mr Brooke's 126 patients

The ileal stoma calls for considerable care at the initial operation, and the technique of its construction is evidently becoming standardised In all centres the importance of fixation of the mesentery in order to avoid ileostomy prolapse or recession is appreciated At the Lahey Clinic, as elsewhere, a separate stab wound is now found to be more satisfactory than the main incision for accommodating the stoma, eversion of the mucosa *and direct suture to skin* is also becoming widely practised Complications such as fistula, prolapse, and recession, which render the stoma inefficient, call for operative revision, a further operation for excision of the whole or part of the bowel provided an opportunity for such revision in 9, and a separate operation was required in 4, of 106 cases in which Mr Brooke did the original ileostomy

The maintenance of electrolyte balance is of vital importance in reducing mortality *after ileostomy* Sodium is lost in direct proportion to the volume output, which may be as much as 3 litres in twenty-four hours shortly after operation, decreasing to 500 ml later, Brooke has found its concentration to be roughly 300 m eq per litre falling to 150 m eq per litre from the *long* established stoma Accordingly sodium requirements can be estimated from the daily volume excreted through the ileostomy

When the stoma is efficient, so *that an* adherent bag may be applied to it, patients express satisfaction with an ileostomy, even five years or more after its institution, and they remain at full and arduous work Nevertheless some maintain that an ileostomy is unnecessary Mr Stanley Aylett has undertaken ileorectal anastomosis in 38 patients, of whom 1 died, he has found that the state of the rectum improves after anastomosis, though healing, judged histologically, is not perfect This finding is supported by the *experiences of* Mr Lawrence Abel and Mr A Dickson Wright A sharp division of opinion

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[1] *Lancet* 1954 i 409

COMMENT

We suggest that in this patient the association between he spinal anæsthetic and the subsequent paralysis is rrefutable. A latent period of seven days before the nset of symptoms is not uncommon, and it distinguishes his type of injury from that following direct damage to he spinal cord. The progression of the disease is due to radual constriction of the cord by the extension of ibrous adhesions, and consequent impairment of the lood supply. An erroneous tentative diagnosis of pinal tumour, followed by laminectomy which establishes the correct diagnosis is a common sequence in cases of adhesive arachnoiditis.

Discussion

Adhesive arachnoiditis is not confined to patients who have had spinal anæsthesia.

As long ago as 1909 Sir Victor Horsley reported a series of 21 patients in whom the gradual onset of weakness in one leg was ultimately followed by paraplegia. Adhesive arachnoiditis was diagnosed usually at laminectomy, because the clinical features were indistinguishable from those of spinal-cord tumour. Characteristically there were dense adhesions obliterating the subarachnoid space in the mid dorsal region and extending caudally. The spinal cord looked shrunken, and in many cases it was compressed by cystic accumulations of C.S.F. In addition, there was often evidence of ischæmic changes in the cord substance.

In 1936 Elkington published a review of 41 cases with similar symptoms and signs. He admitted that the cause of the adhesive arachnoiditis was obscure but suggested that trauma, infection, or syphilis could be responsible. In 18 patients, however, he was unable to show any cause. Elkington emphasised that the essential change was the formation of adhesions and cysts in the subarachnoid space, and he drew attention to the poor prognosis in patients with secondary ischæmic changes in the spinal cord.

Adhesive Arachnoiditis Following Infection

More recently Turner (1948) has shown that diffuse adhesive arachnoiditis may complicate cerebrospinal meningitis either during the acute phase or in the convalescent period. Of the 13 cases described, bacteriological evidence of meningococcal infection was obtained in 9, but in the remainder the diagnosis was based on clinical evidence.

The single case reported by Barker and Ford (1937) is interesting in that the arachnoiditis complicated acute benign lymphocytic meningitis. Improvement followed laminectomy, but after an attack of influenza the patient again became paraplegic.

Attention was first drawn to the relation between virus infections and adhesive arachnoiditis by Horsley (1909), who described paraplegia following an attack of herpes. Many years later Brook et al. (1936) reported 3 cases of paraparesis after spinal anæsthesia and suggested then that the paraparesis was caused by a virus infection superimposed on the effects of spinal anæsthesia. The suggestion that a subclinical virus infection might precipitate adhesive arachnoiditis after spinal anæsthesia was again made by Terp (1950) when describing 5 cases; in 4 the anæsthetic had been a 1/1500 "light" solution of cinchocaine hydrochloride and in the 5th a 1/200 solution of 'heavy' cinchocaine hydrochloride. Thorough investigation failed to establish the cause of the arachnoiditis, but Terp pointed out that, although his technique had been the same for many years, all the cases occurred within a period of six months. Such a grouping certainly suggests an infection with a long incubation period, and in the absence of positive evidence a virus infection would appear most likely.

Adhesive Arachnoiditis Following Spinal Anæsthesia

After the administration, in the same operating-list, of a 1/1500 "light" solution of cinchocaine hydrochloride to 2 patients who later became paralysed, judgment was given in the High Court that this complication resulted from contamination of the anæsthetic by phenol (*Times* 1953). It was postulated that contamination was caused by the permeation of phenol through minute cracks in the anæsthetic ampoules. This judgment was far from generally accepted by anæsthetists; a subclinical virus infection seems as likely a cause of the complication as phenol contamination. It is, of course, possible that the damage was caused by the anæsthetic alone—an explanation for which there is considerable clinical and experimental evidence.

Davis et al. (1931) gave clinical doses of cinchocaine and procaine intrathecally to dogs, in which unequivocal pathological changes in the subarachnoid space developed; the most constant change was a meningeal reaction, which was found in every animal. The inflammatory response was accompanied by thickening of the arachnoid membrane, which contained collections of proliferated arachnoidal cells.

Further investigation by Lundy et al. (1933) established that procaine has a direct toxic effect on the spinal cord of cats and that the concentration of the drug is as important as the total quantity administered.

Lundy's work was confirmed by MacDonald and Watkins (1937), who, also working with cats, obtained conclusive proof that the incidence of paralysis after spinal anæsthesia by procaine was related to the concentration of procaine introduced into the theca. They pointed out that in the cat the bulk of spinal nervous tissue was large in relation to the space within the bony canal and that therefore the volume of fluid available for diluting the anæsthetic was small. They suggested that in man paralysis was usually avoided because of the rapid dilution of the anæsthetic by C.S.F.

"*Light*" *cinchocaine anæsthesia.*—Clinically, since the publication of Hewer's account (1933) of adhesive arachnoiditis after the use of "light" cinchocaine, many similar cases have been reported. In particular Thorsen (1947) investigated the complications of spinal anæsthesia in a series of 2493 cases. 1749 of the patients were given procaine, and in none of these did adhesive arachnoiditis develop; but among the 744 patients to whom "light" cinchocaine was administered arachnoiditis developed in no less than 6. The likelihood of "light" cinchocaine anæsthesia being followed by arachnoiditis is also shown by Terp's (1950) report, already mentioned.

The most likely explanation for the increased risk of injury from "light" cinchocaine is probably related to the volume used. When 10–20 ml. of anæsthetic solution is injected into the spinal theca, there is considerable risk of displacement of C.S.F., so that the membranes and cord, particularly in the immediate vicinity of the injection, are bathed in a solution which remains relatively undiluted.

Continuous spinal anæsthesia.—A further group of patients in whom adhesive arachnoiditis is particularly liable to develop are those exposed to continuous spinal anæsthesia. This involves continuous or repeated injections of small quantities of the anæsthetic, so that a limited area of the spinal cord and meninges tends to be in prolonged contact with the potentially noxious solution.

Kennedy et al. (1950) reported 12 cases of severe spinal-cord paralysis caused by spinal anæsthesia, including 5 cases of adhesive arachnoiditis following continuous spinal anæsthesia. A year later Woods and Franklin (1951) reported progressive spastic paraplegia in a patient who had had continuous spinal anæsthesia, and who died from pulmonary embolism four days after laminectomy.

At necropsy adhesive arachnoiditis was found; the pathological changes were confined to that portion of the cord and meninges which had been in contact with the anæsthetic. It was concluded that the cause of the spastic paraplegia apparatus Dr A Lacassagne points to some of the events that took so startling a turn in 1945 when "radiobiology ceased to be a discipline interesting only a small number of experimenters and medical specialists", and finally Dr James T Case, whose radiological experience goes back to 1903, looks briefly at some of the more prominent developments in diagnosis and therapy

From year to year these exciting happenings have been recorded and discussed in the pages of the *British Journal of Radiology*, which has deservedly won a high place in the world's scientific literature We wish it, and its editors and contributors, many more successful jubilees

COLONIAL-SERVICE CANDIDATES FOR THE F R C S

TOWARDS the end of last year Lord Malvern, F R C S, Prime Minister of the Federation of Rhodesia and Nyasaland, discussed with Sir Harry Platt, P R C S, the position of candidates from the Colonial Medical Service for the final examination for the F R C S Lord Malvern pointed out that the new regulations require a candidate to complete two years' appointments in recognised hospitals, including six months' service as casualty officer These regulations virtually preclude any doctor in the Colonial Medical Service from taking the fellowship unless he happens to have worked in recognised hospitals before joining the service

Subsequently the council of the college agreed that candidates from the Colonial Medical Services who can show that their experience has been at least equivalent to that obtained in two years at recognised hospitals shall be regarded as special cases In a letter to Lord Malvern, the President suggested that candidates who wish to be considered in this way should provide a brief description of the number and types of surgical patients dealt with by them, together with special references to operative experience and opportunities for close liaison with the hospital pathological department, and that each application be supported by the medical director of the territory Such candidates will be eligible to apply for examination after two years, but, said the President, in many cases no doubt they will need longer surgical experience

The discussions and correspondence are to be set out more fully in the Central African Journal of Medicine

SICKNESS AFTER ANÆSTHESIA

SICKNESS after a general anæsthetic is still common enough to leave quite a lot of patients with unpleasant memories of their operation Knapp and Beecher[1] have described some interesting investigations into this problem, and they have studied the value of certain anti-emetic drugs in a series of patients over 15 years of age who underwent practically every type of operation

They first differentiated between nausea, retching, and vomiting Nausea they defined as a subjective sensation of the desire to vomit but without any attempt at expulsive movements It is often accompanied by such objective symptoms as the secretion of saliva, sweating, an increase in the pulse rate, and variation in the rate, depth, and regularity of respiration, so that some attempt can be made to measure its severity Retching and vomiting, both active expulsive mechanisms, are differentiated by the results vomiting always produces some gastric contents, retching produces nothing, and they can be graded according to the number of times they take place and the duration of the episode

In Knapp and Beecher's series the sequence of anæsthesia was invariably nitrous oxide, oxygen, and ether, and it was chosen because it seemed likely to lead to more post anæsthetic sickness of all types than any other combination of agents, and it would therefore provide a reasonable trial for the three anti emetics These were dimenhydrinate ('Dramamine'), chlorpromazine ('Largactil'), and pentobarbitone sodium ('Nembutal') A controlled series of patients was investigated with these agents and with a placebo The problem of the placebo reactor was eliminated by giving each drug intramuscularly to the unconscious patient shortly before the end of the operation, moreover, the observations and their object were not made known to the patients All patients were studied closely and continuously for the first four hours after operation, and all were interviewed at the end of twenty four hours A large proportion were also observed frequently throughout the whole of this period

Knapp and Beecher showed that the incidence of sickness of all types after their chosen anæsthetic sequence was 82% In the placebo group they found that there was no difference in the incidence between the sexes during the first four hours after operation After this initial period, when the greater part of the ether had been exhaled and the patient was returning, or had returned, to consciousness, women had significantly more symptoms than men Age did not affect the issue except that those over 40 seemed to be most helped by an anti-emetic A further interesting result of the placebo studies refuted the widely held view that intraperitoneal operations—and the consequent visceral palpation—increase the incidence and severity of post-operative vomiting There was no evidence from these figures that intraperitoneal operations were more likely to produce complications of this sort than non abdominal operations

Chlorpromazine proved to be an effective anti emetic During the first four hours after operation 50 mg produced a significant reduction in nausea, retching, and vomiting, and this reduction continued for twenty four hours In fact, the 82% incidence fell to 59% This result was matched during the first four hours only by 150 mg of pentobarbitone Dimenhydrinate, in a dose of 100 mg, did not reduce the frequency of these symptoms at any time

There are other important effects, however, besides anti emesis The average awakening time of the patient was prolonged by all three drugs, chlorpromazine extending it by almost an hour But whereas patients were peaceful and sleepy when they awoke after chlorpromazine, they were much confused after pentobarbitone Moreover, all drugs in the doses given caused significant hypotension, chlorpromazine being the worst offender Hypotension appeared about forty-five minutes after giving chlorpromazine and usually persisted for two to four hours, though occasionally it lasted much longer

In establishing the effectiveness of chlorpromazine as an anti-emetic in these circumstances, Knapp and Beecher have given a timely warning that success can be achieved only at a cost In attempts to reduce such a common and unpleasant, rather than dangerous, complication of anæsthesia, the risk of less obvious but potentially more disastrous effects must be borne in mind

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Surgeon Vice-Admiral Sir SHELDON DUDLEY, K C B, F R C P, F R S, formerly medical director general of the Navy, died on May 6 at the age of 71

We also regret to announce the death on May 7 of Major-General Sir CUTHBERT SPRAWSON, C I E, F R C P, a former director-general of the Indian Medical Service

Prof KNUD FABER of Copenhagen, internationally known for fifty years for his work in gastro enterology died on May 2 at the age of 93

THE INDEX and title-page to Vol II, 1955, which was completed with THE LANCET of Dec 31, is published with our present issue A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W C 2 Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now

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[1] Knapp, M B Beecher H K *J Amer med Ass* 1956, 160 376

On examination the signs were typical of a hypoglycæmic attack and after the intravenous administration of 50% glucose the patient rapidly became normal physically and mentally.

He later stated that in the past two years he had had intermittent blackouts, which were increasing in frequency. The episodes usually took place before the midday or the evening meal and he related them to being tired or without food for some hours. The premonitory symptoms always included hunger, dizziness, and diplopia. If he felt an attack to be imminent sudden exercise would precipitate it but he found that it could be averted by taking glucose tablets or food. There was nothing relevant in the past or family history.

Investigations

An islet cell tumour of the pancreas was tentatively diagnosed and the patient was admitted for further investigations. *A glucose tolerance test* gave the results shown in fig 1. It was only necessary to continue the test for three hours to demonstrate the hypoglycæmia but usually the recommended duration of the test is six hours. The low fasting blood sugar level, the rapid fall from the peak following the ingestion of 50 g of glucose, and the final low value at the end of three hours suggested that glucose was rapidly removed from the circulation. *Liver-function tests* were normal.

Plasma insulin assay.—the patient was starved on two separate occasions: the first time to produce an attack, to observe any clinical changes immediately before the attack, and to ascertain the period of starvation required for this purpose; and the second time to obtain blood immediately preceding the attack for the plasma insulin assay. On the first occasion the patient was starved for nineteen hours. Towards the end of this time he became restless and was behaving like a mischievous child. Suddenly he became violent, shouting and screaming, and it required three men to restrain him. The clinical signs were again typical of a hypoglycæmic attack which responded immediately to intravenous glucose. The blood-sugar level was 53 mg per 100 ml while the attack was taking place. The second time the test was made the blood-sugar level was estimated at intervals (fig 2). When the patient showed signs of an impending attack blood was taken for the plasma insulin assay. An impending fit was diagnosed by comparison with the previous test in which the duration of starvation and the premonitory symptoms and signs had been noted. The plasma insulin assay, made by Dr J Vallance Owen and his colleagues at the Hammersmith Hospital, showed that there were 300 micro units per ml. compared with the normal value of 31–82 micro units per ml. On this result an islet-cell tumour of the pancreas was firmly diagnosed.

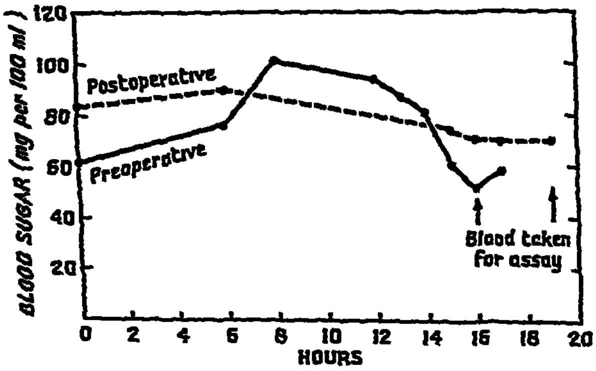

Fig 2—Plasma insulin assay

Operation

The pancreas was explored by Mr Norman Tanner on April 21, 1955. A pink tumour 2 cm in diameter was found near the surface of the pancreas and 5 cm from the tail. It was attached on its deep surface to the underlying pancreatic tissue but was easily enucleated. The remainder of the pancreas and other likely sites of ectopic pancreatic tissue were palpated but no further tumours were found; the liver and other abdominal viscera appeared normal on palpation.

Histological Report (Dr G T Allen)

A section (fig 3) showed an encapsulated tumour with a collagenous matrix in which lay scattered irregular masses of islet tissue and ducts. The more compact areas of islet tissue were recognisable as such but many areas were in the form of strands of irregular islands. Specific stains for granules failed. In view of the encapsulation of the tumour and in spite of the irregularities of the islet tissue, this was reported as a benign tumour. Another section (fig 4) showed easily recognisable islet tissue near the capsule. Some of the histological features of this tumour suggested a mixed tumour of a fibro adenomatous type rather than a pure islet cell tumour more commonly seen in the substance of the gland. All the sections presented the difficulty of deciding the benign or malignant nature histologically, of some of these tumours.

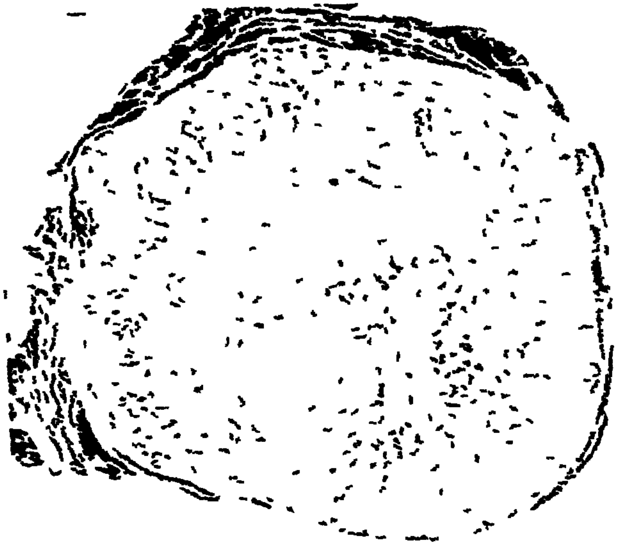

Fig 3—Section of islet-cell tumour

Postoperative Course

Next day the fasting blood sugar level was 136 mg per 100 ml, and on two further occasions the levels were 116 mg and 104 mg per 100 ml. *The starvation test* and plasma insulin assay were repeated but no symptoms or signs of hypoglycæmia appeared in nineteen hours. The results of blood sugar estimations throughout the test are shown in fig 2. On comparing the preoperative and postoperative results it will be seen that the blood sugar level remained more constant after removal of the tumour. The plasma-insulin level at the end of nineteen hours was 50 micro units per ml.

Discussion

These cases nearly always present as attacks of spontaneous hypoglycæmia the causes of which are numerous. Those of clinical significance in adults are functional hypoglycæmia, islet-cell tumours of the pancreas, disease of the liver, and endocrine disorders of the pituitary, thyroid, and adrenal glands.

The first two conditions are the most important and although clinically they are distinguishable, plasma-

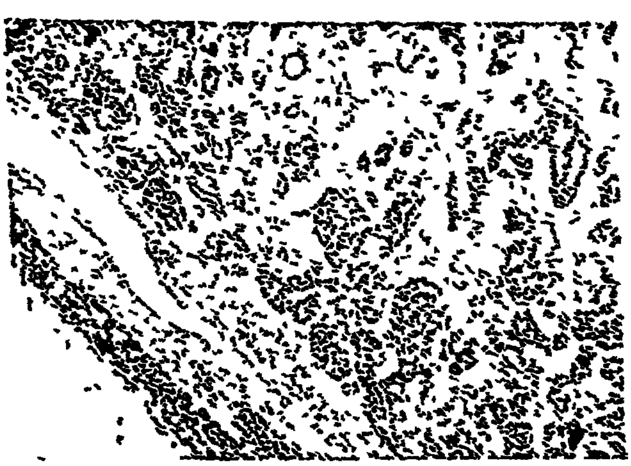

Fig 4—Section showing islet tissue near capsule

we might not even agree on what constitutes good midwifery In midwifery, as so often in medicine, we are faced with a dilemma—are we going to trust the natural processes most of the time, or are we going to try to improve on them? If we follow the first course, we shall leave much midwifery in the hands of midwives if the latter, then we shall get more medical interference, higher episiotomy and forceps rates in primiparæ, and perhaps rather more cæsarean sections

To allow or insist that the woman largely works out her own salvation may be a reasonable attitude, but as a consultant I cannot get out of my mind the innumerable labour difficulties—some trifling, some serious—that crop up from time to time quite unexpectedly Indeed, it may be true that normal midwifery only exists in retrospect, and that a normal case can be diagnosed as such only after the various stages of labour have been completed and the patient has completely recovered Perhaps the young lady was right when, to the question "with whom would you like to be wrecked on a desert island" she replied "an obstetrician" She may have been voicing the opinion of the public, who are making a great demand on hospital confinement and specialist care, because "they know it is safer"[5]

The proportion of live births in England and Wales which took place in institutions, rose from 15% in 1927 to 65% in 1953, though the rise by 11% between 1946 and 1953 was due to a fall in the number of births rather than an increase in the number of institutional beds

Home Confinement

Regional Variations

There are wide regional variations in the proportion of home and hospital births In Southport 90% of births take place in hospital, in London the figure is said to be approaching 80%, in some places it is as low as 30% It would thus appear that with 60% we in Sheffield hold an intermediate position Parallel with this rise in institutional births there was the striking fall in maternal mortality, largely due to other factors, but possibly in part at least related

Essential Requirements

Home confinement can without doubt be very safe, but it presupposes that those in charge of the patient know enough about midwifery to recognise and treat danger in good time We can diagnose only those conditions whose names are in our minds, so we must first be familiar with the possible sources of danger The high head at term may just be a manifestation of parity, but it may also be a sign of placenta prævia—long before there has been any hæmorrhage—or a pelvic tumour, or a brow presentation, or a hydrocephalic head, or a full-term ectopic pregnancy, or some combination of these abnormalities, just to mention a few One must have the right thoughts

> Some years ago a senior resident in a maternity hospital was asked on the telephone to take in a midwifery case He was rather short of beds and thought he ought to ask the general practitioner some questions He learned that the patient was in mountainous labour, but some of the other replies were so equivocal that finally, in desperation, he asked just what was presenting, was it a vertex? "Oh, no," came the reply, "nothing abnormal like that"

But even with the right thoughts, a correct diagnosis is still unlikely to be made without the appropriate clinical examination We who work in hospital still have to admit far too many patients who have not had what I would call proper care

Abnormal midwifery is difficult, even for those with much experience therefore all who want to practise it should have enough experience to become reasonably competent, and should be willing to learn But who has this experience, and how is it to be maintained? For the trend towards institutional births has redu the number of home confinements with the result th general practitioners and midwives are now compet for fewer and fewer cases Besides this being a po it source of friction, it seriously restricts the opportun a practitioner gets of keeping in touch with the subject and tends to make him a less and less suitable person f doing any midwifery at all

Dr S Wand[6] reports that he has recently "led a dep tion to a Committee of one of the Regional Hospital Boa in an area where the amount of hospital midwifery was 83 and the local doctors were complaining that they were n getting enough obstetrical experience" In Sheffield we ar not as bad as this Taking 1953 as a representative yea of the 175 doctors on the obstetric list 136 provided a com plete maternity service for one or more patients, and 3 (25%) of these did so for twenty one or more cases Th experience of 63 doctors not on the obstetric list is that l provided full obstetric service for one or more patient, *but of these only one did so for ten or more cases*

Review of a Sample of Sheffield Births

Early last year I decided to try to find out just wh was happening in Sheffield, and to this end I reviewed the records of every twelfth birth notified in 1953 (th equivalent of one month's cases)

About 30 cases were delivered privately at home o in nursing-homes, and I have no record of a further 2 Of the remaining 600, 310 (51%) were booked for hos pital, the rest being equally divided between those booking a doctor in the first instance, and those bookin the maternity services of the local authority

Welfare Cases

From this sample, we know that of the 161 women booked for home confinement by the maternity service of the local authority, 73 wanted a hospital bed, and from this we may estimate that during the whole year about 850 of this group would have preferred to be delivered in hospital Some of them would not take "no" for an answer, and were eventually admitted

We may look more closely at this sample Their parity and age distribution are given in table I

TABLE I—PARITY AND AGE DISTRIBUTION OF 161 WELFARE CASES IN THE 1953 SHEFFIELD SAMPLE

Parity					
No of patients	35	53	35	21	17
No of pregnancies	1	2	3	4	5 or more
Age					
No of patients	8	93	34	21	4
Age	10–19	20–29	30–34	35–39	40–

There was no age record in 1 case

In regard to their past obstetric history, there were 1 who had had one or more abortions previously, 8 who had had an abnormal pregnancy or labour, and 10 who had had a previous stillbirth or neonatal death O paper, at least, it looks as though some of these women would have been better booked for hospital confinement, and I believe that, except for the few who did not take the clinic doctor's advice and insisted on staying at home, such an arrangement would have been made if a bed had been available

The reasons why some were finally delivered in hosp varied 24 developed some pregnancy or labour complicatio 2 got in because their husbands objected to the arrangements, 1 moved to a house where there was a case of op pulmonary tuberculosis, 1 chose a private nursing home 2 eventually were persuaded to come in because of grand-multiparity and previous stillbirth, and 1 successfully solicited the support of her Member of Parliament

The question may therefore be asked "Are these arrangements satisfactory?" Certainly 73 women in this sample were dissatisfied and some exerted great

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[5] Wrigley A J *Ibid* 1955 ii 142

[6] Wand S *Ibid* p 143

erger, gynæcologist, Hadassa University Hospital, Jeru-
lem, for carrying out the artificial inseminations, and
r E Steinitz, of Jerusalem, for performing some of the
ntrathecal injections

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Preliminary Communications

ABLATION OF THE PITUITARY GLAND FOR SECONDARY CANCER

In 1955 Rothenberg et al[1] described the treatment of certain forms of secondary cancer by destroying the pituitary gland by injecting radioactive substances Technically this procedure is not difficult, but, since many of the patients are in poor general condition and there may be secondary deposits in the skull and/or the scalp, it is essential that the operation should be as simple and safe as possible

The risk of introducing infection by intranasal injection and the added accuracy obtainable by exposure of the pituitary gland encouraged us to persevere with the ntracranial approach

It is necessary to ensure that the volume of fluid injected is small but contains optimal radioactivity Too little radioactivity would be ineffective in destroying the gland, too much would damage the neighbouring vital parts of the brain, and too large a volume of fluid might burst through the diaphragma sellæ and spill over on to the surrounding structures A needle is used with a bore just large enough for the radioactive substance to flow through easily

A sucker attachment is essential to prevent any contamination of the surrounding brain by any radioactive material that might escape from the sella or from the needle after injection

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[1] Rothenberg, S F Jaffe, H L, Putnam T J Simkin B *Arch Neurol Psychiat, Chicago* 1955 73 193

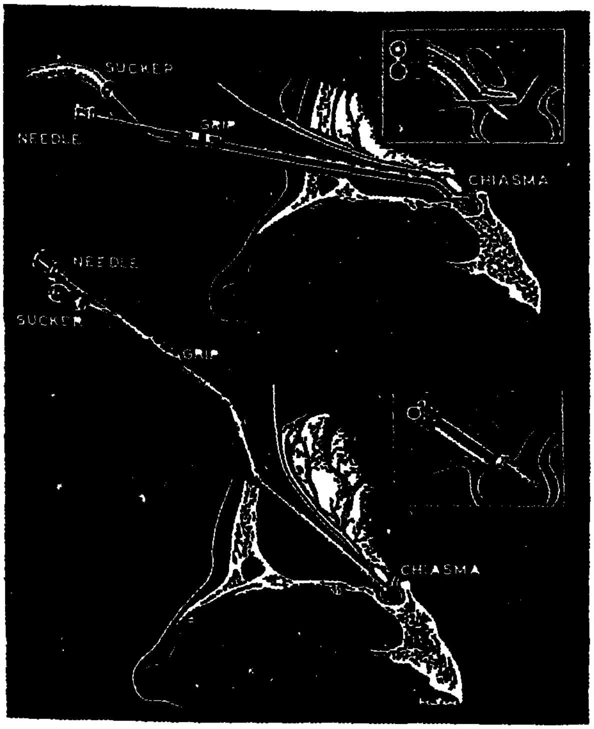

Fig 1—Injection of radioactive fluid into pituitary gland *upper register*, usual approach from just above right orbital margin, *lower register*, ordinary transfrontal approach

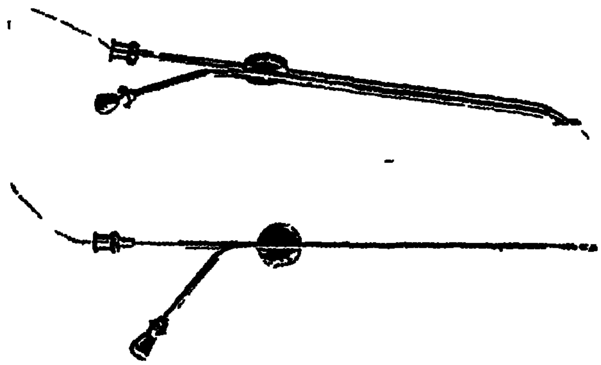

Fig 2—Needle for usual approach from just above right orbital margin

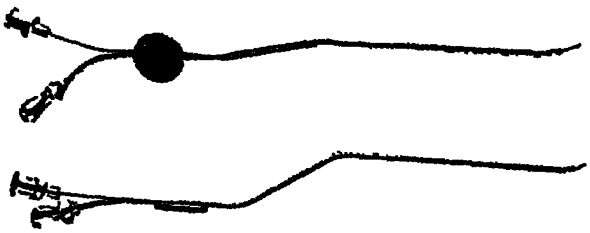

Fig 3—Needle for ordinary transfrontal approach

The usual approach is shown in the upper part of fig 1 Through a small skin flap a trephine hole is made just above the right orbital margin and overlapping the midline by about 0 5 cm The dura is opened, and the frontal lobe is raised and retracted laterally The combined needle sucker (fig 2) is inserted gently along the floor of the anterior fossa until the needle aperture is over the fossa, the end slipping under the chiasma The sucker tubing is attached, the needle pushed home, and the radioactive fluid injected After a minute or so the needle is withdrawn The sucker is left in situ for a few more minutes

When the frontal sinuses are very large, or when there is any abnormality in the region of the pituitary fossa, the ordinary transfrontal approach to the pituitary gland is used, as shown in the lower part of fig 1 After the bone flap has been raised, the frontal lobe is raised extradurally as far as the sphenoidal ridge and thereafter intradurally The optic nerves and chiasma are exposed, and the needle with sucker attached (fig 3) is inserted through the diaphragma sellæ into the pituitary gland The injection is made into the four quadrants of the gland without completely withdrawing the needle The sucker prevents contamination After a few minutes the needle is withdrawn and a lintine patty is placed over the hole in the diaphragma sellæ for a few minutes, after which it is withdrawn and tested with a geiger counter Leakage is minimal by this technique

The needles are of stainless steel The needle for the usual approach (fig 2) is 15 cm long and projects 0 75 cm beyond the sucker, which is of gauge 15 S W G The needle tube is of gauge 23 S W G When the ordinary transfrontal approach is used the needle (fig 3) is 18 65 cm long, the sucker-needle guide tube is of gauge 13 S W G, and the outside diameter of the needle 15 S W G

My thanks are due to Prof B W Windeyer, Dr J D N Nabarro, Miss M D Snelling, and the late Miss Diana Beck for permission to operate on their cases, to Dr A M Jelliffe, who is collaborating with me in this work, Mr R A Millard and his colleagues of the instrument department of the Middlesex Hospital, for the needles, Miss E Hewland, medical artist of the hospital, for the drawings, and Mr M Turney for the photographs

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Midwives' Board It would make it possible to train an aristocracy of general practitioners, such as Mr Arnold Walker, chairman of the C M B, has advocated [9]

Dabbling in midwifery must be discouraged, in much the same way as dabbling in surgery is discouraged, and in fact this is the implication of the general-practitioner obstetric list I would like to push out of domiciliary midwifery those who are afraid of it, for they have no courage, and those who are not afraid of it, for they have no imagination, those who say there is nothing to it, and are prepared to go and do a case now and then, just to keep their hand in, for they have no understanding, and those who have no interest—for they have no soul

A prerequisite of a good maternity service is the proper training and selection of doctors, and this training and selection must be in the hands of those with experience of the frightful effects of bad midwifery

Of course every general practitioner, unless he has had a six-month training in hospital, must make a start somewhere, and I believe that once he is on the Medical Register he should continue to have the right to practise midwifery This right, however, should be subject to the proviso that he should not be allowed to attend the delivery in the home where conditions may try even the most experienced man Let our beginner make his beginning in some institution where he will be under the eye and control of more experienced colleagues, and let him graduate to home confinement when he has proved his worth Similar rules might very well apply to the midwives In the maternity home too, the doctors and midwives can pool their experience and knowledge, and both be the wiser for it

Education in Midwifery

Whether or not my view is accepted, and we are to move towards more institutional beds and an aristocracy of general practitioners, matters of medical education arise with which I am very intimately concerned

Every doctor runs the risk of meeting the unexpected, and we must therefore give the student a good grounding in the anatomy, physiology, and pathology of parturition We must also teach him how to deal with emergencies—but in no way encourage him to think that without post graduate training he will be competent to practise midwifery except in an emergency Teaching in regard to home confinement is now very limited in Sheffield, because for many years the district of our teaching hospital has been so small This may not be altogether a bad thing, and I have not thought fit to try to change matters The pattern of obstetric care is changing more attention is being paid to the education of the expectant mother in motherhood and mothercraft, and—because there are fewer of the abnormalities, such as contracted pelvis and puerperal sepsis, which used to occupy so much of our time—intrapartum care is becoming simpler So far as the general practitioner is concerned there are only a few operative procedures which he should nowadays practise *outside fully* equipped homes or hospitals The episiotomy and its repair, and the repair of perineal tears, low forceps under local anæsthesia, the use of ergometrine for abnormalities of the third stage, are the main treatments required I myself see no reason why students need go into the patient's home to learn these intrapartum techniques

Joint Advisory Committee

I have mentioned some long term objectives The short term policy should be the formation of a local advisory committee for midwifery, where the difficulties and problems that confront us can be ventilated from time to time indeed, it may be argued that this is a pressing matter, for at the moment I know of no way by which representatives of the local authority, the general practitioners, and the board of governors, the regional hospital boards, and the midwives, can be brought together to discuss matters of common interest and responsibility The difficulty of course is to know who is to set up this committee Frankly, I do not think it matters which authority does it, so *long as it is done*

It is to be hoped that the committee to inquire into the maternity services recently set up by the Ministry of Health will give this and related matters full consideration

Conclusion

A review of the present position in regard to home confinement in Sheffield suggests that extra beds should be made available for those women who desire institutional care and for those unsuitable for home delivery There are, according to my estimate, about 1000 of them, and if they were all delivered in hospital instead of at home as at present then the proportion of hospital confinements in Sheffield would be about 70%—a figure which happens to correspond with that advised by the Royal College of Obstetricians and Gynæcologists in it Report on a National Maternity Service (May 1944) A *close study of a random sample* of those women delivered in Sheffield in 1953 suggests that those seeking hospital beds attend earlier for their antenatal care than those making other arrangements The present divided responsibility for maternal care is underlined, and a plea is put forward for the formation of local advisory committees

I wish to thank our medical officer of health, Dr L Roberts, and his staff for facilities put at my disposal, Dr A K Black, senior assistant maternity and child welfare officer, who very willingly spent many hours going over case records with me, and Mr J H Cargill, clerk of the executive council for Sheffield, for information I also acknowledge help from Mr T E Durrant, my technician at the time, for work in connection with filling in, punching, and counting the punch cards used in this survey

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A GENERAL-PRACTITIONER MATERNITY UNIT

JOSEPH SLUGLETT
M B Glasg
GENERAL PRACTITIONER

SARAH WALKER
M D Lond, D P H
SENIOR MEDICAL OFFICER

MATERNAL AND CHILD WELFARE SERVICE, BRISTOL

WOMAN in her labour ought to be confined in the best possible place and under the best possible conditions At present there are two opinions as to where these are to be found On the one hand there are those who think that all confinements should take place in a hospital or institution, on the grounds that, even with the most careful antenatal care, unforeseen complications may arise affecting either the mother or baby On the other hand there are those who claim that for the normal confinement the home and family setting is best for mother and baby and that institutional confinement tends to convert a natural process into a surgical operation The trend throughout Britain is towards hospital delivery, and in Bristol during the past year only a quarter of all deliveries took place at home

The scheme we put forward is one which we consider combines the best features of hospital and home care Moreover, it ensures that those concerned with the welfare of the mother—i e, the family doctor, midwife and, when necessary, the obstetric consultant—will supervise her during her labour Throughout her pregnancy the mother will have been under the care of her own doctor and will have been seen regularly at his own surgery or

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[9] Walker A J Obstet Gynæc Brit Emp 1955, 62, 782

Medical Societies

MANCHESTER MEDICAL SOCIETY

Surgery of Peptic Ulcer

OPENING a discussion in the section of surgery on March 13, Mr H. T. Cox said that dissatisfaction with partial gastrectomy—a well-established procedure with a low mortality-rate—mainly centres around its side-effects. Numerous procedures have been devised to reduce or eliminate these, but, if the various gastric operations are not to rotate in popularity, their results must be compared by means of a simple clinical yardstick. In 100 cases of duodenal ulcer treated by gastro-enterostomy plus vagotomy, he found the side-effects markedly less than in 100 cases treated by partial gastrectomy.

Mr IAN M. ORR (Preston) said that in the stimulation of gastric acid secretion two factors play a part—namely, nervous stimuli via the vagus, and hormonal stimulation due to the activity of cells in the pyloric half of the stomach, in the lesser curvature, and in the duodenum and upper jejunum. Hypersecretion does not occur in every peptic-ulcer patient, and in cases of duodenal ulcer the flow of nerve-secreted acid may be normal or low. The general level of the unstimulated night secretion curves was high in more than half of a duodenal-ulcer group, but even among normal people a few have exceptionally high nerve-secreted acid. This suggests that vagotomy is indicated in only a proportion of duodenal-ulcer cases and might do harm if practised indiscriminately; and, as night acid readings may be high in people without ulcers, high readings are not necessarily an indication of the activity of the ulcer. Surgical treatment must take into account not only the hormone-secreting activity and the nervous secretory activity of the patient, but the age, sex, and physical fitness, and the type of ulcer—duodenal, gastric, or anastomotic.

In a series of 734 operations for peptic ulcer, patients with gastric ulcer had Billroth-I gastrectomies, while those with duodenal ulcer had two-thirds gastrectomies of the anterior Finsterer-Lake type, plus vagotomy if the night secretion was unduly high. A small group, mainly elderly women, had *gastro-enterostomies with or without vagotomy*. In the gastrectomy group 2 patients had a two-stage resection because of gross œdema and inflammation of the duodenal ulcer. The mortality-rate for the series was 1·1%, and a follow-up of 210 patients over five years showed that 5 developed anastomotic ulcers after gastrectomy, without vagotomy, for duodenal ulcer. Of those treated by gastrectomy plus vagotomy none have so far developed anastomotic ulcers. In the late results no striking difference is apparent between the various groups, apart from the incidence of stomal ulcer in 2·4% of patients having gastrectomy without vagotomy.

Reviews of Books

Cancer Cells

E. V. COWDRY, director, Wernse Cancer Research Laboratory, Washington University, St Louis. Philadelphia and London: W. B. Saunders. 1955. Pp. 677. 112*s*.

THE author is an individualist, already well known from his *Textbook of Histology* and his *Problems of Ageing*. It is therefore not surprising that in covering a very wide field he lays more emphasis on certain subjects in which he excels. In fact, he says himself that "no single individual can take the place of all the specialists now investigating cancer."

None the less a well considered plan has been followed, "each chapter constituting more or less of a unit, carrying the account a step farther and supplying a basis for what comes next. . . . The order of presentation was changed again and again as the writing progressed in efforts to gain some measure of continuity." For convenience, a clear summary of the contents is given at the end of each chapter.

The first chapter explains the distinction between malignant and benign tumours. The next three chapters describe the properties of malignant cells, including abnormalities of function, multiplication, and spread, and changes in the cytoplasm and nucleus. Then follows a description of the agents capable of bringing about malignant transformations, the theories concerning their actions, and the susceptibility of normal cells to these carcinogens. The latent period and the factors modifying the production of cancers are next discussed. The last 100 pages deal with general data on diagnosis, prevention, and treatment, and with the history and achievement of modern cancer research. The bibliography includes about 3000 references, compiled with great care.

Those concerned with cancer research are all too familiar with the man who "has an idea" about the cause or cure of cancer. No better book could be placed in his hands, for it is an accurate and up-to-date summary of a great deal of the effort which has been made during the past fifty or sixty years in trying to identify the cause and the cure for cancer. Those who seek information on how the malignant cell differs from the normal will find a reasoned account of the present state of knowledge in this field. Those already tackling this problem may find the section devoted to their special field rather superficial, but this is inevitable in a general book on cancer. For those who gibe at the slow progress which has been made in clinical and experimental studies of cancer and who complain that more time is devoted to mice than to men, the reading of this book will be a salutary experience.

Mind and Body

Psychosomatic Pathology. PEDRO L. ENTRALGO, professor of medical history and rector of Madrid University. London: Harvill. 1955. Pp. 150. 12*s*. 6*d*.

THIS erudite but extremely interesting and readable book is both a critique and a historical survey of what is now known as psychosomatic medicine. The main theses which Professor Entralgo puts forward, with skill and persuasiveness, are:

(1) The term "psychosomatic pathology" *has two complementary meanings*. One is literal and superficial: the study of human disease from the point of view of the two aspects which it presents, the psychological and the somatic. The other is derivative and comprehensive: "the scientific consideration of human disease in conformity with the personal conditions of man's psychophysical reality."

(2) Understood in this derivative and inclusive sense, psychosomatic pathology is a relatively new development. Medicine has always been, in one guise or another, "psychosomatic", but the same cannot be said of pathology.

(3) Primitive Christianity first suggested the possibility of a true psychosomatic pathology. "Sin" was distinct from "disease," and this view opened the way to a theoretical and practical consideration of the possible relationships between "moral disorder" and "physical disorder."

(4) "Western" pathology, from the School of Salerno to Freud, has not succeeded in becoming fully psychosomatic. It has been hampered in this respect by its fundamental "naturalism," a continuation of the Hellenic, and by too exclusive an adherence to the "visive" concept of knowledge.

(5) Twentieth-century psychosomatic pathology has regained—in a different form—certain of the possibilities that primitive Christianity offered to the knowledge and practice of the physician, and has revealed the simple underlying reason for the "personalism" of the ancient Semite.

Beginning with the concept of disease in primitive times, Professor Entralgo sketches the beliefs held by two important cultures, the Assyro-Babylonian, in which the sick man was regarded as having sinned, and the Hellenic, in which the disease is considered more as a departure from man's "nature." This led to the naturalism and physiological bias of Greek medicine, which in turn through the teachings of Galen influenced Christian medicine towards physiology. The concept of disease in "occidental" medicine is then discussed, and in his concluding chapter "Towards an anthropological medicine," Professor Entralgo examines the ideas about neurosis before the time of Freud, the work of Freud, and the creation of what he terms "anthropological" medicine, which includes psycho-analysis and psychosomatic medicine in its scope and practice.

The breadth and clarity of Professor Entralgo's survey will stimulate any physician or psychiatrist who is of general practitioners particularly experienced in the work Unfortunately this has not always worked out in practice, and for the most part it is open to any general practitioner to undertake midwifery if he so chooses We should like to see this work restricted to keenly interested practitioner-obstetricians who, though probably with smaller lists, would continue in general work so as to remain in touch with the whole field of general practice Family doctors not doing maternity work should refer their cases to these colleagues A group practice would almost always include at least one practitioner-obstetrician Future entrants to the "obstetric list" would gain their experience and qualify for admission to the list by association with practitioner-obstetricians

Where local-authority medical officers continue in the service they should be given the opportunity to conduct their midwifery practice on the same terms as general practitioners—i e, he, or she, must be able to visit the expectant mother at home where necessary and attend the confinement in this labour-ward unit

In any maternity scheme the needs of the mother and baby are paramount For some years now it has been our experience that mothers approach their confinement with much less fear than formerly This is due, we feel, to over-all antenatal supervision as well as instruction in relaxation We make a point of telling the mother, by discussion, film strips, and diagrams, as much as we think she ought to know about the course of labour and assure her that we will be with her when she needs us All the same there remain the hazards of any normal delivery, and many mothers are aware of these It may be said that "the only normal delivery is the absolutely normal one which has just been completed"

We feel that our scheme would have a wide appeal, for the mother would know that she could be delivered in a place where all the resources of a maternity hospital were readily available should things go wrong, and yet be able to return home immediately for her subsequent care

We should like to record our appreciation to Dr R C Wofinden, medical officer of health, Bristol, for his advice and constructive criticism in the preparation of this article

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HOSPITAL FARMS

In his reports[1] on the National Health Service accounts for 1954–55, the *Comptroller and Auditor-General, Sir Frank Tribe*, again refers to hospital farms and market gardens An expert committee reviewed the farming activities of 190 hospitals with 40,000 acres of farmland and nearly 4000 acres of market gardens They found that, in a number of instances, farming had been developed for its own sake, "and the maintenance of pedigree herds and dairy farming had become a major preoccupation with some hospital authorities" In the light of the committee's report, the Ministry of Health advised hospitals that they had no authority to run farms except in so far as they were an essential part of hospital management, and they asked hospitals *to review their farms* By Oct 31, 1955, 207 farms had been surveyed by regional boards Decisions had been reached about the future of 126, and it had been decided that farming should cease at 47 hospitals and be *reduced at a further 38, involving* the disposal of 17,598 acres of land

Trading accounts for hospital farms and gardens in England and Wales in 1954–55 showed an excess of income over *expenditure of £60,000* Farms showed a surplus of £140,000 and market gardens a deficiency of £80 000 (these figures do not include small market gardens) In Scotland farms recorded a net profit of over *£56,000* but *market* gardens showed a loss of just under £10 000

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[1] National Health Service Acts 1946 to 1952 Accounts 1954–55 H M Stationery Office Pp 41 2*s* 6*d* National Health Service (Scotland) Acts 1947 to 1952 Accounts 1954–55 H M Stationery Office Pp 26 1*s* 9*d*

In England Now

A Running Commentary by Peripatetic Correspondents

ART critics have come under the brush at Burlington House this year Sir Alfred Munnings leads the way Besides the usual reliable nags from his stable, he has entered a likely outsider—his witty but good-natured satire on modern art, *Does the Subject Matter?* Of his circle of critics, I got the feeling that Munnings was backing the dog Mr A R Thomson urbanely offers us *The Selection Committee 1955* in an entertaining and elegant crescent before a red curtain But with Mr Richard Eurich the gloves are off and his version of *The Critics* is as harsh as it is accomplished

There is no formal royal portrait of the year, and the place of honour is given to a large study of *The Duke of Wellington* in ducal robes People seemed to be turning with relief from its uncertain grandeurs to the smaller portraits, such as Sir Gerald Kelly's blue and grey picture of *Sir Geoffrey Jefferson, M S, F R S*, who sits at ease looking out sleepily yet shrewdly from beneath heavy lids Though Mr A R Middleton Todd has painted *Lord Adrian, O M, F R S*, in academic robes he too sits at ease before a not too tidy bookcase, looking over his well-known half spectacles In Mr Frederick Elwell's picture, *Mrs Rosemary Adams, F R C S* sits in a draped dress of rich red before a small open desk. Mr Eric Kennington's effective pastel of *Sir Russell Brain, P R C P*, hangs in the select small south room Among the sculpture there is the now almost inevitable head of *The Late Sir Alexander Fleming, F R S*—this time a less familiar one of him in his early 50s—and a bronze of *Dr Roger Bannister*, by Josephina de Vasconcellos Mr Allan G Wyon's silver medallion will later be a suitable prize for meritorious anatomy students at Leeds

Sir Winston Churchill, who has been an honorary R A longer than he has been an honorary F R C S, has two pictures hung, including a dark but attractive interior of *Sir John Lavery's Studio* After-dinner speakers will turn with a shudder from Mr Ruskin Spear's *Unaccustomed as I am* But surely no medical dinner was ever half as horrible as this macabre postprandial occasion

* * *

Now that automation is so much used in anæsthesia, I am occasionally able to contemplate phenomena not directly concerned with the unconscious patient in front of me

I have two long orthopædic sessions each week and here some curious problems have so far eluded solution

A popular method of securing a bloodless field in limbs is to apply an Esmarch's bandage and then to inflate a modified sphygmomanometer cuff, after which the rubber bandage is removed On the pressure gauge of the instrument are two red lines at 250 and 500 mm Hg respectively marked 'arm' and 'leg" Now why use a pressure considerably higher than the systolic blood pressure and why use twice this pressure on the leg? I have posed these queries to two orthopædic surgeons, a physicist, and a hydraulic engineer, and they all gave different answers

I pass over briefly the peculiarities of orthopods as to the time for which tourniquets or their equivalents can be applied One is insistent that I remind him when twenty minutes have elapsed in the case of an arm while his opposite number seems quite annoyed if I venture to remark that an hour has gone by

Even more remarkable is the attitude towards asepsis In the private wing of a London teaching hospital, if a general surgeon drops an instrument it is boiled for ten minutes by the clock and handed back If, however, an orthopædic surgeon does the same thing in the same theatre, twenty minutes elapse At an equally famous London teaching hospital, they boil dropped instruments for two minutes "just to make sure" as their professor of bacteriology has shown that thirty seconds is ample provided that the water in the steriliser does not go off the boil when the instrument is dropped in

It is all very puzzling and I think that in future I must keep my mind on really simple matters of anæsthesia, such as the mode of action of chlorpromazine

* * *

Dangerous Leg ulcer unhealed since 1916 Photograph taken before treatment with F99

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It has been shown beyond question by large scale serum-lipids studies that a good proportion of patients suffering from intractable skin conditions have a deficiency of the essential fatty acids It is not possible to carry out these studies in everyday practice, but any patient with eczema or furunculosis who fails to respond to symptomatic treatment should most certainly be tried with essential fatty acids "F99" A high proportion of these patients will be found to respond.
In gravitational ulcers, where the skin is "under-nourished," the application of additional essential fatty acids rarely fails to heal the wound.

Literature on request

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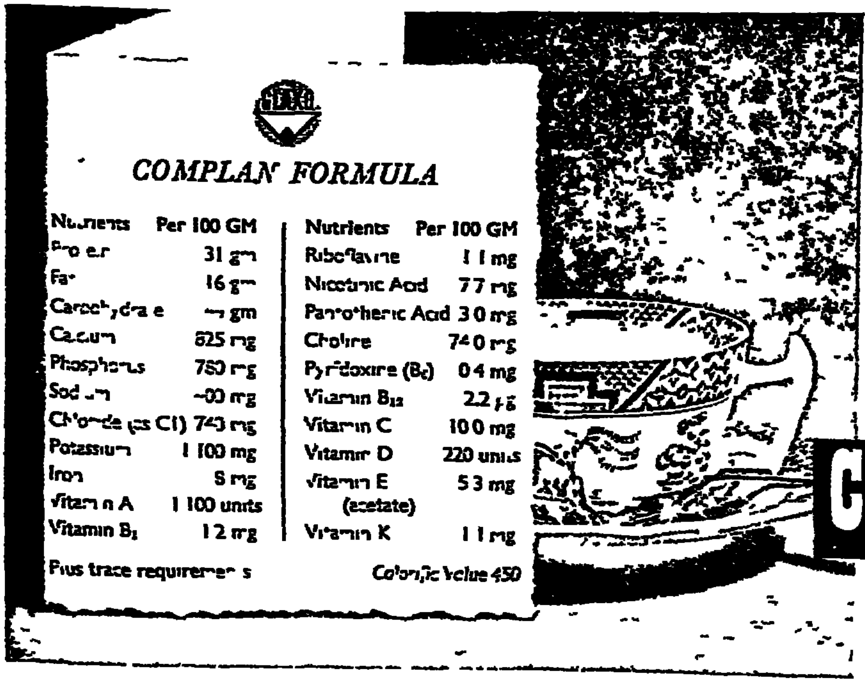

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Denmark reports only half the mortality (taking the male rate in middle age as *the most reliable indicator*) of Finland, or Canada, or New Zealand [4] At probably a somewhat lower, though still high, level of fat consumption, the Stockholm rate is only half that of Edinburgh, or Aberdeen, or Newcastle, or Cardiff

Our own experience of fat-rationing, starting from 1940 is also adduced in support, but, again, the available data do not fit There was a decline of mortality at the beginning of the war, but the climbing pre-war trend was resumed in 1943,[5] although fat restriction was continued for several years longer and reached its greatest severity (such as it was) in 1947 *If margarine and kindred products are the villains, the story might hang together a bit better*, because, of course substantially more margarine was eaten from early in the war [6,7] In that case, why the decline of mortality in 1940–42 ? The record is anything but straight, and it is good to know that we are soon to have first approximations at least to the facts about E F A consumption in this country during recent years, and not only courageous extrapolations from a few of the figures

The war-time experience of Norway is probably the *most quoted evidence*, *and once again the statistics are* rather different from the common impression of them The actual decline in cardiovascular mortality in Norway is difficult to estimate, and it was salutary to find when I visited there last autumn how much less excited the Norwegian experts were about it than others The fall among men seems indeed to have started *before* food shortages were at all serious [8–10], it was seen in several cause groups, and it affected young persons—i e, non-coronary cases—more than the middle-aged Moreover, it occurred in a period when not only was there restriction of total calories and drastic reduction of fats, but also several *other factors* which *are probably related to the* frequency of ischæmic heart disease were all being influenced in a favourable direction smoking, habitual physical activity, diabetes, *and possibly blood pressure* levels and body weight Those interested might refer to Professor Strom's fascinating account [10] of Norway's war-time increase in infectious diseases, and the decline in dental caries, childhood enlargements of tonsils and adenoids, maternal mortality, stillbirths, infant mortality, various cancers, suicide, and schizophrenia and other psychiatric disorders [11] There almost certainly was some fall in coronary heart disease during the Occupation a reasonable estimate might put it in the order of 20–25% (How unexpected if the substantial increase in the eating of fish and fish products was in some measure responsible But to claim this, or the interference with hydrogenation, as *the* cause in what was so obviously a multifactorial situation, is surely to court the errors of the over simple *tale about fats*) As interesting as this decline is the fact that pre war Norway, although enjoying a high-fat diet, seems to have had rather *low* mortality from coronary heart disease, and after war-time food restrictions were lifted there has again been *a return to relatively low* rates, low at any rate for a " Western " country—little more than half those of Scotland or a third of New Zealand's

I am not suggesting that national death-rates certified to coronary heart-disease should be used in considerations of the ætiology of this condition or, indeed, that they have any value, *and I am well aware that* diverse juggling with the data can yield diverse results I am only making the point that if the data are used at all it should be with greater circumspection In this respect it may be fair to place on record that it was not the vital statisticians, epidemiologists, or social medicine workers in general who first engaged in these exercises, and their hesitation was only partly due to their well known indolence With much experience *of the snares of time* series and international comparison in well tilled fields like infant mortality and tuberculosis their reluctance *was perhaps understandable*

The other principal source of information about the experience of different countries, and at different times is the ad-hoc field survey These, however, are only at their beginnings The difficulties of standardising techniques, population samples, &c, are enormous, for the peoples that need to be studied often differ in such a great many respects Keys himself [12] is pioneering a truly mid century approach to these matters

The second observation I should like to make is that it would help to clarify ideas, and to make communication easier, if there was less premature simplification of the complex of problems into the measurement of serum cholesterol, or β-lipoproteins, and if the term " atherosclerosis " were not used indiscriminately to include anything from experimental fatty lesions in the aorta of rabbits to the whole of the natural history of ischæmic heart-disease in man This widespread contemporary woolliness has had unfortunate results It is a reasonable proposition that several causes and several mechanisms are involved in the human disease, and it is conceivable that some of them are not related in simple fashion to serum-cholesterol, &c But it is a *fallacy to suppose* that this automatically renders them unimportant *The* U K pathological survey which we are now analysing seems to suggest that, in terms of morbid anatomy alone, different factors may operate at different stages in the long journey from flecking of the coronary arteries to the fatal heart disease—age at one stage, " social class " at another, physical activity of work at yet a third, and so on However that may be, the notion of " multiple causes " is crucial for preventive medicine if only because it would be more sensible to propose to the people *that they should modify* their diet *and* other ways of living (should such a programme appear hopeful) than to clamour for a revolution in diet alone Moreover, it may be easier to control the modern " epidemic " of coronary thrombosis than the more ancient coronary atheroma

The main consequence of the prevalent misconception has been the relative neglect of clotting and thrombosis in modern research There are the strongest indications that thrombosis in human coronary arteries should be a major focus of investigation the historical evidence which suggests that coronary atheroma has not increased in recent years, though thrombosis and infarction have the observation which can be made by any pathologist who views his material in epidemiological terms that only a minority of *men* with much or severe coronary atheroma suffer infarction, at any rate in middle age (and also that some with little atheroma can have serious obstruction and ischæmic heart disease), the *precipitate nature of such decline as did in fact* occur in war time Norway, and the striking fall in thrombosis—embolism observed in their hospitals during those years [14], Duguid and related work, and the difficulty of inducing thrombosis and infarction on the experimental atheroma of

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[4] Statistics kindly supplied by national offices of vital statistics or from W H O

[5] Registrar General's Statistical Reviews of England and Wales 1938–54 Tables part I Medical H M Stationery Office

[6] How Britain was Fed in War Time H M Stationery Office 1946

[7] Domestic Food Consumption and Expenditure 1950 H M Stationery Office 1952

[8] Strom A Adelsten Jensen R *Särtr Nord Hyg Tidskr* 1950 31 123

[9] Strom A Pygh A *Sartr Nord Med* 1952 47 396

[10] Strom A The Influence of War time on Health Conditions in Norway Oslo 1954

[11] Odegard O *Acta Psychiat Kbh* 1954 29, 333

[12] Keys A *Minn Med* 1955 38 758

[13] Morris J N *Lancet* 1951 i 1 69

[14] Dedichen J Strom A Adelsten Jensen R [illegible] K Factors Regulating Blood Pressure Transactions of the 5th Conference Josiah Macy Jun Foundation New York 1951

THE LANCET

LONDON SATURDAY, MAY 12 1956

The Maternity Services

We welcome the announcement that, following a recommendation in the Guillebaud report, a committee has been set up to inquire into the maternity services.[1] The lack of unity in maternity work under the National Health Service has been much criticised, for it has led to duplication and confusion. It is not uncommon to hear of patients attending in the same week a hospital antenatal clinic, a local-authority clinic, and her own doctor. More serious are misunderstandings whereby patients receive little or no antenatal care because each authority thinks that this being provided by another. In some areas coördination has been achieved by advisory obstetric committees which include representatives of the various bodies concerned. The Royal College of Obstetricians and Gynæcologists[2] has recommended unified control at national, regional, and area levels, and on a later page of this issue Professor **Scott Russell** emphasises the urgency of the need for coördination.

Further problems will be before the new committee. Of these perhaps the most important are the place of the confinement and the personnel who should man the obstetric services. The picture of the family doctor and trusted friend bringing the son and heir into the world in the patient's own home is attractive but hardly realistic today. The factors that have caused the trend towards confinement in hospital are well known, and it seems likely that both the wishes of the community and the greater safety for the mother in hospital will cause this trend to continue. But the hospital is not necessarily the safest place for the newborn: the risk of cross-infection by resistant strains of staphylococci is a factor strongly in favour of the type of scheme suggested in this issue by Dr **Sluglett** and Dr **Walker**. They propose that normal cases be delivered by the family doctor and domiciliary midwife in a simple labour-room attached to a maternity hospital and not in the patient's own home. The patient and her baby would be taken home by the midwife within a few hours after delivery. Such a scheme might be extended to include the earlier discharge from hospital of those at present booked for institutional confinement. It has been suggested that if all patients fit for discharge went home on the seventh day, existing maternity beds would suffice for the delivery in hospital of all women who need or desire this. On the other hand, during these seven days babies would run the risk of infection, and it might prove wiser to discharge such patients twenty-four hours after delivery, once careful observation had shown that the condition of mother and baby was satisfactory, before transfer to a lying-in ward. When from time to time the bed state necessitates early discharge from hospital the mothers and babies come to no harm, but inevitably the domiciliary midwife resents having to visit patients whom she has not delivered. It seems that a prerequisite for routine early discharge from hospital would be unification of the midwives' services, so that patients would not be passed from the care of one organisation to that of another. Such unification is in fact recommended for wider reasons in the report of the Royal College of Obstetricians and Gynæcologists.

The place of the general practitioner in the maternity services was discussed at a conference held last November by the College of General Practitioners,[3] at which arguments were voiced in favour of increasing the maternity beds at the disposal of general practitioners. This is certainly desirable, provided it is recognised that if every practitioner does only his own numerical share of obstetrics he will not have enough continuing experience to remain efficient. (In one large executive-council area more than half the doctors who had expressed their willingness to conduct obstetric cases were found to have dealt with 5 cases or fewer in a year.) Professor **Russell** elaborates this theme and declares that "dabbling in midwifery must be discouraged in much the same way as dabbling in surgery is discouraged. The majority of women will be safely delivered of live infants whatever the standard of work, and the very normality of the reproductive function may blind us to imperfections in care. The practitioner dealing with only a few cases each year may well think that he is rendering an efficient service if only one baby is lost every two years, but this may represent a stillbirth-rate of 5% compared with a possible 1–2%." There are very strong arguments for limiting obstetric practice to a smaller number of general practitioners who have a special interest in the subject and who by training and continued experience can maintain efficiency and merit the name general-practitioner obstetrician.

In replanning the maternity service the importance of the contribution by local-authority clinics should not be overlooked. The staffs of clinics are at present handicapped by lack of direct knowledge of the outcome in cases that come under their care antenatally, and Dr **Sluglett** and Dr **Walker** suggest that these doctors should have the opportunity of attending confinements. There is evidence that in some areas the clinics are being used less than formerly, and where this is so steps should be taken to ensure that the help they offer—notably blood tests, dietary supplements, and education—is not overlooked.

However the service is reorganised, the midwife, the general-practitioner obstetrician, the local authority with all its ancillary services, and the specialist and hospital services will each have a part to play. Once coordination has been improved, there will be room for experiments in the distribution of work between these groups, including experiments with discharge home after different periods.

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[1] See *Lancet*, April 28, 1956, p. 574.

[2] Royal College of Obstetricians and Gynæcologists. Report on the Obstetric Service under the National Health Service. London, 1954.

[3] College of General Practitioners. Conference on General-Practitioner Obstetrics, Nov. 20, 1955. London, 1956. Pp. 40. 3s. 6d.

There can be no doubt that food is far and away the greatest single controllable factor affecting health and disease, but existing knowledge can influence the picture only if effectively applied to the community by means of health education

You point out that research into the origins of degenerative diseases in man is beset with difficulties Not the least of these are encountered in the planning, conduct, and interpretation of controlled human feeding experiments A consequence of this is that even potent nutritional factors affecting human health may continue for a very long time to elude demonstration under conditions which will satisfy the statisticians Moreover, such experiments as have been attempted have often of necessity been carried out under abnormal conditions and for too short a time Results have been inconclusive or even contradictory so that the health educator finds it difficult to be decisive enough to be effective

The most striking improvements in the national health during recent years have been in the younger age groups of the community Whilst in no way minimising the achievements of curative medicine, the fact remains that the children of today are better specimens largely because of the adoption by the community of healthier ways of living encouraged by health education and assisted by improving social conditions

I personally have not the slightest doubt that far and away the biggest factor has been the acceptance by the community of the so called "balanced diet," reinforced by the school meal

Careful inquiry in the home as to what constitutes this "balanced diet" all too often causes me grave concern, but the fact remains that even the orthodox 20th century teachings on fats, carbohydrates, proteins, vitamins, and minerals &c, has achieved a notable improvement on the fodder meted out to the average family fifty, thirty, and even twenty years ago As a direct consequence, and associated with measures to improve the cleanliness of food and milk supplies, we now raise children who mostly survive the perils of infancy, who grow and gain weight at reasonable rates, and who are free from obvious crippling deformities

This is very solid achievement, but a closer look at some of these children will remove any cause for complacency How rare is the bright eyed child, mentally alert, firm of flesh and limb, of good posture, who causes little anxiety to the parents in the matter of general health How very common is the dull and listless child with rotting teeth, deformed dental arches, bulging tonsils, pale and limpid flesh, indifferent posture, constipated, and drifting throughout the winter and most of the summer from episode to episode of sepsis, pyrexia of unknown origin, and general malaise All too often indeed has one encountered this picture even in doctors' families As regards the health of the adult population it may be arguable that that too has shown comparable improvement Nevertheless the appalling volume of digestive, rheumatic, respiratory, circulatory, and mental disorders, reflected in sickness absenteeism, consumption of drugs, and demands on hospital facilities are little short of a national scandal and must surely be a challenge to preventive medicine

Not the least significance of this recent work on the relation of the fats to morbidity is the revelation of further vital substances in common foodstuffs capable of exercising profound physiological influences on the body With scarcely a week passing without that number being added to and the demonstration of deficiency syndromes associated therewith, one cannot but be astounded at the arrogance of those who blandly assure us of the adequacy of denatured diets reinforced piece meal by what they regard as the essential vitamins, &c All the more relevant, therefore, are Sinclair's observations concerning the hazards arising from the national consumption of cereals of low extraction rates and the more timely your own reiterated warning in this respect regarding our daily bread

It seems likely that we shall remain largely at a standstill if we await a strong lead from the laboratory or the field Where can we turn for a clue to the way ahead?

I *contend*, Sir, that we can no longer afford to ignore the fruits of the experience of McCarrison,[1] Picton,[2] Weston Price,[3] Wrench,[4] and many others inspired by them, who have proved for themselves that positive health is attainable by giving due attention to wholeness, freshness, and quality of food, including due regard to the soil in which it is grown

The proof of the pudding is in the eating, and any family who, for instance, will take the trouble to bake their own bread from compost grown, stoneground, wholemeal flour who will eschew, so far as is practicable refined sugars, manufactured sweetmeats, and processed foods and who will include in their dietary significant daily quantities of raw, fresh fruit and vegetables, will reap unmistakable dividends of health even after relatively short periods I single out bread (and would include, of course, other cereal foods, such as cakes and pastries) because I believe in the quantities in which it is normally consumed it is capable of exercising the greatest influence on the family health

The first reaction of the busy housewife may well be to hold up her hands in horror at the thought of the added chore of home breadmaking The ladies assure me, however, that the process can soon be reduced to a fine art Moreover, even the sceptical, having sampled it, seem prepared to make the effort on the commendation of its flavour, texture, and aroma Their testimony to its health giving properties comes later I am informed that at least a hundred housewives in this town alone regularly bake wholemeal bread for the family There is also considerable experience of this sort emerging from residential nurseries and institutions where enlightened dietaries are in force

In view of the urgency of the situation, it would be an encouragement if others with similar family or institutional experiences were to reaffirm them at the present time

Finally, it is to be noted that Dr Sinclair justly *dissociates himself from long-haired naturalism* The fact that, even in his learned treatise, he feels the need to do so suggests to me that as a profession, in consequence perhaps of the extravagent claims and vicious attacks of the naturopaths, we have come to regard the concept of fresh, whole, unadulterated, and naturally grown food as the province of the crank, whereas in truth the only really healthy communities which have ever been demonstrated anywhere in the world were found to be subsisting on just such a diet

Public Health Department,
Eastbourne
KENNETH O A VICKERY

RESERPINE IN SEVERE HYPERTENSION

SIR,—Professor Platt and Dr Sears report (April 14) that in three of their female patients lactation developed as a side effect of the administration of reserpine I was much interested in this as my wife has recently observed an apparently adverse effect of reserpine on lactation

A few weeks before term slight hypertension and fluid retention developed 'Serpasil' was prescribed No further rise in blood-pressure occurred, but water retention increased greatly and was only partly controlled by acetazolamide For the first few days after delivery she took no serpasil and diuresis was profuse Lactation started normally and she had a plentiful supply of milk About a week after delivery, serpasil was again prescribed since the blood pressure was still slightly elevated Within a few days, water retention set in and at about the same time the milk began to go back At the end of a week, she had difficulty in satisfying the baby giving him both breasts, whereas formerly she had had more than sufficient milk in one breast She decided to stop taking serpasil Approximately twelve hours later normal diuresis set in again and the breasts became heavily engorged The next day there was again more than sufficient milk and there has been no further trouble

Presumably a good many lactating women have taken reserpine, and it would be interesting to know whether any other similar observations have been made

Arlesheim Switzerland
A M WOOLMAN

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1 McCarrison R Nutrition and Natural Health London, 1944
2 Picton, L J Thoughts on Feeding London 1946
3 Price W A Nutrition and Physical Degeneration Los Angeles 1939
4 Wrench, G T The Wheel of Health London, 1938

us week the administration of exogenous hormones in do something to alleviate symptoms in advanced ises He emphasises the need to give hormone herapy in general a more rational basis and he nphasises the difference in response to hormone herapy before and after the menopause Of 17 patients ho responded to androgens 14 had had their first ymptom before the menopause whereas of 14 who nproved with œstrogens, 13 had had their first ymptom after the menopause and there were other ifferences in the behaviour of the two types of cancer **Ellis**[15] and his colleagues also concluded that estrogens were more effective in postmenopausal vomen Foss's view that present techniques are nadequate to detect hormone dependence may be too loomy What is lacking is not the methods but rrangements whereby individual attention can be iven to each patient with breast cancer The recent efinements in the technique of urinary œstrogen etermination, such as those recorded by **Brown**[16] have given these estimations a validity not previously known, and their extended application to problems of this kind, although tedious, is sorely needed

Salute to Adventurers

After the Metropolis Management Act was passed in 1855, forty-seven medical officers of health were appointed to the London districts (they were almost the only ones in the country) and in April, 1856, eight of them met at the house of Dr **Pavy** in Finsbury Square At a further meeting on May 13 the Metropolitan Association of Medical Officers of Health came into being this became the Society of Medical Officers of Health in 1873, and next week it celebrates its centenary

The M O H s of those early days were embarking on a new venture they had scant support from the vestries (who were often openly hostile), they had no textbooks to consult, and they were faced with "those difficulties and perplexities which must inevitably arise from so novel a departure in municipal administration"[17] It was for these reasons, and "to promote efficiency in the discharge of their duties and to aid the progress of sanitary science" that they felt the need for an association Their choice of Sir **John Simon** as the first president must have been automatic After 7 years as the first M O H for the City, he had in 1855 become the first central medical officer of the Board of Health, but the minutes of the association's first meeting show that he was chosen solely for his own qualities "and not in any way because of the office he held under the government" Among his many distinguished successors were Sir **George Buchanan** (1875–77) and Sir **Shirley Murphy** who, as president in the jubilee year (1906), described the society's first fifty years in an address which, with the other contributions to the jubilee number of *Public Health*,[18] gives us a mass of information, not only about its activities but also about the progress of public health in this eventful period Since its jubilee the society's presidents have included Sir **Francis Fremantle**, Sir **William Savage**, Sir **Alexander Macgregor**, Prof R H **Parry** and Sir **Allen Daley** Now in the centenary year this office is fittingly held by Dr **Charles White** who until his retirement a few weeks ago was like the first president M O H for the City of London, but is perhaps even better known both at home and abroad for his previous work in the adjacent post

At first the society concerned itself mainly with sanitary reform and the control of infectious diseases, and it soon began a liaison with Government departments which has steadily improved and which has often influenced legislation An outstanding achievement as long ago as 1877 was the inauguration of a weekly return of infectious diseases among recipients of relief but this was discontinued after a year, despite repeated appeals to the Government, and thirty years were to elapse before the first notification Act was passed in 1889 As time went on more and more attention was paid to personal health and discussions took place on domestic and school hygiene and physical culture, the teaching of hygiene in schools and the control of tuberculosis The early years of this century saw legislation on midwives, maternity and child welfare, school health, and tuberculosis, and after the first world war special groups of the society were formed for the benefit of the assistant medical officers doing this work A fever group was also established a dental officers group came into being, and what is now the Services group, with a membership of 300 past and present officers of the Armed Forces, was started in 1920 Describing, in the centenary number of *Public Health*,[19] the changes that have taken place in the membership and activities of the society, Dr **Stanley Walton** points out that medical officers of health are now in the minority the fellows include university teachers, officers in central government departments, chest physicians, medical journalists, factory doctors, and consultants in infectious disease Partly for this reason many feel that a second change of title would now be appropriate, and it is interesting to see that as long ago as 1905 the alternative name of "United Public Health Society" was suggested—one that would not be out of place today

The society's work was much affected by the National Health Service Act, but its history is full of examples of its ability to adapt itself to such changes It can congratulate itself, among other things, on having continued, after the Act was passed, the activities of its tuberculosis group and on retaining many chest physicians and sanatorium doctors as fellows, for this has done much to counteract the division of responsibility in tuberculosis control which the Act created The fever group has played a similar part But the Act gave the public-health service more than it took away for instance its section 28, dealing with care and aftercare and the prevention of disease, affords (*subject to Ministerial sanction*) almost unlimited scope for excursions into new preventive territory These opportunities have not been overlooked by the society, and its deliberations during the past decade show that attention is now being paid, for example, to mental ill health, the problem family, the care of the elderly, and the expanding work of health visitors, social workers, and

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[15] Ellis F *Proc R Soc Med* 1944 37, 731
[16] Brown J B *Lancet* 1955 i 320
[17] *Public Health* 1906, 18 2
[18] *Ibid* p 211

[19] *Ibid* May 1956, p 6

America, have obtained good results by orbital irradiation to a dose of about 900r, this evidently does not work in every case Hermann[2] in Edinburgh has reported 12 cases in which pituitary irradiation brought about most satisfactory results, and in 4 cases improvement was dramatic The dosage she gave varied between 3000r in ten days ,and 5000r over two months Many cases were reviewed four years after treatment, when results remained satisfactory, and there was no mention of any undesirable sequelæ

The value of radiotherapy in this condition should be recognised, and there may be a tendency to exaggerate the dangers of irradiation in the neighbourhood of the pituitary With modern technique, dose calculation is accurate , and, provided excessive dosage is avoided, no ill effects are likely In some cases where pituitary cachexia or interference with hypothalamic structures has followed irradiation of a pituitary tumour, the damage may wrongly have been attributed to the treatment, when actually the tumour was responsible Insertion of radon seeds into the pituitary can cause serious damage, not only to the functional activity of the gland, but to the neighbouring visual tracts , but this should not happen with properly administered external irradiation

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D K SAMBROOK

REVISION OF THE CURRICULUM

SIR,—Dr Ellis's plea last week to free the medical curriculum from the restrictions imposed by the G M C recommendations and let it loose for experiment by the various medical schools may be ideal in conception but would, I feel, be chaotic in practice

The result might well be training schemes throughout the country ranging from four to eight years, each reflecting the dominant influence of the particular school or university, and varying in content from my utilitarian ideas to the quite serious suggestion that courses in Latin and Greek should be compulsory for medical students In addition, with the dwindling number of medical students and consequent competition, there would be the temptation to indulge in the " Come to X School " campaigns with attractive slogans such as " Graduate at Y—No Anatomy Required "

I have no doubt that the medical curriculum is, from time to time, considered by the College of General Practitioners, but I have yet to hear of any medical school with G P s on the faculty or committee dealing with medical courses

If the Royal College of Physicians instigated a survey of opinion on the medical curriculum from the medical graduates of this country, I think they might well be surprised at the support for the utilitarian approach

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G M WYBURN

FLUIDS FOR INTRAVENOUS INFUSION

SIR,—Dr Barnard, in his letter of April 28, rightly stresses the need to scrutinise each bottle of infusion fluid when it is opened Pressures above or below atmospheric do not, however, of necessity indicate a fault

Consider, for example, the standard M R C container This holds 540 ml of solution and 70 ml of gas When it is filled and autoclaved the seal being tightly screwed down the gas pressure inside rises and falls to normal again on cooling If the seal is loosely inserted, so that the rubber may move slightly, gas is displaced during heating , but directly the pressure drops, the seal clamps down again In this event there exists a partial vacuum in the bottle, which, tapped smartly with the hand, produces the characteristic rattle known as the ' water hammer " effect

Increased internal pressure may be due to (*a*) slight pressurising of the filling room, to maintain an air flow away from the aseptic area, or (*b*) the difference in temperature during filling and during opening A range of only 10°C, which is moderate, would account for the 10 cm water pressure observed It may happen, too, that at filling the liquid itself is chilled

The fundamental criteria are the sterility and freedom from pyrogens of the solution These are not synonymous, and demand separate tests before the sample is released for use My own handling of several hundreds of thousands of intravenous infusion solutions has convinced me that contamination by micro organisms is exceedingly rare—they are found in one bottle in perhaps fifty thousand Almost invariably the organism is a mould, and it accompanies hair cracks of the base or gross pitting or cracking of the neck of the bottle, presumably as a result of rough handling Bottles which are faulty before sterilising nearly always explode during that process

It is a wise precaution always to scrutinise the sample against a good light, just before administration of the fluid If there is any obvious damage to glass or rubber, or if the solution shows any suspended solid, it should be put aside for further investigation

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PETER COOPER

RESERPINE IN ANXIETY STATES

SIR,—Reading the conclusion by Dr Hare and his colleagues (April 28) that there was no general tendency to alleviation of anxiety symptoms in 32 patients who were given reserpine prompts me to comment on the application of the term " tranquilliser " to this drug and cruder preparations from *Rauwolfia serpentina*

The effects of these drugs include depression, usually with extreme agitation and anxiety, insomnia, nightmares, and lethargy—all by now well recognised and frequently reported Now the term " tranquil " usually implies a peaceful, contented state of mind Only " lethargy," the commonest effect (occurring in 16 out of 40 cases of mine), could possibly be mistaken for this but the description given by patients has not led me to believe that such a frame of mind has developed It is described in such words as " I've had all the stuffing knocked out of me," " I've no energy at all," " a nauseating weakness " Tiredness or sleepiness are other terms used To describe such an effect, the word " depressor " would be more accurate , it would also include the quietening effect on noisy psychotics and the mood depressing function which has occurred in varying degree in 14 out of 40 patients

My other objection to ,the term " tranquilliser " is based on the fact that of 12 patients who had obvious mild anxiety symptoms when treatment with reserpine or ' Rauwiloid ' was started, only 2 improved in any degree at all, and 1 of these later developed troublesome dreaming " all night long " 3 became more anxious and agitated and developed marked or severe agitated depression One man who said he was always apprehensive, stated that he was rather more so when on rauwiloid This may not have been due to the drug, but it did not " tranquillise " him This lack of " tranquillising " effect has been remarked on by Joiner and Kauntze[1] among others

The term " depressor " would not of course cover the production of agitation or nightmares and insomnia I would be interested to have a psychiatrist's opinion as to whether the agitation is an effect of the drug or a reaction to depression The insomnia may well be a result of diurnal lethargy and drowsiness, but it is uncertain whether nightmares can be explained in this way

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P S TWEEDY

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[2] Hermann, K *Brit J Ophthal* 1952, 36 1

[1] Joiner C Kauntze R *Lancet* 1954 i 1097

is therefore arisen Those who do ileostomy and excision as a routine admit limited indications for resection and anastomosis (in children, the mentally deranged, and patients with circumscribed involvement of the bowel), but experience has taught them that retention of the rectum, whether anastomosed or isolated, can lead to severe exacerbation of the disease and its remote complications, such as arthritis Indeed perforation and exsanguinating hæmorrhage have been known to arise in the rectum alone The Gordon Hospital group have not, however, experienced any such difficulties, they contend that a low anastomosis with excision of the last inch of colon is the secret of success Time will tell

RECORDS IN GENERAL PRACTICE

THE latest publication[1] in the General Register Office series, Studies on Medical and Population Subjects, carries forward the account of the study[2] of general-practitioner records begun by Dr W P D Logan in April, 1951 Before this date attempts had been made by a few general practitioners to observe and record morbidity in their practices, but this study, in which 8 practices in different parts of the country were covered, represented the first coordinated effort of its kind The inquiry was extended to 2 more general practices, and the latest report includes returns from 13 family doctors, with lists totalling some 37,000, who have recorded each item of service given to their patients

The results are doubly interesting—both as an example of the use of a new research method in a new research field, and for the information gained on the distribution of morbidity in the community The item of service rendered by the practitioner, as reflected in the consultation rate, has been accepted as a valid and useful measure, when considered in relation to the total number of patients at risk While it is easy enough to record that a consultation has taken place, it is less easy to be certain that the cause of the consultation has been correctly assessed From the published tables it is clear that the number of medical certificates of all kinds issued in the practices concerned is high, and it may be inferred that many of the attendances and consultations recorded arose from the administrative need of the patient to obtain a certificate of his disability rather than from the disability itself

The conditions from which the patients were suffering have been classified according to the International Classification, and allowance must be made for the difficulties which were, no doubt, experienced by the Registrar-General's staff in fitting the practitioners' definitions into this pattern Accurate clinical definitions are seldom possible in general practice, and the analysis may be weakened rather than strengthened by attempts at too strict a classification In bronchitis, for example, it is clear that the practitioners who took part had their own ideas about the difference between "acute bronchitis," "chronic bronchitis," and "bronchitis" unqualified It remains to be seen how far agreement can be reached about definitions of disease as first seen in the practitioner's consulting room, and those concerned with statistical evaluation in this research field have to give close attention to this point

The broad morbidity picture recorded in the second and third years of the survey confirms the earlier pattern,[2] and it is now possible to rank the causes of illness and disability in order of frequency of occurrence This study cannot, however, show with accuracy how far the incidence and prevalence of particular conditions are influenced by geographical situation, or, except within broad limits, by type of practice It is to be hoped that the larger investigation which is being conducted by the College of General Practitioners and the General Register Office as a combined operation will provide more precise and useful information Much remains to be learnt about the conduct of morbidity surveys, both large and small, and about specific as well as general aspects of morbidity This work must certainly go on, for an accurate assessment of the community's state of health at any given time can be a valuable starting point not only for further research but for administrative decision and action

B M A AND G M C

THE qualifications and opinions of its direct representatives on the General Medical Council ought to be a matter of some interest to the profession but only by the enterprise of two independent candidates Dr Whiteside and Dr Dillon, was the recent election saved from being a formality Their letter on p 687 will, we hope, lead the British Medical Association to reconsider its procedure over these elections Of course, the association may, as before, see no reason for change it may say, reasonably enough, that like any other medical group it is entitled to propose its own candidates and try to persuade people to vote for them, using its machinery for the purpose But it should understand that this reply will not in fact satisfy those doctors (both outside and inside the association) to whom it has long seemed that election to the General Medical Council takes place by automation from B M A House The fact that the representatives chosen have always given long and useful service to the profession is irrelevant in relation to the real issue—namely, whether damage is being done by depriving a democratic process of its meaning Nobody could expect the B M A to resign its right to nominate candidates, but perhaps thought could be given to some such suggestion as we made six years ago, when we said[1]

> "As things stand, an independent candidate would have to have quite exceptional claims before he could succeed against the B M A 's official nominees, and we suggest that the elections would be given more reality and usefulness if the B M A , *instead of asking voters to keep rigidly to an official list, were to present them with a choice of a dozen or more candidates all of whom would be acceptable to the association If this incidentally improved the chances of an occasional outsider, so much the better* both for the G M C and the B M A , for unreal elections are seldom quite healthy "

A RADIOLOGICAL JUBILEE

ON Jan 6, 1896, the first news reached this country that Professor Rontgen of Würzburg had discovered a remarkable and so far unrecognised form of energy Little more than three months later there appeared the first journal to be devoted entirely to the new science of radiology it was called the *Archives of Clinical Skiagraphy* and it was edited by Sydney Rowland, a young graduate of Downing College, Cambridge From this vigorous ancestor, the *British Journal of Radiology* can claim descent, and this month it celebrates its diamond jubilee In its May issue, senior members of the British Institute of Radiology survey the achievements of these sixty years Prof Gilbert Stead a distinguished teacher of radiological physics, traces the astonishing progress that has brought us face to face with the awesome discoveries of nuclear physics with their enormous potency for good or evil Dr Russell Reynolds, who has studied X rays since Rontgen's day, discusses some of the notable advances in technique which have made diagnostic radiology an increasingly powerful aid to the clinician, and Dr N S Finzi writes, from his long experience, of change and expansion in the methods of radiotherapy Mr Cuthbert Andrews manufactured X-ray tubes for nearly forty years and he has interesting things to say about changing fashions in

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[1] Studies on Medical and Population Subjects no 9 (in continuation of study no 7) General Practitioners Records H M Stationery Office Pp 80 6s 0d

[2] See *Lancet* 1953 ii, 978

[1] *Lancet* 1950, i 627

FOOTBALLER'S ANKLE

SIR,—We have read with much interest Mr McDougall's article[1] Most osteo articular lesions in athletes give rise to no symptoms, as Mr McDougall points out, but they are clearly demonstrated by radiographic examination, which shows areas of calcification in the articular ligaments or at the insertion of tendons In boxers, for instance, La Cava[2] has found areas of calcification on the dorsal aspect of the hands at the tendinous insertion of the radialis muscle

The lesion of the astragalotibial joint in soccer and rugger players, wrestlers, and skiers has been well known for more than twenty five years[3,4] According to Biolato and Foà,[5] in trained subjects there is notable increase in elasticity of articular ligaments and therefore a wider range of excursion of the joint itself In the ankle joint there is enlargement of the tibiofibular mortise so that the astragalus takes part in dorsal and plantar flexion, abduction, and adduction of the foot This abnormal mobility is the cause, according to Allaria,[6] of the arthrosis of the tibiofibular syndesmosis found in skiers

Such conditions may be due partly to repeated slight trauma to the articular surface[7], but they are largely due to repeated severe stretching of ligaments and tendons This is in agreement with the concept of "chronic entesitis," recently described by La Cava at the Argentine Congress of Sporting Medicine

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Stadio Torino, Rome, Italy

A VENERANDO
G LA CAVA

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[1] McDougall A *Lancet* 1955 ii 1219
[2] La Cava G Le fratture della mano nel pugilato Rome, 1948
[3] Baetzner W Sportunfall und erste Hilfe Berlin 1928 Sport und Arbeitschaden Leipzig 1936
[4] Giannotti M Chirurgia delle lesioni da sport Turin 1939
[5] Biolato D, Foà A *Congr int Méd Sport* 1933
[6] Allaria A *Chir Organi Mov* 1950 1 25 *Studi Med Chir Sport* 1950 10 353
[7] Venerando A Terzani G Atti 3 Giornata Reumatologica Rome 1953 p 169

PARAMETRIOGRAPHY

SIR,—Hysterosalpingography, pelvigraphy, and gynæcography are approved methods for the X-ray examination of the female genital organs Arteriography can give some information about adnexal tumours, but we lack a good objective method for studying the extension of a parametrium tumour or an infiltration of the parametrium Gynæcological palpation gives information on the size of the tumour, but it is often impossible to decide whether the tumour belongs to the parametrium or not In order to overcome these difficulties the following method has been worked out

The patient is placed in the lithotomy position Two long, slightly curved injection needles are inserted 2–3 cm into the tissue about 5 mm lateral to the cervix on each side parallel to the long axis of the uterus The usual intra uterine cannula is inserted into the external os and fixed, and a third needle or thin cannula is introduced into Douglas's pouch The patient is then placed in the supine position on the trochoscope table During fluoroscopy 30 ml of a solution consisting of equal parts of 0 25% lidocaine solution and 35% iodopyracet ('Umbradil') plus 500,000 I U penicillin are injected into each parametrium Then the first postero anterior film is taken After that 10–20 ml of 'Endografin' (Schering) or similar viscous water soluble contrast medium is injected through the uterine cannula during fluoroscopy Films are taken in posterior anterior, lateral, and oblique projections If a tumour found on *gynæcological palpation is not seen* in the parametrium, the patient is placed in the prone position The foot end of the table is elevated about 15° 600–1000 ml of carbon dioxide is instilled into Douglas's pouch during fluoroscopy, and new films are taken

This method has been practised since July, 1955, in patients with acute adnexitis, in order to follow the development of the inflammation, in some cases of sterility and in cases where the findings on gynæcological examination have been inconclusive In all, 40 women, including outpatients, have been examined, and so far no complications have occurred On the contrary, in cases of acute adnexitis injection of penicillin into the parametrium seems to be of value, and is now used in therapy

The results have been very promising In several cases a correct diagnosis of endometriosis was established where "adnexitis" had previously been diagnosed, and in others the presence of extra uterine pregnancy or ovarian tumour, diagnosed by this method, was invariably confirmed at subsequent laparotomy

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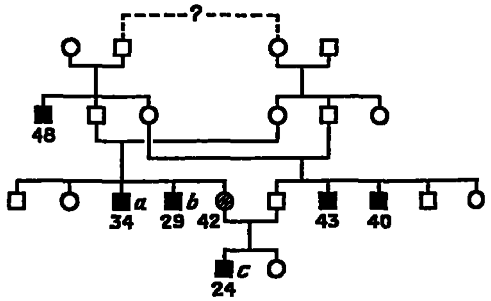
AXEL INGELMAN-SUNDBERG

PEPTIC ULCERATION IN A FAMILY

SIR,—The accompanying figure, showing the pedigree of an intermarrying Tripolitanian Jewish family, may be of interest in view of the stress now laid on the psycho somatic ætiology of duodenal ulcer 7 members of the family had peptic ulcer, of these I know personally (*a*), (*b*), and (*c*), and in the remainder the diagnosis was confirmed radiographically Wright et al[1] recently described a family in which 9 out of 13 living siblings, have duodenal ulcers



Family with 7 cases of peptic ulcer (black = duodenal ulcer, hatched = gastric ulcer) Figures indicate age at onset

Dorot Negev Israel

A YUVAL

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[1] Wright J T Grant, A Jennings D *Lancet* 1955, ii 1314

KETONURIA—A FALLACY IN ROTHERA'S TEST

SIR,—The standard textbooks on sideroom work and urine-testing state that there are no fallacies in Rothera's test for ketones There would appear to be one fallacy which may occasionally cause confusion

A male diabetic, aged 56, was admitted to hospital for review and stabilisation Mild ketosis and glycosuria were present on admission The glycosuria rapidly disappeared on adjusting the insulin dosage, but, despite the absence of other clinical or biochemical evidence of ketosis, routine urine tests by the nursing staff repeatedly showed "acetone present" The ferric chloride test was negative, and on checking the nitroprusside test the addition of ammonium hydroxide led to an immediate colour reaction, but the colour was not the typical purple normally seen in ketonuria Investigation revealed that the patient was receiving an aperient containing a small amount of phenolphthalein, and this drug, excreted in the urine, was producing the colour change in the presence of free alkali

This fallacy in Rothera's test is not generally recognised and might, if overlooked, lead to insulin overdosage It was found that urine containing phenolphthalein did not produce a colour change on 'Acetest' tablets, and the Ames Company Ltd, which manufactures these tablets, has kindly confirmed this by more accurate investigations The use of the tablet method of testing for ketones will, therefore, avoid this fallacy, which should perhaps be recognised in the teaching of medical and nursing students

I am indebted to Dr J A W McCluskie for permission to publish this case

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A CAMERON MACDONALD

Special Articles

HOME CONFINEMENT *

C S RUSSELL

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PROFESSOR OF OBSTETRICS AND GYNÆCOLOGY IN THE UNIVERSITY OF SHEFFIELD

Professor Claye, of Leeds, has recently said that domiciliary delivery deserves to be as dead as the odo and already it is in that desirable condition two of the more civilised countries in the world "[1] e was speaking of Australia and New Zealand He went n to say that "alone among the more populous countries the English speaking group Great Britain remains ld fashioned" Against this opinion may be set the ct that in Holland an efficient home service has been ported by Professor ten Berge[2], and Dr L Roberts, ur medical officer of health in Sheffield, has expressed he opinion that the home should be the best place for woman to have her baby[3]

The General Practice Review Committee of the ritish Medical Association were firmly of the opinion hat midwifery, and not only home confinement, is an ntegral part of general practice, and that every possible ncouragement should be given to general practitioners to ndertake it About half the practitioners answering questionary said that they liked midwifery, and ished to increase their experience, a third undertook ases only when specially asked to do so, and the emainder wished to discontinue it[4]

Maternity Medical Services in the Home

he General Practitioner

Under the present arrangements an expectant mother nay, if she wishes, make arrangements for a doctor to rovide her with maternity medical services These ervices include

(*a*) Antenatal care throughout pregnancy (including an nitial antenatal examination and one at the thirty sixth veek of pregnancy)

(*b*) Attendance at any emergency in connection with the regnancy if the doctor is summoned on the patient's behalf

(*c*) Attendance at the confinement if the doctor thinks it necessary or is called in by the midwife

(*d*) Medical supervision of the mother and child during he puerperium

(*e*) Postnatal care of the mother, including a pelvic xamination at or about the sixth week after confinement Why the postnatal pelvic examination is named, rather than an antenatal pelvic examination, is not clear to me I should have thought the latter was much more important]

The family doctor may provide maternity medical ervices for a patient who is on his medical list, and he is paid a special fee for these services There are, however, certain doctors whose obstetric experience has been approved by the local professional committee The names of these doctors are shown separately or are specially mentioned in the executive council's list They are entitled to a higher fee, if in an emergency they are called in by midwives to patients for whom they have not previously arranged to provide maternity medical services, they are entitled to a fee from the local health authority If the family doctor does not wish to undertake the maternity care of one of his ordinary patients, he will advise her to consult one of his colleagues on the obstetric list

The mother receives the services free of charge, and the doctor is paid a comprehensive fee by the executive council

The Local Health Authorities

Besides the services given by general practitioners, the local health authorities have a duty to provide ante natal and postnatal clinics for the regular supervision and care of expectant and nursing mothers Routine medical examinations and special investigations are undertaken by these clinics, welfare foods and simple medicaments are supplied, detailed advice on mothercraft is given, and where practicable, priority dental care is provided The clinics are in fact centres for all the educational and social work that is so desirable for pregnant and nursing women They are held at the maternity and child-welfare centres, where the authority's midwives and health visitors normally work

Under the 1936 Midwives Act the authorities also have to secure that there are enough midwives in their area If the mother chooses to have a midwife rather than a doctor, to attend her, the midwife will call in medical aid only if this is required The cost of this is met by the local health authority The authorities also have the power, though not the duty, to provide domestic help in households where this is needed

The Midwife

A word must be said at this stage about the midwife In the past she was often decried, sometimes with much justification, and even today some people think of her as a modern Sarah Gamp The Working Party on Midwives remarked that "with past intolerance equally distributed (between doctors and midwives) the way should be smoother today for that integration of midwifery and medicine which we regard as essential to the most profitable employment of both" But encroachment of the doctors they said, is not in itself sufficient to account for the failure of midwifery as a profession for women Another reason is that, while the public has gradually become nurse-conscious, it has not, at the same time, become midwife conscious Victorian prudery which shrouded everything connected with childbirth in an almost impenetrable mist, is not yet dead

In 1948 a municipal midwife, because of shortage of accommodation, was quartered in a small private hotel She was requested not to use the general lounge because her presence might embarrass the other guests

My view is that the woman who is in attendance at labour must be someone of education, who is properly trained, and who has a pride in her work But how can she have the sense of a job well done unless she is encouraged to take responsibility both during labour and in the antenatal and postpartum period? This encouragement must come from medical men and women, for nobody else is likely to give it to her I am sure that unless we adopt a proper attitude to the best of our midwives, we shall be laying up for ourselves and for our children a store of trouble Midwifery recruitment will fall, and a profession which is not yet all that respectable will fall on evil days

It is quite clear to me that neither the doctor nor the midwife must monopolise the patient but that they must work together as a team, and I accept the Royal College of Midwives' view that "the function of the midwife should be substantially the same whether she is engaged in institutional or domiciliary practice"

The Divided Responsibility

The responsibility for maternity care is divided between those employed by executive councils, local authorities, boards of governors, and regional hospital boards, so we cannot easily agree as to what are the best arrangements for each patient This need not surprise us for reason to be proud of estimates for the present financial year True, another £12 million was provided for hospital boards, an increase of about 4%, but a little over £7 million of that would go to meet wage-claims and rising food costs Precious little improvement of the service would be available out of the extra money

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* Based on a lecture given to the Medico Chirurgical Society of Sheffield on Feb 2, 1956

[1] Claye A M *J Obstet Gynæc Brit Emp* 1955 62 784

[2] ten Berge B S *Ibid* p 785

[3] Roberts L Personal communication

Brit med J suppl 1953 ii 109

Training of Mental-health Workers

Raising this subject in the House of Commons on April 30, Mr KENNETH ROBINSON said that ideally the future of the mental-health services lay not so much in having more and more beds as in emptying the mental hospitals and in preventing people from having to be admitted to them This could only be achieved by extending and improving outpatient facilities and community and domiciliary services The local health authorities were responsible for these latter services, and their instruments in carrying out these duties were the mental-welfare officers and the psychiatric social workers He thought it odd that though both carried out highly responsible duties the P S W s were highly trained and the officers not trained at all

In 1951 the Mackintosh Committee recommended that there should be a substantial increase in the number of P S W s and pointed out that the mental-health service demanded a large number of trained mental-welfare officers These officers were responsible for prevention and aftercare among mental patients and perhaps their most important work was done in their capacity as duly authorised officers The duly authorised officer often initiated the whole procedure of certification, and he might indeed be the first contact between the members of the public and the mental-health service He could, and often did, override the opinions of general practitioners on patients suffering from mental disorder One would imagine that these officers would undergo a rigorous and extensive course of training and obtain some kind of national qualification, but nothing of the kind happened The Minister of Health in reply to a question had admitted that there was no national scheme of training, though some local authorities arranged courses The Minister had added that the position was being studied by a working party But immediately after the issue of the Mackintosh report, Mr Robinson recalled, an ad-hoc committee was formed, with representatives from the universities, the Royal Medico-Psychological Association, the National Association for Mental Health, and the Society of Mental Welfare Officers They had submitted proposals about training to the Minister in 1952 After 18 months the Minister wrote saying that the question could not be considered until the Working Party on Health Visitors, under Sir Wilson Jameson, had reported The mental officers themselves appreciated that their increasing responsibility demanded a high standard of competence, national training, and qualification, especially for new entrants into the service

Some months after the receipt of the Minister's letter the various bodies worked out an actual syllabus for a year's course The National Association for Mental Health agreed to organise a scheme and a further approach was made to the Minister with the same negative result Now, when the Jameson Working Party was almost ready to report, the bodies concerned were asked to await the findings of yet another committee, the Younghusband Committee on social workers, which meant a further delay of anything up to two years

Turning to the psychiatric social workers, Mr Robinson said that for them there was an established training of a high quality, but there were not enough training facilities and not nearly a large enough output In its recent report the Committee on Maladjusted Children estimated that for a satisfactory child-guidance service alone four times as many P S W s were needed—420 instead of the present 109 , hospital authorities also needed more, for vacancies existed in every mental hospital There was thus an acute shortage of these workers and the training was stiff In his view the salary range of £495–750 p a was not sufficient incentive for the right kind of people

Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said there were 1100 mental-welfare officers in the local health authority services Many had considerable experience from the days when the local authorities ran their own mental hospitals, and it should not be suggested that they were not doing their job satisfactorily The advice of those who had had long experience was available to new comers Many local authorities were providing training courses, some at universities and some within their own organisation, including secondment to a mental hospital She realised, however, that more courses were needed and she appreciated that the professional associations representing welfare officers felt strongly that there should be a properly recognised training

The Mackintosh Committee were set up before the new pattern in the mental health service evolved By their terms of reference they necessarily considered mental health workers in isolation But barriers between the mental and the physical health services were breaking down and we no longer regarded mental-health work in a vacuum It might well be that from the reviews of the Working Parties on Health Visitors and Social Workers there would emerge a new concept of social welfare workers and the kind of training suitable for them

Another report which the Government could not ignore in plans for mental-health work was that of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency (now sitting)

She sympathised with welfare officers who had waited so long and patiently, but while it was essential that they should be properly fitted to discharge their functions she did not agree that social work for the mentally ill could never be combined with work for those who were in difficulties in other ways Sometimes it might be an advantage in obtaining the cooperation of a family if the trained worker came to them as a welfare visitor and not exclusively as a mental-welfare worker There was also an advantage in the hospital P S W having a wider sphere of activity, since he was the link between the patient and his home and friends and the medical and nursing staff of the hospital or clinic These workers took a two-year social science course at a university, followed by a year's practical experience, and then a university mental-health course The Minister assisted with grants for the university mental-health course Since 1949–50 the grant had been £8000 and the average yearly intake of students for these courses was about 50 She did not deny that there was a shortage of these workers, but estimates of the number needed varied from 870 to 1500 According to the Association of Psychiatric Social Workers the number of qualified workers was 447, but that did not include many local-authority workers who, though they had not taken the recent specialised training, were qualified by long experience Similarly hospital returns showed that they had 311 whole-time workers of whom only 182 were included in the association's estimate The Government did not believe that greater numbers of students would automatically be forthcoming if more courses were provided or if the scale of the Government contribution were increased

QUESTION TIME

Smoking and Lung Cancer

Mr J K VAUGHAN MORGAN asked the Minister of Health whether he was now in a position to make a public statement as to the effect of smoking in producing carcinoma of the lung —Mr R H TURTON replied Since my predecessor made a statement in February, 1954, investigations into the possible connection of smoking and cancer of the lung have been proceeding in this and other countries Two known cancer producing agents have been identified in tobacco smoke, but whether they have a direct rôle in producing lung cancer, and if so what, has not been proved The extent of the problem should be neither minimised nor exaggerated The number of deaths from cancer of the lung has risen from 2286 in 1931 to 17,271 last year To place the figures in perspective—in 1954, out of every 1000 deaths of men aged between 45 and 74, 77 were from bronchitis, 112 were from strokes and apoplexies, and 234 were from cancer, of which 85 were cancer of the lung Deaths of women from cancer of the lung are still not very significant and represent a small fraction of the total

The chairman of a committee of the Medical Research Council which has been investigating the subject considers that the fact that a causal agent has not yet been recognised should not be allowed to obscure the fact that there is, statistically, an incontrovertible association between cigarette smoking and the incidence of lung cancer The statistical

TABLE II—AGE DISTRIBUTION OF 160 WELFARE CASES AND 103 DOCTORS' CASES IN THE 1953 SHEFFIELD SAMPLE

	Age groups	
	Under 20	Over 20
No of welfare cases	8	152
No of doctors cases	1	102

pressure to get a hospital bed. We who have the responsibility for deciding who should occupy the beds under our care may find ourselves in an uncomfortable situation. On the one hand, we have those who are trying to get another case into hospital, and, on the other, those in hospital management and nursing who have to provide all the non-medical services, and who often want to keep the case out.

Doctors' Cases

The age and parity distribution of those booking family doctor first, but who do not normally have antenatal care at the welfare clinics, is not remarkable, except when their ages are compared with those attending the welfare clinic first (table II). Those under 20 years of age usually went to the clinic first.

Whereas before 1948 comparatively few women booked doctors as well as midwives, under the National Health Service the services of both are available without charge, and over half the women now confined at home book a doctor. He accepts responsibility for the case and may, at his discretion, attend the confinement or leave it to the midwife.

More and more general practitioners are also providing antenatal care for their booked patients, and local health authorities are encouraging midwives to work in association with the doctors. "There is thus at present a transitional stage in which medical antenatal care for domiciliary cases is changing hands"[7]—and, if general practitioners and midwives give a better service under the new conditions, this change is all for the good.

Personal preferences of the patients also play a part. As the wife of a traffic manager said, "Everybody doesn't like to meet what you have to meet at antenatal clinics"—though it is only fair to add that she was equally critical of her own doctor's supervision.

A history of previous abortion, difficulty with pregnancy or labour, or stillbirth or neonatal death, is less frequently encountered in the group booking the family doctors than that which attends the maternity service of the local health authority. Social class probably still largely determines whether the patient goes first to a family doctor or to a welfare clinic, and as social class and reproductive performance are closely linked, there is nothing surprising about this difference. There is, however, one other conclusion that can be drawn from this comparison. The domiciliary midwives in Sheffield, working on their own, have a more difficult type of case to look after than those who only assist the family doctors. Whether we should praise them for their enthusiasm or criticise the arrangement is debatable.

Are More Hospital Beds Required?

The Ministry of Health advises that "unquestionably most multiparæ who have had four or more children would be within the group having medical reasons for admission"[8]. If we accept this view, and if we add all patients over the age of forty, all who have had a previous abortion, previous pregnancy or labour difficulty, stillbirth, or neonatal death, we find that 41 of our 161 welfare patients (and 17 patients booked with general practitioners) should not have been booked for home confinement. To these we may add 26 primigravidæ and 32 parous women, who wanted a hospital bed, then we may deduct those whose booking arrangements were subsequently changed, and reach the grand total of 95 cases, the equivalent of just over 1100 cases a year.

This figure does not take into account primigravidæ who have booked a doctor but would have preferred a hospital bed if it had been available, or parous women who have given up trying to get a bed, nor does it take into account the relatively short stay in hospital (not more than ten days) that is all that can be offered to patients who are taken in. This last point is a matter about which some senior hospital midwives hold strong views, maintaining that if only we kept our patients for the full fourteen days, very much would be gained, especially in respect of breast-feeding. For myself, I am not convinced that an extra few days in hospital would make so much difference. What concerns me more is that the rapid turnover in institutions makes it very difficult to keep the risk of cross infection negligible.

In round figures it may be said that at least 1000 extra deliveries might well take place in institutions, which—surprisingly enough—would bring the proportion of institutional deliveries for Sheffield up to only 70%.

Selection of Cases by the Hospitals

Could the hospitals improve their ways of selecting cases, and could they find beds for these hundreds of women who perhaps ought to come in? No doubt some better selection is possible, but it is extremely unlikely that any substantial adjustments can be made.

I do not altogether hold with the policy of first come, first served, but there is much to be said in its favour. At least it encourages early antenatal care, which allows us to examine patients when their natural state of health is not materially altered by the pregnancy, and to deal with any gross abnormality, such as an ovarian tumour, expeditiously and with the least risk.

My figures show that in the teaching hospitals patients attend early—a practice which must, by modern standards, be encouraged. In the non teaching hospitals a substantial proportion of cases are booked because of adverse home conditions. If they keep out patients who should come in for more obstetrical reasons, it is just one of the deficiencies of the service. Examining such data as I have, I cannot see how beds can be found for any but a handful of the many hundred cases who really should come in.

Possible Improvements

In my view, all is not well with our maternity services, but to find ways to improve matters is not so easy.

More Maternity Beds

Taking the long view, we should, I believe, press for extra maternity beds, but who is to provide them, and who is to look after them when they are provided?

Taking the first point first, I like the idea of the local authority and regional hospital board providing them as a joint centre for domiciliary midwives and for selected general practitioners. The local authority must be included, for they have many responsibilities for the care of the pregnant woman over and above what the general practitioners have time for. The day to day running of such a home could very well be in charge of the local authority midwives who are already doing this in the patient's home, and general practitioners could be appointed to do the day-to-day minor obstetrical procedures. I feel very strongly that some supervision, maybe even control, should be in the hands of the consultants, or at least doctors who have the necessary experience to advise on obstetrical matters.

Aristocracy of General Practitioners

Though we should have extra maternity beds, I do not think that we want more hospital maternity beds—with the full complement of consultants, registrars, and house-surgeons—for an increase in the number of hospital beds would still further dilute the material available to the general practitioners. The arrangement I have suggested would have the support of the Central pulled down and 75,000 people were rehoused This year he hoped that these figures would be substantially higher, and he was confident that before long we should reach the target—namely, to rehouse every year at least 200,000 people from the slums

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[7] *Minist Hlth Rep* 1952

[8] Selection of Maternity Cases for Admission to Hospital Ministry of Health circular Aug 11 1951

London's Drainage

The London County Council is to consider next week the proposals of the rivers and drainage committee for a major programme of improvements estimated to cost about £9³/₄ million at the council's southern outfall main-drainage works The scheme involves large civil, mechanical, and electrical engineering works and buildings, and will, together with the equally large improvements already well advanced at the northern outfall works, considerably improve the condition of the Thames

Infant Mortality in Scotland

In Scotland the infant-mortality rate in 1955 was 30 per 1000 live births [1] This rate is the lowest recorded in Scotland, being 1 below that for 1954 and 5 below the five years' average

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[1] Quarterly Return of the Registrar General Scotland quarter ended Dec 31, 1955 H M Stationery Office Pp 40 2s 6d

Infectious Diseases in England and Wales

Disease	Week ended April			
	7	14	21	28*
Diphtheria	4	7	5	8
Dysentery	1336	1442	1125	1319
Encephalitis				
Infective		2	7	1
Postinfectious	2	1	3	1
Food poisoning	153	185	166	190
Measles, excluding rubella	3354	2972	2105	1993
Meningococcal infection	40	35	18	27
Ophthalmia neonatorum	39	30	39	27
Paratyphoid fever	3	7	12	7
Pneumonia, primary or influenzal	698	631	433	369
Poliomyelitis				
Paralytic	8	12	15	10
Non paralytic	2	8	6	5
Puerperal pyrexia	258	246	253	222
Scarlet fever	681	537	516	647
Smallpox				
Tuberculosis				
Respiratory	561	738	701	801
Meninges and C N S	15	12	13	12
Other	62	70	75	77
Typhoid fever	2	1	3	2
Whooping cough	1346	1451	1545	1767

* Not including late returns

Appointments

COPELAND, W A, M B Aberd, D M R D whole time consultant in radiodiagnosis, Edinburgh Northern group of hospitals

DARNBOROUGH, JACK M B Edin whole time deputy director Sheffield regional blood transfusion service

GORDON, DOUGLAS M B Edin, D M R D D M R part time consultant radiologist, Moorfields, Westminster and Central Eye Hospital (Westminster Branch)

MURPHY, E F, M D N U I, M R C P E asst physician in infectious diseases, Seacroft Hospital, Leeds

READER, D M M B Lond D OBST registrar in obstetrics and gynæcology, Gloucestershire Royal Hospital Gloucester

TREVAIL ARCHER C J M B Manc asst anæsthetist, Northampton area

WATT P A M B Camb, D OBST medical registrar, Royal United Hospital Bath

The Hospital for Sick Children, Great Ormond Street, London

CLAIN ALLAN, M B Cape Town F R C S part time surgical outpatient assistant

MACKENZIE D Y M D Lond M R C P D C H house physician

O DONNELL, BARRY, M CH N U I, F R C S senior surgical registrar

WALLIS G C W M M B N Z D L O resident registrar to the ear, nose and throat department

Manchester Regional Hospital Boards

DANZIGER ARNOLD M R C S, D A asst anæsthetist (S H M O) Burnley and district hospitals

JONES W K M R C S F F A R C S consultant anæsthetist Manchester Royal Infirmary and South Manchester hospitals

TURNBULL F W A, M B Edin, M R C P consultant chest physician Manchester chest clinic, Baguley Withington and Wythenshawe Hospitals

WOOLLEY, P B M B Manc M R C P asst chest physician (S H M O) Manchester chest clinic and Monsall Hospital

Notes and News

THE TEACHING HOSPITAL AND THE UNIVERSITY

AT the annual meeting of the United Sheffield Hospitals on April 26, SIR FRANCIS FRASER considered what a teaching hospital should aim to provide for its university, in the light of Wilfrid Trotter's assertion that clinical medicine is compounded of practical art, applied science, and experimental science

" Science, or rather the scientific method," said Sir Francis, " requires that a conclusion in any situation be reached only when the evidence is complete and that until then judgment must be left in suspense In the practice of medicine it is clearly unjustifiable to suspend judgment and its consequent actions in this way, and so the clinician brings to his aid a practical art For this he requires experience of similar situations, a cultivated intelligence, and knowledge of and sympathy with human beings of all types " It is in the teaching hospitals that the future practitioner forms his habits and his attitude to sick persons " Is there perhaps a tendency in teaching hospitals, occupied as they must be in providing for the more material requirements of diagnosis and treatment of serious disease, to let this aspect of the care of patients look after itself and to take it for granted ? Each of you must have received on frequent occasions the story of the patient anxious and fearful of the unknown being kept waiting in unattractive surroundings for hours perhaps before an overworked member of the staff is able to give him or her a few minutes' attention, only to refer him to another department where the same thing happens What the patient wants above all is to pour out a story to a sympathetic and understanding physician and to receive comfort and encouragement That is the essence of the art of medicine Are the practitioners of the future who are being trained as much, or perhaps even more, by example as by precept receiving the influence which it is our duty to provide ? "

Turning to clinical medicine as an applied science, Sir Francis remarked that clinical trials, based on observations in animals, can be adequately provided for only in teaching hospitals, where clinicians can cooperate with the staffs of the university's basic science departments " Every teaching hospital should be sufficiently elastic in accommodation and staff to be able to contribute to investigations of this type, and teaching hospitals have the responsibility to encourage them " The development of medicine as an experimental science—now usually known as clinical science—has led to the appointment of whole time heads of departments of clinical medicine and clinical surgery, with whole time staffs to assist them and with laboratories close to the wards A few pædiatric departments are similarly staffed and equipped, and before long workers in other specialties will need similar opportunities " I have visited many teaching hospitals in this and other countries, and no matter how recently they have been planned and built there is always the same experience—that the laboratory accommodation for the clinical departments is much too small I would suggest that laboratory accommodation adjacent to wards is likely to be wanted in the near future on a scale that may well seem fantastic at present "

In conclusion Sir Francis urged that the main teaching hospital of a university should contain at least small departments and a few beds devoted to each of the specialties " Only in this way can each specialty be inspired by the advances taking place in the others and enabled to share in the new knowledge and methods For the care of the patients of the community, by means of the applied science and the art of medicine, these special departments may well have larger units in other hospitals in the area, but they should all share in the invigorating intellectual environment of the university clinical centre "

THE NATURE OF GENIUS

THE centenary of the birth of Sigmund Freud was commemorated at a meeting held in London last Sunday by the International Psycho Analytical Association, when Dr HEINZ HARTMANN, the president, took the chair, and Dr ERNEST JONES gave the Freud memorial lecture

The question whether there really is such a thing as genius—that is to say, any attribute that differs in its very nature from those present in all human beings—Dr Jones answered with a decided No the differences between individuals, and between races, are quantitative rather than qualitative ith the district midwife at one of the local-authority linics In Bristol general practitioners can already ndertake the antenatal care of their own patients, hether booked for hospital or home confinement, in ocal-authority clinics The scheme is closely linked ith the consultant service, obstetricians from the main ospital centres holding regular sessions at each clinic, o which patients can be referred by the general practitioners The local authority's medical officer covers the antenatal supervision of mothers whose own doctors do not practise midwifery The district midwives share with he doctors the antenatal care of mothers booked for domiciliary confinement The expectant mother is thus able to attend at one centre near her home, where all members of the obstetric team are available (Redman and Walker 1954)

General Outline

The scheme we have in mind would require a block of labour wards attached to a maternity hospital Each would consist of a suitably heated room with simple equipment such as would be found in a good household which has been prepared for a confinement—i e , bed, cot, wash-hand basin, and so forth Except for preparing and cleaning the room, no extra staff would be needed When the woman went into labour she would inform the district midwife who would arrange for her admission to this labour-ward and accompany her there If the midwife undertook pupil-training, a pupil would also attend The patient would not be left by herself at any time during her labour Her own doctor would be informed at once and, with the midwife, would be responsible for the conduct of the case When the mother had been safely delivered and had recovered from the effects of her labour, she would be taken home by ambulance with her baby, accompanied by the midwife Nursing would then be continued as for a home confinement This scheme would have the following advantages

1 The delivery would be conducted under ideal conditions If any complications should develop, all the resources of the maternity hospital would be easily available

2 The mother would have a sense of reassurance knowing the resources of the hospital were there if wanted

3 She would be attended at her delivery by her own doctor and midwife Continuity of care and personal relationship is extremely important As one mother said "I should feel more confident if I knew I was being looked after by people who not only knew my case but knew me."

4 A relative or friend would be allowed to accompany the mother, if desired

5 The risk of exposure of mother and baby to hospital cross-infection would be greatly reduced

6 Most mothers in hospital begin to fret after the first few days and we feel sure they would be glad to go home so soon

7 There would be considerable saving of public money

Discussion

With the excellent transport now available, there is no clinical reason why most mothers who have had a normal confinement should not go home soon after delivery Owing to shortage of beds this sometimes happens now, and no harm follows We see little difference between transporting the patient by trolley from a labour-ward to an ordinary ward and transporting her from the labour-ward to an ambulance, under cover and so to her own home In fact, we believe that a return home so soon after delivery is preferable to discharge from hospital on the 4th or 5th day If the patient goes home at once, arrangements will certainly be made for domestic help, but if she goes home later she may well have to start household duties long before she is fit

The time for sending the mother and baby home will, of course, vary and must be left to the judgment of the team It would normally be about the time when a midwife would leave a case after completing a home delivery The midwife would have to give extra time here to see the mother and baby safely home and comfortably settled A similar procedure of immediate return home has been reported in a fairly large series of hernia repair operations with excellent results (Farquharson 1955)

The incidence of hospital cross-infection, especially with resistant strains of staphylococci, is a matter of concern and maternity hospitals and their attendant nurseries are not immune In the labour-units we have described, neither mother nor baby would normally come into contact with hospital personnel or other patients

There would have to be more strategic planning of the actual confinement, and detailed arrangements for the reception and care of mother and baby on their return home would need to be made well in advance The scheme would need more domiciliary midwives and a larger and more flexible home help service but it would still cost far less than a greatly enlarged maternity unit or a new maternity hospital Midwives in maternity and general practitioner hospitals could be released to work on the district

In our opinion these cases must be regarded as home confinements and qualify for the full maternity grant After all, the grant is intended to cover not the actual delivery but the puerperal period when home help is most needed We also think that consideration should be given at a national level to reducing the charges made for the home help service in maternity cases The differential grant of £4 does not cover the cost of a home-help for the lying-in period except for a few cases who qualify for a reduced charge under existing assessment schemes We think it unfair that the mother delivered and nursed in hospital should have this economic advantage over her sister who is nursed in her own home

If the majority of mothers came to be delivered in these G P labour-wards, arrangements for training medical students and pupil midwives would need modification We see no reason why training should not be carried out under the ægis of this general-practitioner/midwife team We do not think it unkind to say that many of us are not happy about the way some medical students have floundered through the district-midwifery part of their training In the scheme we propose the young student or pupil midwife would be closely supervised at each delivery until he or she were confident enough to be in charge of a case

The scheme would be best suited to large towns, but there is no reason why it should not apply to the less-scattered rural communities The labour-wards would have to be opened where accommodation at a maternity hospital could be found and according to population requirements Where there is already a maternity hospital we suggest that one of the wards could be divided into rooms All dressings, instruments, and the like would be provided by the hospital. Put in homely language we should be simply renting a room for a short time The conduct of the case would be in the hands of the G P -obstetrician/midwife team with or without a pupil, and be completely outside the jurisdiction of the medical or nursing staff of the hospital The scheme would deal only with "normal" confinements Abnormal cases booked for hospital and emergencies would pass out of the care of the general practitioner or the local authority on admission to hospital Some "social cases," where home conditions were unsatisfactory, would need to be retained in hospital for the lying-in period and would therefore come under the supervision of the hospital staff

The original intention of the "obstetric list" was that midwifery should be practised by a limited number

University of Cambridge

On April 28 the following degrees were conferred

M Chir—C Q Henriques *
M B, B Ch—A B L Peake *
M B—Rachel D Hudson Frank Summers
* By proxy

University of Oxford

On April 26 the following degrees were conferred

D M—G A Rose *
B M—Geoffrey Barraclough,* I J F Smallwood
* In absentia

University of St Andrews

Dr James Walker has been appointed to the chair of midwifery and gynæcology in succession to Prof Margaret Fairlie, who retires this year

Dr Walker graduated M B with honours in the University of Glasgow in 1938 and was awarded the Brunton prize as the most distinguished graduate of his year In 1940 he was appointed Jardine research scholar in midwifery and the same year he joined the Royal Air Force and served with Fighter Command as a medical officer until 1942 when he was posted to India In 1945 he returned to this country and was responsible for medical administration of Transport Command stations in South East England and Wales On demobilisation, he was appointed to a specialist training post in gynæcology at the Glasgow Royal Infirmary Afterwards he was appointed surgeon to outpatients (gynæcology) at the infirmary and was appointed Hall tutor in midwifery In 1947 he took the M R C O G and became senior lecturer in midwifery and gynæcology in the University of Aberdeen In 1954 he took his M D with honours At present he is reader in the Institute of Obstetrics and Gynæcology University of London and consultant in obstetrics and gynæcology at Hammersmith Hospital

Royal College of Physicians of London

In our last issue we inadvertently omitted from the list of newly elected fellows of the college the name of Dr E N Rowlands, of London

King's College Hospital Medical School

Dr B S Cardell has been appointed to the readership in morbid anatomy at the medical school

The Sir Charlton Briscoe research prize for 1955 has been awarded to Dr P C Harris for his thesis on the effects of disease on the pressure in the pulmonary artery and right ventricle

Royal Society of Medicine

On May 4, Sir William Gilliatt, president of the society, presented the Hill Hickman medal to Dr Harold Griffiths of Montreal

Royal College of Physicians of Edinburgh

At a meeting of the College on May 1, with Sir Stanley Davidson, the president, in the chair, the following were elected to the membership

K Cowan A Girdwood Fergusson W M Jamieson J Marshall E D Caldwell, S Vaishnava M V Phadke N L Sharma M F Barry, T L Bhatia J K Baird, G A Tait H S Moore F L Blair, D H A Boyd, G F Harris D T Crichton S Omer E W Poole R D Montgomery, S A Stephen, W C Walker C N Best, P C Bajpai H Weiskopf, M J Craft, S A Yeoh R P Benson, N Islam, B P Winn, G L Asherson

A New Kind of Nursing Course

The Secretary of State for Scotland and the Nuffield Provincial Hospitals Trust have appointed a committee to keep under review the progress of the experimental scheme of training for student nurses to be undertaken in the Royal Infirmary, Glasgow (see *Lancet*, April 7, 1956, p 394) The medical members are Dr May Baird, Prof L J Davis, and Sir Walter Mercer

Society for the Study of Fertility

On Thursday and Friday, June 14 and 15, this society will hold a conference in London Further details may be had from the hon secretary 31, Weymouth Street, Portland Place, W 1

Medical Research in Scotland

The Secretary of State has appointed the following new members to the Advisory Committee on Medical Research in Scotland Prof I G W Hill F R C P E Prof J W Howie, M D, Prof G F Marrian, D SC, F R S and Prof J S Young, M D

How Many Doctors?

The committee set up last year by the Minister of Health and the Secretary of State for Scotland, under the chairmanship of Mr Henry Willink, to consider the future numbers of medical practitioners and medical students, has fixed June 30 as its closing date for receiving written evidence Organisations and persons who intend to submit written evidence should send it to the secretary of the committee, Mr Philip Muston, at the Ministry of Health, 14, Russell Square, London, W C 1, as soon as possible, and in any case not later than June 30

CORRIGENDUM *Association of Clinical Pathologists*—In our report of April 28 (p 554) the second sentence in the second paragraph about the paper by Dr W H Taylor and Dr J V O Reid should have read "*Only* 11 patients had oliguria "

Diary of the Week

MAY 13 TO 19

Monday, 14th

ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street, W 1
5 P M *Epidemiology and Preventive Medicine Section and the Chadwick Trust* Dr Huntington Williams (Baltimore) Influence of Chadwick on American Public Health

Tuesday, 15th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S W 1
5 P M Dr F T G Prunty Chemical and Clinical Problems of the Adrenal Cortex (First of two Humphry Davy Rolleston lectures)
ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields W C 2
3 45 P M Prof David Slome The Vestibular Apparatus (Arnott demonstration)
WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY
5 P M (St Mary's Hospital Medical School W 2) Prof W E van Heyningen Research on Bacterial Toxins (Almroth Wright lecture)
INSTITUTE OF DERMATOLOGY, Lisle Street, W C 2
5 30 P M Dr P F Borrie Rosacea

Wednesday, 16th

ROYAL SOCIETY OF MEDICINE
5 P M *Comparative Medicine* Dr W H Thorpe Mr B B Boycott Dr H Kay, Prof H J Eysenck Learning in Man and Animals
POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W 12
2 P M Prof Ronald Hare Transmission of Infections of the Respiratory Tract
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S W 3
5 P M Dr J R May Bacteriology of Chronic Bronchitis
INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver Antibiotics
HYPNOTHERAPY GROUP
8 P M (1, Wimpole Street, W 1) Dr W A H Stevenson Place of Hypnotherapy in Psychiatric Practice

Thursday, 17th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P M Dr Prunty Chemical and Clinical Problems of the Adrenal Cortex (Second of two Humphry Davy Rolleston lectures)
ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Mr E F Chin Surgery of Funnel Chest and Sternal Prominence—Pigeon Chest (Hunterian lecture)
UNIVERSITY OF LONDON
5 P M (Guy's Hospital Medical School, S E 1) Dr Louis M Hellman (New York State University) Uterine Dysfunction
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr M D Milne Periodic Paralysis
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE
7 30 P M (26, Portland Place W 1) Dr B B Waddy Medical Field Units of the Gold Coast
HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place Edinburgh) Mr G P Mitchell Congenital Dislocation of the Hip

Friday, 18th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A M Dr I R H Kramer Differential Diagnosis of Lesions of the Oral Mucosa
ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington W 2
5 P M Mr Aleck Bourne The Non Malignant Cervix
SOUTH WEST LONDON MEDICAL SOCIETY
8 30 P M (Bolingbroke Hospital Wandsworth Common S W 11) Sir Clement Price Thomas Carcinoma of the Lung

Births, Marriages, and Deaths

BIRTHS

BAKER—On May 2 to Dr Hazel Baker (née Hill) wife of J A C Baker M A of Wednesbury, Staffs a fourth son—Edward James

JACKSON—On May 1 to Eileen (née Greenwood) M B and John W Jackson M CH F R C S—a daughter, Jennifer Mary

She was 74 She had severe claudication When she as admitted to hospital there had been small areas gangrene on one foot, but these had now separated ad she was up and "pottering" Soon she was to be ischarged and sent home

Let me see Mrs ——, you live by yourself don't you ?

No doctor, with my sister

How old is your sister ?

She s 80

Then I suppose she is in no state to look after you

Oh, yes, she is doctor, but I have to look after her because he goes out to work.

Goodness gracious, at 80 What does she work at ?

She works on a capstan

Part-time ?

No, whole time We get up at half past five in the morning to get her off and she gets back to her supper at even

Well, could you get a home help to come in each day ?

But who s going to pay for it, doctor ? I've only my pension

What about your sister ? She earns big money

So she may, doctor, but she saves for her old age

* * *

First Child ($5^{1}/_{2}$) has just been to his first film My husband selected *The Wizard of Oz* as suitable, enjoyable, and not terrifying I was assured there were no witches and it was all lovely colours and mild as milk. So I got a school-teacher friend to come too, with her carefully brought-up little girl ($4^{1}/_{2}$) We arrived just after the beginning, which was monochrome and about a farm in Kansas The children didn't seem to mind, though we wondered if it was the right performance · After what seemed a long time to us and $^{1}/_{4}$ lb mixed sweets to them glorious colour sequences ran riot over the screen, and the magic word "Oz" was mentioned, so we knew we hadn't made a mistake (or had we ?) From then on there was hardly a witchless moment, not to mention clouds of sulphurous smoke, bangs, orange flashes, and scarlet-mouthed hydrocephalic familiars First Child crouched very close to me, completely absorbed, refusing stoutly to come out, though frankly admitting terror $4^{1}/_{2}$ was made of sterner stuff and bounded up and down, inexorably questioning her mother The songs bored both of them, and finished the sweets I kept assuring my son that all would be well, as it always was in films, but he reminded me vividly of a rabbit too near a stoat The whole party was relieved when the worst witch was melted, and $4^{1}/_{2}$ was hurried off to seek a different kind of relief To the strains of *Home Sweet Home*, with the heroine mysteriously restored to her Kansas farm, we left in good order to catch our long-past-bedtime bus $5^{1}/_{2}$ said it was a smashing film, and of course he was frightened, but he wouldn't have missed it for anything $4^{1}/_{2}$ said were there any more liquorice allsorts My friend said she didn't *think* it would do any lasting harm I said I'd have a word or two with my husband on the subject of nightmarish films for impressionable children

Guess who had the nightmare ? $5^{1}/_{2}$ and $4^{1}/_{2}$ slept peacefully till morning "I wish you'd stop kicking and screaming about witches," my husband said irritably "Heaven knows what you'd be like after an A film !"

* * *

Not every diabetic's mind
Is mathematically inclined,
(Nor, parenthetically, is mine)
And so we seek a standard sign
No wonder, then our reason teeters
Between ccs and millilitres
Between the barrel and the label
There mounts a metric tower of Babel ,
Yet since it gets beneath our skin
We must inject our insulin
So Makers, though our ampoule smiles
Approve your standard colour phials,
However lunatic our fringe
We must employ a marked syringe—
So make your vitreous incisions
Not, please, in units, but divisions

Letters to the Editor

G M C ELECTION

SIR,—We were the two younger and unsponsored candidates at the General Medical Council election Each of us stood because he wished to represent the active practitioners of the National Health Service, who are at present inadequately represented on the General Medical Council We had lunch together and then attended the count at Hallam Street, being the first candidates to do so in living memory We should like to take this opportunity to thank Mr W K Pyke-Lees, the registrar, and Mr C O Weston who showed us the electoral machine in action This was of exceptional efficiency, and we were both much impressed by it

Our abiding memory, however, will be of the way in which the whole might of the British Medical Association was thrown into the fight to keep us off the council There were two paragraphs in separate issues of the *British Medical Journal* extolling B M.A candidates, and about 45,000 members of the profession in England received two well-timed circulars We estimate that the cost of this was some £2000 of Association money Neither of us was in a financial position to act likewise, nor do we agree with the principle of canvassing by pressure groups

We still hold that the direct representation on the General Medical Council should be representative of the profession at large, not excluding the younger groups We therefore believe that reform of the electoral procedure is necessary We hope that our candidature will have pioneered the way towards this Finally, we should like to thank the doctors who voted for us with 16,000 votes Perhaps we shall have better luck and a fairer chance next time

Herne Bay Kent — C T H WHITESIDE
Rugeley Staffs — STANLEY DILLON

FATS AND DISEASE

SIR,—Like many of your readers, I am sure, I wonder whether this work on E F A[1-3] may be a major breakthrough into the explanation of coronary heart disease I have been mulling over the data on fat consumption and "atherosclerosis" for years, but have always come away with the feeling that, though there *must* be something in it, the story as usually told—whether in terms of total fat in the diet the proportion of calories derived from fat, or animal *v* vegetable fat—just would not stand up It may well be, as is now suggested, that what we were getting was a blurred version of a more complicated story that includes the ratio of E.F A to other fatty acids

Permit me, therefore, to make two observations that may help to clarify future discussion, now that an additional factor has been introduced First, there is the common idea that the prevalence of coronary heart-disease in different countries is in step with what is known of their fat consumption Second is a question about possible misconceptions in current research

The facts about prevalence are mainly of two kinds mortality-rates produced in the various national offices of vital statistics , and the results of ad-hoc clinical surveys As regards the former, the frequent statement that total fat in the diet is closely correlated with mortality from ischæmic heart-disease is incorrect, at any rate for comparable Western peoples There is wide variation in the certified mortality from coronary heart-disease among countries with very high fat diets Thus

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[1] Bronte Stewart B Eales L Antonis A , Brock, J F *Lancet* Jan 14 1956, p 101

[2] Sinclair H M. *Ibid* April 7 1956, p 381

[3] Bronte Stewart B Antonis A Eales, L , Brock, J F *Ibid* April 28, 1956, p 521

difficult to identify in its earliest stage Such terms as "invasiveness" and "invasion of the stroma" are thus difficult to define To take one example the histological characteristics of lymphosarcoma in its earliest stages are not at all sharply defined—hence the occasional use of the term "diffuse lymphocytoma" to describe the pattern of the lymph-node which has lost most of its normal architecture but whose constituent cells are not yet frankly malignant—but one of the criteria frequently accepted as indicative of malignant behaviour is "invasion (or transgression) of the capsule" In the advanced case transgression of the capsule is likely to be obvious, but if one looks for this in all surgically removed lymph-nodes one will see it remarkably often This fact illustrates the circular argument into which we are so apt to fall when trying to lay down diagnostic criteria The argument is that, since lymphosarcoma always shows capsular transgression, capsular transgression always indicates lymphosarcoma, whereas, in fact, it does not There are also sites such as the thyroid and prostate where "invasion of the stroma" is commonly diagnosed, although in fact this diagnosis is rarely justifiable on the microscopic appearances alone Indeed, if the epithelial elements still remain within the anatomical capsule of the thyroid or the prostate it is doubtful if the microscopist can rightly recognise invasion of the stroma at all

We thus seek a finer criterion of invasion Can it lie in "*rupture of the basement membrane*"? Nearly all epithelium has a basement membrane, and rupture of this membrane should, one would think, provide a fairly reliable criterion of malignant growth Again, however, the histopathologist is disappointed The exact nature of a basement membrane is still not known for certain, nor are the factors which may lead to its disappearance It may certainly disappear, or at least become undemonstrable by ordinary staining techniques, in areas where there is chronic inflammation, as in chronic cervicitis or peptic ulceration—an unfortunate fact from the diagnostic point of view since it is so often the small, ulcerating lesion that causes diagnostic difficulty In my own view, the integrity or otherwise of the basement membrane is of little or no value as a criterion of malignancy

A final criterion is the presence of *neoplastic tissue within blood or lymph vessels* Provided that both the vessel and the neoplastic tissue can be indubitably recognised, this criterion may certainly be of great value, but such a finding is unlikely in the early stages of a cancer

Using the Clinical Data

All the criteria just discussed are purely histological and, difficult though they may be at times to define, they are the best criteria of malignant growth, short of metastasis, that we have Ideally our recognition of "malignancy" in a section should be based on these purely histological criteria alone, and we should be able to answer the question "malignant or non malignant?" or decide that it is unanswerable, by examining the section without knowing anything of the third source of information—the clinical data With one possible exception—that of melanotic growths, where the significance of identical histological appearances possibly does vary with the age of the patient—a verdict of "malignant" or "not malignant" given on histological evidence alone should not be altered by any subsequent learning of the clinical data

It may be objected that a proper and comprehensive opinion on a section cannot be given without full clinical data This is indeed true, but the time for the histopathologist to read the clinical data is after he has assessed the section, not before The almost invariable practice, when given a section, is to read or ask for the clinical data first, then to examine the section and give an opinion This, in my view, is the least profitable and the least accurate way of assessing a section Foreknowledge of the clinical data introduces into our mind a quite ineradicable bias—a bias such that some degree of prejudgment of the section is almost impossible to avoid For example, if a histopathologist is given a section to examine, with the information that it was part of a paranephric mass, associated clinically with paroxysms of hypertension, he is quite unlikely, on finding a somewhat polymorphic slightly glanduliform neoplasm, to say other than that the mass was a phæochromocytoma He may, of course, be correct, but, by learning the site and the clinical associations of the tissue he will have rendered himself virtually incapable of assessing the tissue pattern as a purely histological problem, or of recalling how closely such a growth may resemble a neoplasm of thyroid or parathyroid, or indeed an undifferentiated glandular carcinoma of almost any origin If the same material be examined by a pathologist who, at the outset, intentionally ignores the clinical data, he is likely to argue thus "This is part of a neoplasm whose pattern is not obviously diagnostic If it comes from the region of the adrenal, phæochromocytoma is the likeliest diagnosis, if from around the carotid bifurcation, carotid body tumour is the likeliest If it comes from within or beneath the thyroid, a thyroid or parathyroid adenoma is possible [and he might prefer one rather than the other] If an abdominal lymph-node is the source, secondary glandular carcinoma, of unidentifiable origin, is admissible" Then, and only then, having extracted the maximum information (and the maximum instruction) from the section, he turns to the clinical data and finally, on clinical grounds, narrows down his diagnosis to that one of his histological possibilities which now seems the most appropriate He does this final part, however by virtue not of his histological, but of his clinical, knowledge Similarly, a neuroblastoma, a small cell bronchial carcinoma, or a lymphosarcoma may be more rapidly diagnosed by the pathologist already in possession of clinical data, but, compared with his counterpart who has the habit of examining sections "blind," he will be so much the longer in learning the similarities commonly presented by these tumours Not only is he slower to realise how relatively non specific are many of the tissue patterns which we are apt to accept as diagnostic, but almost inevitably he is also slower to incorporate within his experience such fine differences of pattern as do in fact exist

Now, it clearly matters little to the patient with a frankly malignant neoplasm whether the pattern of his neoplasm resembles that of another frankly malignant neoplasm or not But there are other occasions when identity of histological pattern obviously does matter to the patient very much These are the occasions when the lesion is of "borderline" appearance—occasions when we most need, yet most lack, sharp definition in our criteria of malignancy Here again, the best hope of achieving increased sharpness and specificity in our criteria lies in increasingly frequent practice of "blind" examination of sections

In illustration of this, an instance may be quoted where a histologist, having examined a section "blind," had decided that it showed part of a highly cellular, organising hæmatoma The section itself gave no indication of the site, which was alongside a recently ruptured tendon The section was then shown to two other histologists with the information that the material came from the region of a tendon, and both said, "probably a synoviosarcoma" In the circumstances this was a not unreasonable evaluation of a highly cellular tissue of polymorphic pattern containing clefts and spaces Yet it is doubtful if this diagnosis would have been preferred had they not been biased at the outset by the mention of tendon

The criteria for diagnosis of some examples at least of synoviosarcoma certainly lack specificity and sharp mals There has been some improvement in the last years in the distribution of research, as you describe pril 28), but the balance is still not redressed

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SIR,—I was much interested in your leader of April 28 id in the admirable paper by Dr Bronte Stewart and s colleagues which appeared with the critical letter of rof Ancel Keys in the same issue I feel that the verage medical man might be somewhat bewildered and onfused by the sudden weight of evidence incriminating ur until recently much praised Western diet for the apid increase in the incidence of coronary-artery disease t is perhaps pertinent, therefore, to recall that when I rst presented some of the fundamental evidences of the ietary theory of coronary heart disease in your columns,[1] hey provoked such adverse criticism that Professor Keys elt obliged to intervene [2] Now, less than two years later, he question is not any more whether the increase of the at calories as a percentage of total ingested calories is esponsible for the increased incidence of coronary athero clerosis, but whether all kind of fats are equally esponsible for it

I was greatly intrigued by some of the "fascinating peculations" of Dr Sinclair (April 7)

I have no doubt that he is on sound ground when he raises he question of essential fatty acids (E F A) with reference to oronary atherosclerosis I am however afraid that he tried o cover too much ground in his letter As Professor Keys ays the idea that deficiency of E F A in the diet may be elated to atherogenesis is not new The vexed question of egetable versus animal fats, especially as far as their influence on hypercholesteremia is concerned, cannot yet be decided with certainty Much work has been done in recent years, but, despite the interesting work of Groen et al [3] and Donath et al [4] on vegetarians, both Hardinge and Stare [5] and Mayer et al [6] in their controlled experiments still came to contradictory results More recent work, however, mainly by Ahrens,[7] Kinsell,[8] and especially Malmros,[9] seems to indicate that not all kinds of vegetable fat have the same lowering effect on serum cholesterol Using corn oil which contains about 57% of linoleic acid, Professor Malmros reduced the blood cholesterol level in 8 patients with familial hypercholesteræmia from 450–500 mg per 100 ml to about 300 mg and kept some of the patients on that level for two months [9] I repeated this experiment, and I did indeed lower the cholesterol level substantially in a healthy person, and in a hypercholesteræmic patient I doubt however, whether our patients will be prepared to face this ordeal unless we can find less repulsive carriers of E F.A Dr Sinclair's observation [10] on increased permeability, and his emphasis on the link with vitamin B_6, might help in the explanation of some of these results, although to prove any, even relative, deficiency of E F.A would need a great deal of additional research

I quite agree with you, Sir, that the great importance of the admirable work of the Cape Town group lies in the assumption that any dietary factor which raises, or lowers, the β lipoprotein level in the blood will also raise or lower the liability to myocardial infarction Incidentally this assumption, by implication, was clearly expressed several years ago by others [11] [12] I am, however, much more impressed by the systematic and careful work of Dr Bronte Stewart and his colleagues in following up the fluctuation of blood-lipids after feeding "on many occasions malodorous oils" for up to 172 days Furthermore, they are most cautious in the interpretation of their results Unfortunately balance studies of fæcal fats have been only sporadically carried out so far, and I am looking forward to seeing the results of more detailed studies, as promised in their paper, for the following reason

According to the authors the physical activity of the volunteers was minimal throughout the study Their fig 1 indicates that a male Bantu, aged 37, with a body-weight of approximately 140 lb , having consumed as much as about 2200–2300 calories daily, lost around 7–8 lb of weight in seven weeks Another male Bantu, aged 65, with an initial body weight of only 110 lb (figs 2 and 7) on a daily calorie intake of about 2300 lost weight in the first month and regained his lost weight on an average daily intake of about 2600 calories in the second month , he gained afterwards slowly less than 5 lb in weight in the following two months on a 2500–3000 calorie diet, and gained again less than 5 lb in weight in the fifth and sixth months averaging about 3000 calories daily (fig 7) Thus 65 year old man was certainly grossly overfed with 50–60 calories per kg body-weight on minimal physical activity, and gained only about 8 lb in six months These two weight curves, which can be read only approximately, strongly suggest that a considerable part of the ingested fats was not fully absorbed and utilised If this assumption is correct, the fat calories of these volunteers were in reality considerably lower than the calculated 36%, 45%, and 60–70% It may also be of some interest that most of the weight gained by the 65 year old Bantu coincided with the two periods when ten eggs were added daily to his diet I am confident that the Cape Town workers will be able to clarify these points soon

We have to keep in mind that the dietary theory of atherogenesis, as it stands at present, was only elaborated in the past few years, and I fully agree with you that more research is urgently needed and that in this type of research the unit of time is the decade But the death-roll from coronary-artery disease is still rapidly increasing Are we going to wait for another decade to take the appropriate measures ? Whilst the elucidation of the influence of E F.A on atherogenesis appears to be, at this moment at least, as important as that of the sex hormones,[12] [13] are we going to condemn our patients to substitute E F A for butter and bacon or demasculinise them with female hormones ? I myself, have had my share of corn and wheat germ oil, and, like Professor Keys,[2] I am convinced that, unless the E F A can be made much more palatable (without hydrogenation), most patients in this country will prefer a diet substantially reduced in those fats which they are used to (or which they like) In other conditions it has been shown in long term observations that such diets work quite satisfactorily in practice [14]

London W 1 Z A LEITNER

SIR,—I am sure I am not alone among public-health medical officers, now liberated from preoccupation with infection and gravely concerned at the ravages of degenerative disease, in regarding the last few issues of *The Lancet* as momentous

First we are treated to Dr Sinclair's fascinating postulations on the relationship of fats and disease This is closely followed by the interlocking findings in the publication of Dr Bronte-Stewart and his colleagues and your own thoughtful commentary in the same issue

Sinclair's work is evidently continuing, but it appears that he has been moved to issue what amounts to an interim report in a genuine endeavour to assist in halting us on the alarming and slippery slope of premature degeneration lesions of quite the same histological pattern, and present for the same length of time, do not A granulosa cell tumour which behaves as a carcinoma may be histologically indistinguishable from one that does not, and a similarly unpredictable future is associated with carcinoid tumours and with occasional melanotic growths The fleshy, spindle cell sarcomas, of whatever type, especially those in the subcutaneous region, form another tumour type whose future behaviour is far from predictable, some recur repeatedly and finally metastasise, others of apparently the same histological appearance do not Retained placental tissue provides a good example of this kind of difficulty Two excised uteri may show foci of persisting, hyperplastic trophoblast of apparently identical type, yet one patient will die of chorionepithelioma, and the other live Quite similar tissue may be found in uterine curettings from patients who have no subsequent hysterectomy and yet survive There is little difficulty in finding evidence of atypical cell growth in such retained trophoblast—the trophoblast may consist of little else but atypical cells—or in finding evidence of invasion, possibly on a grand scale The histopathologist's problem is that there is no dependable correlation between these appearances and the later occurrence of metastases (Park and Lees 1950) The same lack of correlation applies in varying degree to the other neoplasms in this group, and for this reason accurate figures for incidence and curability are again extremely difficult to obtain

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[1] Leitner Z A *Lancet* 1954 i 1078
[2] Keys A *Ibid* 1954 ii, 37
[3] Groen, J Tjiong B K , Kamminga C E , Willebrands A F *Voeding* 1952 13, 556
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[12] Oliver M F Boyd G S *Brit Heart J* 1953 15 387 , *Ibid* 1955, 17 299
[13] Leitner Z A *Proc R Soc Med* 1955, 48 672
[14] Leitner Z A *Voeding* 1955 16, 107

“ BORDERLINE ” CASES

The third group of tumours comprises the so called borderline cases—those cases where the surgeon wants an answer to the question, Has this growth crossed the borderline to malignancy ? It is very likely that there is no such definite borderline, but the pathologist will remember that the surgeon nearly always has to act as if there were

This borderline group is the main cause of worry in the diagnosis of biopsy material When the pathologist uses the term “ difficult ” to describe these cases, he is not referring so much to purely histological difficulties (he can still recognise the various tissue components, and their arrangement) as to the lack of available knowledge of the clinical behaviour to be expected with such histological appearances—in other words, to a low level of clinical correlation In these circumstances he cannot give his diagnosis with the same degree of confidence as in the straightforward group nor can this be expected of him

Here we find ourselves in conflict with scientific discipline For *scientific* purposes, remembering our obligation to provide as accurate data as we can for cancer study as a whole, we should, if we feel the evidence in favour of a diagnosis of malignancy to be inadequate, say that a diagnosis of cancer cannot be given For *practical* purposes, since the welfare of the patient is in the balance, the scientific outlook has to be put on one side, and a diagnosis of cancer made if there is even a moderate degree of suspicion of malignancy The difference between diagnosis for these two purposes can be reconciled by making the reservation that though, in the interests of the patient, a diagnosis of cancer has to be made, the case very possibly was not one of cancer at all in other words, to quote from an earlier discussion of this matter, “ it is legitimate to treat a patient because he might have cancer but not legitimate always to assume that if he recovers he necessarily did have cancer ” (Park and Lees 1955)

Summary and Conclusions

In all but clinically manifest cases, surgeons and radiotherapists are dependent for their diagnosis of cancer upon the pathologist It is obvious, therefore, that if comparisons of different forms of treatment or of incidence of cancer are to be valid, the pathological diagnoses on which they depend must be accurate It has been pointed out that, even under optimum conditions, histological assessment of malignancy is far from absolute In the case of early cancer, histological criteria of diagnosis are even less satisfactory, and of lower practical value than pathologists would like In such cases there may be quite legitimate differences in interpretation of the histology, and when this happens figures of incidence of early cancer will vary correspondingly

The property of invasiveness, on whose presence or absence depends frequently the diagnosis of “ malignant ” or “ not malignant,” is particularly difficult to define, and therefore to recognise, in its early stages indeed, in an attempt at its definition, I would go so far as to suggest, and not facetiously, that an abnormal overgrowth of cells should be regarded as showing invasion only if it shows what *every* histopathologist would say *was* invasion

Pathologists should, by all means, persuade the clinician to provide them with as much in the way of clinical data as he can, informing him that, usually, the more help he gives them, the more they can give him I would, however, suggest that the habit of always examining sections first, and reading the clinical data afterwards, is a valuable one It should help to sharpen and clarify diagnostic criteria at that stage of cancer where we most need, yet most lack, sure definition—the early stage

It has been shown that a diagnosis of cancer for practical purposes may at times, in borderline cases particularly, be inescapable, but that it is legitimate for scientific purposes to have reservations about the accuracy of such a diagnosis, and to take this fact into account in the retrospective analysis of data

The term “ histologically proved,” when applied to cancer, is admissible only if “ proved ” is used in its original and now almost obsolete sense of “ tried, tested, or assessed ” Its equation with “ proof ” in the legal sense, with the implication that certain objectively defined, specific criteria have been satisfied, is not justifiable

I am most grateful to Prof A C Lendrum for helpful comments during preparation of the script for publication

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URINARY EXCRETION OF ŒSTROGENS DURING PREGNANCY, LACTATION, AND THE RE-ESTABLISHMENT OF MENSTRUATION

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Few reliable figures are available for the urinary excretion of œstriol, œstrone, and œstradiol-17β during pregnancy and lactation Most of the published figures for early pregnancy and lactation were for total œstrogens, and many were obtained by semi quantitative bio assay methods (Pedersen Bjergaard and Pedersen Bjergaard 1948, Venning 1948, Jayle and Crepy 1952) Cohen, Marrian, and Watson (1935), using colorimetry, were the first to determine the urinary excretion of œstrogens during the last 6 months of pregnancy they showed that œstriol is quantitatively the most important urinary œstrogen during pregnancy, and that the amounts

BREAST CHANGES IN FIBROCYSTIC DISEASE OF THE PANCREAS

SIR,—The letter of Dr Stroud and Dr Heppleston (April 21) raises some interesting points I have recently studied a post mortem series of breasts, gonads, and endocrines at the Royal Hospital for Sick Children, Glasgow, and agree that the histological appearance in their first case is a not infrequent variant of physiological neonatal mammary hypertrophy I interpret this appearance of dilatation of ducts lined by a flattened epithelium as an involutional change in a duct ectasia produced by considerable secretion in the active phase of *Hexenmilch* production Sometimes this appearance is seen in conjunction with the more normal picture of hyperplastic columnar epithelium, and in the latter I have observed vacuolation of the free border of the cells and passage of small eosinophilic globules (stainable by the periodic-acid/Schiff method) into the lumen of the dilated ducts (see figure) I have noted moderate to severe duct dilatation in 10 infants up to the age of 2 weeks of 65 such cases examined, and in a further 7 children under 1 year of age of 68 such cases examined It is therefore not infrequent 1 of these patients, a 12-week old female, died of mucoviscidosis and staphylococcal bronchopneumonia, having been treated with aureomycin and chloramphenicol

In my series physiological hypertrophy of the breast is an almost invariable finding in the full term neonatal infant and may be accompanied by changes in the vaginal epithelium, ovaries, and prostate This condition is less frequently seen in the premature infant, where the mammary ducts tend to be of solid, cord-like type Regression usually begins in a few weeks but the condition may persist for several months with duct dilatation more obvious than epithelial hypertrophy That hormonal effects may continue to be produced in childhood is suggested by my finding of follicular ovarian activity, endometrial mitoses, and active budding of the mammary ducts of a girl aged 7 years who died of hepatitis and cirrhosis It is well known that liver disease in the adult male may lead to failure to break down œstrogens and result in gynæcomastia, prostatic hypertrophy, and testicular atrophy

In addition to the case of mucoviscidosis mentioned above I have examined the breasts of a further 5 such children, and none showed significant histological abnormality of the breast or sweat-glands of the skin of the breast Of these cases, 1 died at the age of 1 day and another at 3 days and neither had antibiotic therapy A 3rd, who died with bronchopneumonia at the age of 4 months, had been treated with aureomycin, streptomycin, and penicillin, A further 2 cases each died at the age of 21 months with purulent pulmonary infection, each having been treated with penicillin, chloramphenicol, and oxytetracycline, while one also had aureomycin

It would therefore seem that breast changes are at any rate not invariable accompaniments of the mucoviscidosis syndrome Nevertheless the suggestion that antibiotic treatment may be responsible for mammary enlargement is worthy of further study

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PROGRESSIVE EXOPHTHALMOS

SIR,—Mr Rowbotham and Mr Clarke (April 14) mention radiotherapy in the treatment of this condition, but express the opinion that it is not justifiable to irradiate the pituitary gland and neighbouring structures, although they do not define exactly what dangers they anticipate from such treatment

In the 30 cases which they cite, operated on by their own method of orbital decompression, exophthalmos was relieved in every case, and no eyes were lost However, orbital decompression, at least when carried out by the usual modification of Naffziger's method, does not always save the patient's eyes

It is only in those severe and rapidly progressive cases, aptly termed malignant exophthalmos, that there is acute danger to vision from papillœdema, keratitis, and perforation of the globe In the more chronic progressive exophthalmos, whether accompanied by thyrotoxic symptoms or not, the condition runs a much more benign course, and there is seldom any danger to vision, although ophthalmoplegia, once it has developed, is usually irreversible Dr Arthur Jones [1] cites a case of malignant exophthalmos in which, despite bilateral orbital decompression, perforation of the right eye occurred, necessitating enucleation Subsequently orbital radiotherapy was given, and led to rapid regression of œdema of both orbits and of the proptosis of the remaining eye, the danger to which was averted The improvement appeared to be permanent

The following case may be of interest ·

A tin worker aged 48, had partial thyroidectomy in 1951 for toxic goitre Three weeks after operation pronounced proptosis of the right eye developed A few weeks later the left eye became affected also In August, 1951, left tarsorrhaphy was performed Owing to increasing orbital œdema and exophthalmos, in November, 1951, he underwent bilateral orbital decompression This failed, however, to save the right eye, which later perforated and had to be enucleated In May, 1952, he was referred to me The left eye was much proptosed, with œdema of lids, and great tension could be felt in the orbital tissue and globe The tissues of the socket of the right eye and right eyelids were grossly œdematous also The patient was in acute discomfort, with severe frontal headaches, and he was extremely anxious about the possible loss of his remaining eye The vision in this was not seriously impaired, but it seemed to be straining against the protective tarsorrhaphy, like a hound on the leash In May, 1952, both orbits were irradiated to a dose of 500r There was symptomatic relief, but the alarming tension and proptosis of the left eye remained In January, 1953, it was decided *to irradiate the pituitary gland* A *dose of 2500r* was delivered in three weeks Within a few weeks the condition was obviously improved the left eye was much less tense, watering had ceased, and the œdema of the orbit was subsiding, and he lost all his previously agonising headaches

During the past three years, his condition has remained satisfactory, although there is still some proptosis, and it was felt wise to retain the tarsorrhaphy (with a small central hole through which he sees quite well) The subjective relief has been most striking

In this case orbital decompression failed to save one eye, and the other one might well have been lost too if the disease had not been arrested and partly reversed by radiotherapy Although Jones, and Sosman in described by Brown (1955a), modified, as follows, for urines containing larger amounts of œstrogens than could be satisfactorily measured by the original method

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[1] Jones, A *Brit J Radiol* 1951, 24, 637

The 24 hour urine volumes were diluted to 2500 ml with water, according to the stage of pregnancy, 200, 100, 50, 20, or 10 ml portions of this were used for each determination, and complete specimens of the œstriol fraction, or aliquots of $^1/_2$, $^1/_5$, or $^1/_{20}$ were taken for colour development so that the final œstriol, œstrone, and œstradiol 17β colours were within the convenient range for colorimetry Specimens of urine of less than 100 ml were diluted to 100 ml with water before acid hydrolysis, and half the volumes of hydrochloric acid, ether, and carbonate solutions recommended in the original method were used After the evaporation stage, the original procedure was unaltered, but if necessary, portions of the œstriol eluates from the chromatogram columns were taken for colour development

The loss of œstrogens during acid hydrolysis (Brown 1955a) is less evident when the urine is dilute than when it is concentrated, and is negligible in late pregnancy when the urine is diluted five times or more before hydrolysis To show that the method used in this investigation is reliable at the œstrogen levels encountered in late pregnancy, recovery experiments were performed in which 200 µg of œstriol, 20 µg of œstrone and 10 µg of œstradiol 17β were added to 10 ml of male urine diluted to 100 ml with water *before* acid hydrolysis these amounts are equivalent to daily excretions of 50 mg of œstriol, 5 mg of œstrone, and 2 5 mg of œstradiol 17β In twelve such experiments, the mean percentage recoveries with their standard deviations were œstriol, 81 ± 3, œstrone, 83 ± 1 4, and œstradiol, 81 ± 4—which are within the ranges claimed for the method

Results

The results obtained from subjects 7 and 8 over a period which includes a complete menstrual cycle and the cycle in which pregnancy started are shown in figs 1 and 2 In both women the urinary œstrogen levels were very similar in the two cycles up to about the 24th days—showing the ovulation peaks and the subsequent luteal rise In the first cycle the œstrogen levels then decreased before the onset of menstruation, but in the second cycle, when pregnancy had occurred, they continued to increase, and they began to increase rapidly about 7 weeks after the last menstrual period Subject 7 had nausea at this time

The results from the four subjects throughout their pregnancies are shown in fig 3 on a logarithmic scale Those for subject 8 are also shown for a week after delivery There was a rapid rise in the urinary levels of the three œstrogens throughout pregnancy, greatest between the 6th and 20th weeks The œstrone and œstradiol levels at labour were 100 times higher than those during the luteal phase of the menstrual cycle, the œstradiol levels being about one third of the œstrone levels The urinary œstriol levels rose approximately 1000 fold during this time The results obtained during the last weeks of pregnancy are shown in more detail in the accompanying table

EXCRETION OF ŒSTRIOL, ŒSTRONE, AND ŒSTRADIOL-17β DURING LATE PREGNANCY EXPRESSED AS MG PER 24 HOUR SPECIMENS OF URINE

Subject	Type of œstrogen	Weeks before delivery			Days before delivery						
		4	3	2	7	6	5	4	3	2	1
7	Œstriol Œstrone Œstradiol	16 0 75 0 30	17 0 70 0 28	19 0 75 0 40	22 0 93 0 38						20 0 9 0 38
8	Œstriol Œstrone Œstradiol	31 1 5 0 60	31 1 5 0 58	39 1 7 0 65	35 1 6 0 60	34 1 5 0 63	36 1 5 0 64	41 1 7 0 73	40 1 7 0 70	36 1 5 0 60	41 1 0 68
9	Œstriol Œstrone Œstradiol	24 1 4 0 38	22 1 3 0 38	35 1 8 0 57	28 1 2 0 48	30 1 2 0 46	23 1 0 0 38	30 1 0 0 40	24 0 93 0 35	25 0 93 0 30	21 0 93 0 33
10	Œstriol Œstrone Œstradiol	41 0 29 0 73	33 2 1 0 83	36 1 7 0 70	31 1 6 0 63	36 1 8 0 73	39 1 5 0 70	39 1 8 0 85	30 1 4 0 60	41 2 1 0 90	

Subject 8

During labour, which lasted 3 hours, the urinary excretion calculated on a 24 hour basis was 44 mg of œstriol, 1 7 mg of œstrone, and 0 85 mg of œstradiol 17β After delivery, the urinary œstrogen levels fell rapidly In the case of œstrone and œstradiol-17β there was a linear relationship between the logarithm of the amounts excreted and the time after delivery, and normal non pregnancy levels were reached within 5 days In the case of œstriol this linear relationship did not apply so closely, and normal non pregnancy levels were not reached until 25 days after delivery (fig 4) Levels were low during lactation and reached a minimum (œstriol 1 0 µg, œstrone 3 µg, œstradiol 0 µg per 24 hours) at the time when lactation became inadequate and suckling was discontinued Thereafter the amounts increased slowly

There was slight vaginal bleeding on the 78th and on the 84th days after delivery when the œstriol and œstrone levels were both approximately 7 µg per day Soon

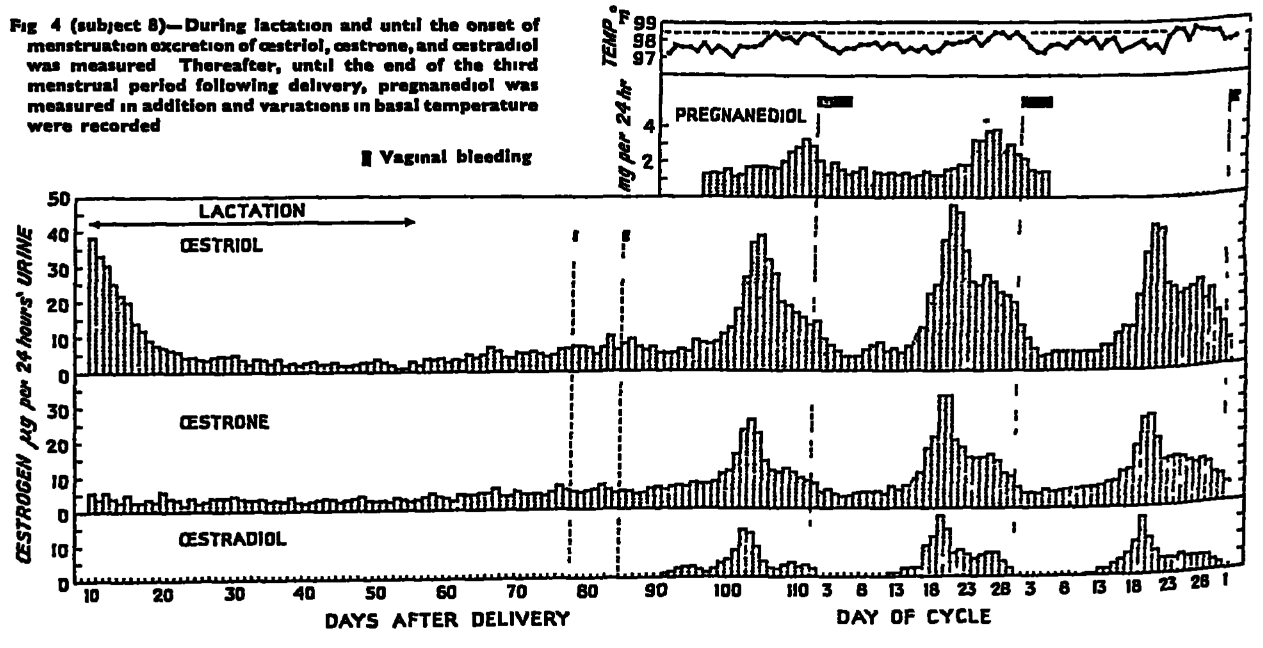

Fig 4 (subject 8)—During lactation and until the onset of menstruation excretion of œstriol, œstrone, and œstradiol was measured Thereafter, until the end of the third menstrual period following delivery, pregnanediol was measured in addition and variations in basal temperature were recorded

NON-DISCIPLINARY ERASURE FROM THE REGISTER

SIR,—It is not generally realised that under the Medical Acts 1858–1950 the name of a registered medical practitioner may be lawfully erased from the Medical Register if he fails to reply to an inquiry from the registrar of the General Medical Council concerning his address and/or possible retirement from active practice Restoration of a name so erased is a costly and tiresome business Application must be supported by an affidavit and at least two certificates of identity and good character together with a fee

Medical defence societies are seriously perturbed at the number of their members whose names are so erased Not only are they unwittingly and illegally engaging in practice in the mistaken belief that they are registered medical practitioners, but they may find themselves removed from membership of their defence society, which would prove a serious matter if they became involved in threatened or actual litigation

It therefore behoves every medical practitioner from time to time to satisfy himself that his name appears in the Medical Register and to furnish an address at which he can be reached by communications from the General Medical Council or from the defence societies In their own interests, both present and future, practitioners are strongly urged to give attention to this matter immediately and thereby ensure that they are not acting illegally or deprived of the necessary legal advice and protection should medicolegal trouble arise in the conduct of their professional duties

ROBERT FORBES
ALISTAIR FRENCH
C C MILLAR

Secretaries of the Medical Defence Union,
Medical Protection Society and Medical
& Dental Defence Union of Scotland

FREUD

SIR,—Who was Freud's "faithful and gifted English biographer"?[1] The standard Life is by Jones, a Welshman[2] And was not John Stuart Mill a Scot?

Bangour Village
West Lothian

JOHN COLLINSON

FŒTAL MORTALITY IN PREGNANT DIABETICS

SIR,—I was interested to note the low fœtal loss in pregnant diabetics reported last week by Dr Pedersen and Professor Brandstrup, particularly because these authors seem likely to be able to assist in confirming the correctness of my theory of the cause of eclampsia[3]

In my paper I suggested that toxæmia and eclampsia originated from damage to the syncytium, produced by maternal opposition to the entry of hormones manufactured by a foreign or transplacental source (a fœtus or mole), after the mother had become intolerant to the presence or activity of these invading hormones This maternal opposition to the entry of fœtal hormones would, I suggested, mean that with the onset of toxæmia (marked first by digital œdema, and later by hypertension and albuminuria) the entry of fœtal insulin into the diabetic mother would diminish, or be cut off, and that her blood sugar would rise and her need for parenteral insulin would increase Conversely, in the absence of toxæmia fœtal insulin would continue to enter the mother freely, and reduce her requirements of parenteral insulin until term

The low fœtal loss reported by Dr Pedersen and Professor Brandstrup is attributed by them "either to the lowering of the mother's blood-sugar level for a long time, or to unknown factors favourably influenced by strict control of the diabetes" during the last eight weeks—i e, those weeks in which toxæmia commonly occurs Their conclusion supports my theory, and I hope that they may be able to supply further details concerning insulin requirements and blood sugar findings in the presence and absence of toxæmia, which will further assist in proving my thesis

Reading

K D SALZMANN

CLUBS FOR THE HARD OF HEARING

SIR,—We shall be grateful if you will allow us the use of your columns to point out that persons who are suffering in any degree from loss of hearing can derive great benefit from joining a club for the hard of hearing There are some two hundred of these clubs in Great Britain and Northern Ireland affiliated to the British Association of the Hard of Hearing

The suffering entailed by loss of hearing is largely psychological and is due to loneliness and the frustration of the social instincts It can be acute Besides purely social activities, the clubs give opportunities for lip-reading practice As they are almost wholly run by people who are themselves hard of hearing, they also offer scope for organisational talents which are often blocked by inability to hear on normal committees The wider work of county leagues and of the association itself gives an outlet for all degrees of ability

Within the clubs, experienced hearing-aid users can often advise novices on the practical use of an aid, thus saving unnecessary calls on the clinics

There is no fear that the clubs will lead to segregation of the hard of hearing On the contrary, many members who formerly shrank from normal contacts have been brought back to a full participation in the life of the community

Our honorary secretary, whose address is 64, Liverpool Road, Chester, will at all times be pleased to answer inquiries and to supply helpful pamphlets

Department of the Education
of the Deaf,
Manchester University

A W G EWING
President

Twickenham

P A REED
Chairman

ACUTE AND LATENT PORPHYRIA

SIR,—Dr Whittaker and Mr Whitehead suggest (April 28) that barbiturates may be related more to neurological complications than to the precipitation of an acute attack of porphyria That this is not always so is shown by the following case of acute porphyria

A housewife, aged 43, was admitted in 1953 with a history of grand mal epilepsy for twenty seven years, for which she had received phenobarbitone for nine months twenty years previously, and again for two months before admission Three weeks before admission she had had intermittent colicky abdominal pain followed in a few days by paralysis of both legs Phenobarbitone was discontinued a week before admission

Her father had died three months previously The cause of death was said to be cardiac failure During the last five years he had been having attacks of abdominal pain accompanied by the passage of dark red urine about every six months

On admission the patient was extremely ill, with signs of peripheral circulatory failure and flaccid paralysis of both legs Repeated examination of the urine showed no porphobilinogen Her condition gradually improved, and four weeks after admission she was given a test dose of amylobarbitone sodium gr 3 About seven hours later she complained of severe colicky abdominal pain and a specimen of urine collected shortly afterwards was found to contain porphobilinogen (Watson Schwartz test) This was confirmed by spectroscopy and examination of the urine under ultra-violet light By the following day she was none the worse for her experience

It would seem from this case that barbiturates can occasionally precipitate an attack of acute porphyria

Llwynypia Hospital,
Rhondda
Glamorganshire

M S PATHY

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[1] *Lancet* May 5 1956 p 617
[2] Jones E Sigmund Freud London 1956 vol 2 pp 47 183
[3] *Lancet* 1955 ii, 953

ANÆSTHESIA FOR OPERATIVE OBSTETRICS

VALUE OF CUFFED ENDOTRACHEAL TUBE

David J Coleman
M B Lond, F F A R C S, D A
SENIOR REGISTRAR

Brian L Day
M A, B M Oxfd, F F A R C S
REGISTRAR

DEPARTMENT OF ANÆSTHETICS, ST GEORGE'S HOSPITAL, LONDON

The dangers of administering a general anæsthetic to a woman in labour or in whom labour is imminent have recently received considerable attention, particularly from obstetricians (Wrigley et al 1955) Aspiration of gastric contents during or immediately after anæsthesia is a serious hazard We seek to show here how this may be averted by the use of a cuffed endotracheal tube

Mortality and Morbidity

The main cause of maternal mortality resulting from general anæsthesia for obstetric surgery is regurgitation of gastric contents with subsequent aspiration, and, with the reduction of the maternal mortality from other causes, this has assumed a greater significance

In 1949 Sir William Gilliatt reported that of 55 maternal deaths associated with 34,146 deliveries at twenty-three hospitals, 3 had been due to aspiration of vomit under general anæsthesia Gilliatt stated that "these are deaths which should not have occurred," and he stressed the importance of a properly trained anæsthetist attending women in labour

Jeffcoate (1953), reviewing the records of the Liverpool Maternity Hospital for the years 1935–50, found that of 6 maternal deaths 3 had been due to the aspiration of vomit He stated that "the greatest danger of forceps delivery under general anæsthesia at the present time is anæsthesia"

Parker (1954) described 7 cases of aspiration of vomit at the Birmingham Maternity Hospital, 6 of the patients died 5 of the cases occurred in a total of 18,524 deliveries in 1943–52

In the U S A Merrill and Hingson (1953) surveyed the experience of 183 hospitals in 1945–49, and found that there had been 59 maternal deaths due to aspiration of vomit from a total of 2,503,921 births

Merrill and Hingson estimated that inhalation of vomit accounted for between 1 5 and 2 5% of maternal deaths in the whole of the U S A At a recent meeting at the Royal Society of Medicine (Wrigley et al 1955) it was considered probable that the figure for *hospital* practice in this country was higher Besides maternal mortality, maternal morbidity and fœtal mortality due to anæsthesia must be taken into account

Hartzell and Mininger (1946) recorded 20 cases of bronchopneumonia due to the aspiration of vomit under ether anæsthesia, while Davis and Gready (1946) reported 45 "aspiration accidents," 8 of which were serious Presumably many more cases occur, but since recovery is complete they are rarely recorded (Merrill and Hingson 1953 McKelvey and Freeman 1954)

As regards infant mortality little is recorded Anoxia brought about by vomiting must weigh heavily against the fœtus, and it seems reasonable to assume that in some cases it proves fatal

The Lancet (1955), summarising the present position, noted "There has been some uneasiness about an apparent increase in the maternal deaths due to anæsthesia but this may well be only a relative increase, brought about by a fall in the number of deaths from other causes" Whatever the exact position, there appears to be a need to improve anæsthesia for the woman in labour

The Problem

Labour may last for hours or days, and at any moment it may be necessary to induce anæsthesia Thus it is impossible both to feed the patient and to prepare her adequately, by modern standards, for operation A compromise has to be found, and it is now the practice to give women in labour an easily assimilated diet consisting mainly of fluid and glucose The glucose administered should be isotonic, Morton and Wylie (1951) have drawn attention to the action of hypertonic glucose in slowing gastric emptying and increasing the volume of fluid in the stomach During labour the gastric emptying-time is prolonged, and Hirscheimer et al (1938) showed that out of 10 primigravidæ in labour 2 had emptying times of up to nine hours In our experience this may often be extended up to eighteen hours, the factors responsible are the presence of a large mass in the abdomen, and the effects of fear and of painful uterine contractions Moreover, the stomach may become dilated, especially in long labours (Greenhill 1943) From the anæsthetist's point of view it is wise to *suppose that the stomach of a woman in labour is never* empty

The obstetrical requirements of anæsthesia are good oxygenation, a light plane of anæsthesia, and moderate muscular relaxation When a conventional anæsthetic sequence (i e, nitrous oxide and oxygen with trichlorethylene, ether, or cyclopropane) is being used, an error of judgment by the anæsthetist or a sudden increase of stimulus by the obstetrician may cause laryngeal spasm, lightening of anæsthesia, vomiting, obstruction to the airway, and anoxia Again, a stormy induction with pronounced excitement and a slow descent through the second stage of anæsthesia will predispose to vomiting To prevent these complications it is essential that the airway be completely under the control of the anæsthetist, and to ensure this a cuffed endotracheal tube must be used

Management

The anæsthetic management of the pregnant woman should begin in the antenatal period when the patient should attend classes conducted by the anæsthetist At these meetings an attempt is made to dispel latent fears of the unknown and of pain by a simple account of the analgesic procedure in labour

After admission to hospital an easily assimilated diet should be given It has been suggested that gastric lavage should be attempted before inducing anæsthesia (DeLee and Greenhill 1943), and that if this fails anæsthesia should be carried *to* the stage of complete sensory loss, and the gastric lavage then repeated effectively In our experience, however, attempting to pass a Ryle's or œsophageal tube on a woman in labour increases her fear and distress, commonly the quantity of fluid and debris recovered is small (Hirscheimer et al 1938), and the Ryle's tube may then be returned on the crest of the vomitus wave We do not attempt to aspirate the stomach unless the patient is *actively* vomiting at the time of induction It is then essential to use a large bore œsophageal tube

There has been considerable discussion as to the ideal position of the patient for a forceps delivery *Those* performing their deliveries with the patient in the left lateral position have been quick to indicate the advantages of this position to the anæsthetist, should vomiting occur Once intubation has been achieved, the position adopted is of little importance to the anæsthetist, and of course if cæsarean section is to be undertaken there is no choice of position

From the anæsthetist's point of view the important position is that used during the induction of anæsthesia If vomiting is expected the Trendelenburg position is usually chosen The reverse Trendelenburg position,

FUND FOR TUBERCULOUS WOMEN

Mr W H **Townsend**, of the Margaret de Sousa Deiro Fund, writes

This Fund exists for the treatment and relief of women who, normally supporting themselves by their own exertions, are temporarily incapacitated by pulmonary tuberculosis There are grants to cover the cost of treatment, when this cannot be carried out in suitable conditions under the National Health Service, and grants towards convalescent holidays following institutional treatment In approved cases the trustees also give financial assistance for rehabilitation, when part-time work yields an inadequate living wage By its constitution the Fund cannot assist chronic cases where there is no prospect of return to employment Further information can be obtained from the trustees at 1, New Court, Carey Street, Lincoln's Inn, London, W C 2

Parliament

The Guillebaud Report

Mr R H **Turton**, the Minister of Health, in opening on May 7 a debate on the Guillebaud report described it as a "welcome vindication of the National Health Service as it now exists" The report made clear that economy and efficiency had increased since the service began in 1948 Thus in real terms the increase in the gross cost of the service between 1949 and 1954 was small —only £30 million out of a total of £400 million— and during these years the service had been substantially improved and extended.

Perhaps the greatest problem of the service, he continued, was the tripartite division of the administrative structure, and the committee agreed that cooperation between the different branches of the service, and even within them, had not yet been fully attained The Government, Mr Turton said, accepted that there should not at this time be any transfer to other authorities of responsibility for hospital or general-practitioner services, any creation of new central or local ad-hoc authorities as the recipients of particular functions, any changes in regional-hospital-board areas or in their methods of appointment, or any transfer to those boards of responsibility for teaching hospitals in England and Wales, or any transfer of dental-clinic services from local authorities to the central health departments The acceptance of these broad principles did not, however, cover the whole ground, and it was indeed dependent on certain minor adjustments of practice, if not of organisation In the hospital service, for instance, the committee had suggested that it should be made clear that the regional hospital boards were responsible for exercising a general oversight and supervision over the administration of the hospital service in their region The Government accepted this principle, but Mr Turton wished to make it clear that this did not mean that the R H B s should set the H.M.C s (or for that matter the Minister the R H.B) in a strait-jacket of prior approvals The conception was rather one of review—and, if necessary, rebuke—after the event, and not of reference upwards beforehand

It was in the home health and preventive services, Mr Turton thought, that the tripartite administrative structure raised most problems, and our first objective must be "to place at the disposal of the patient in his home, equally with the patient in hospital a coordinated team acting under the clinical guidance of his personal medical attendant" This would call for the closest cooperation between the general practitioners and the local health authorities It should be the aim of the home team, which must include welfare as well as health workers, to keep out of hospital, including mental hospitals, all patients who could equally well be treated at home In his view health and welfare were so closely linked that in the domiciliary field at least they ought to be administered as one

Turning to finance Mr Turton recalled that the Guillebaud Committee had suggested £30 million a year as a desirable rate of capital expenditure for the hospital service for the coming seven years The programme for hospital building announced last year, providing £17½ million for new major projects and £13 million for capital expenditure, was a major step in the direction proposed by the committee It would not be affected by the cuts in capital expenditure The committee's recommendation that charges for dental treatment and spectacles should be reduced raised the question of priorities between the different parts of the service and must be reserved for further study

However the service was organised, Mr Turton concluded, so long as unlimited financial resources were not available, questions of priority would arise In his own mind the three needs which could claim precedence were hospital accommodation, the mental-health services, and old people

Dr **Edith Summerskill** agreed with the committee and the Minister that no major administrative changes should be made in the service anyhow at this stage The proposal to restore certain kinds of hospitals to the local health authorities would, in her view, be a retrograde step because it would establish a central and a local hospital authority She would like to see closer collaboration between the local authorities and the general-practitioner service The conditions of service of the practitioner should bear a closer resemblance to those of the medical officer of health The salaried medical officer's approach to medicine, with the emphasis on prevention, had been dissimilar to that of the general practitioner occupied with the curative side Unfortunately the N H S still made the doctor dependent on fees—there were still capitation fees—and that gap between these two doctors, working in two different medical worlds, was unfortunately not made smaller The time was coming when we must consider the best means of remunerating the general practitioner

She was disappointed that the Minister had not accepted any of the financial recommendations of the committee 45% of our hospitals were built before 1891 The capital expenditure on hospitals was three times as high in 1938–39 as it was in 1952–53 The teaching hospitals, she thought, should be integrated with the regional hospital boards It was an anachronism for them to be autonomous The splendid isolation of the teaching hospitals tended to introduce a snob element into the health service which militated against cooperation and the closing of the human gap

The shilling prescription charge was, she held, unjustifiable It had reduced our huge medicine bill of £46 million by £4 million It deterred not the hypochondriacs or the better off but the poorest in the community who should have no financial barrier between them and the doctor With the expensive high-pressure salesmanship of the drug houses, was it any wonder that the Minister had to keep on asking for more money for proprietary drugs? She found it difficult to reconcile the colossal sum spent on drugs, and the Minister's weak attitude towards it, with the decision to cut the milk-supplies to the under-5s in the nursery

Sir **Frederick Messer** regretted that the Guillebaud report had not said more about preventive service In his view it was worth considering whether the maternity and child-welfare services and domiciliary services should not be transferred from the county councils to the large boroughs Mr **John Baird** suggested that, in considering priorities, we should remember that the N H S was in fact a money-saving service Sir **Hugh Linstead** believed that doctors did not need Ministerial protection against the advertising methods of the drug firms

Colonel **Malcolm Stoddart-Scott** thought that the Guillebaud report confirmed that the N H S would become in the very near future the first priority of our social services He besought the Minister to persuade the Cabinet to spend no less than £50 million a year for the next five years or so on building and modernising hospitals He regretted that the Guillebaud report remained so silent on the needs of mental health and of preventive health and said nothing at all about the development of the industrial health service In his opinion there should be one national health service both for industry and for the civil population

Mr **Arthur Blenkinsop** had been impressed by Professor Titmuss and Mr Abel-Smith's financial survey What hope was there, he asked, of the regular production for the public of information about how the health service was going? As the Guillebaud report showed, the service was not extravagantly run, and he thought that everyone had been influenced to some extent by the aura of unfounded charges The Minister, he thought, had little

A SPECIFIC VIRUS-ANTIBODY FLOCCULATION REACTION WITH POLIOMYELITIS VIRUSES

WILSON SMITH
M D Manc , Dip Bact , F R S

F W SHEFFIELD
M B Lpool

L H LEE
M B Malaya

GILLIAN CHURCHER
M B Lond

From the Department of Bacteriology, University College Hospital Medical School, London

IN a recent publication from this laboratory Belyavin (1956) reported a macroscopically visible flocculation reaction between influenza viruses and their specific antisera His subsequent work, much of it still unpublished, has firmly established the value of the reaction both as a research tool for the investigation of virus structure and strain relationships and as a practical method—simple, rapid, and flexible—for the assay of serum antibodies

The question whether such direct flocculation would take place with other viruses, especially those of a different order of size and possessed of quite different biological characteristics, seemed to us to be of great scientific interest and importance Poliomyelitis viruses were chosen for investigation for the additional reason that a simple in vitro method of typing poliomyelitis viruses and of detecting and assaying antibodies is urgently required , present available methods can be used only in specially equipped laboratories and even there impose severe limitations on the amount of work which can be undertaken because they are so expensive and time consuming The urgency of this need is considered to justify present publication of the results of experiments which are obviously of a preliminary nature but which, nevertheless, show conclusively that poliomyelitis viruses react with homologous serum antibodies to form, under appropriate conditions, easily visible floccules, and that the reaction is type specific We are under no illusions as to the amount of further work needed to establish the full significance of this reaction and to determine the range of its practical applicability, but we believe that it opens up a new line of approach to many outstanding problems of poliomyelitis

Materials and Methods

Poliomyelitis Viruses

Virus strains used were Brunhilde (type 1), Lansing and Y SK (type 2), and Leon (type 3) Seed pools of each were prepared as required and stored at –20°C

Cultivation of Virus

The viruses were propagated in HeLa cell cultures The HeLa cells were grown in the medium recommended by Sheffield and Smith (1956) Small cultures in Sanders bottles were used for the routine passage of virus and for titrating virus, but for the production of flocculating antigens larger cultures in babies' feeding bottles made of 'Pyrex' glass were made to obtain sufficient quantities of virus Each bottle received an inoculum of about 4 × 10^6 HeLa cells which, with medium changes on the 3rd and 5th days of incubation, gave cultures of about 10 × 10^6 cells by the 7th day On the 7th day all medium was removed and the cells were washed thrice with Earle's solution An inoculum of 0 05 ml or 0 10 ml seed virus was added to each bottle followed by 10 ml maintenance medium Incubation was continued at 37°C on a roller drum for a further 48 hours, at which time the virus fluids were harvested Two different maintenance media have been used Parker 199' with 10% rabbit serum , and Earle's solution 85%, 5% solution of lactalbumin hydrolysate 5%, and rabbit serum 10% Both of them have proved satisfactory, though we now prefer the second because of its simplicity

Preparation of Virus Antigens

These were prepared by concentration and purification of virus from the culture fluids Batches of pooled virus fluids were first centrifuged in a horizontal centrifuge at 1500 r p m for 15 minutes to remove gross particles They were then clarified by centrifugation in the 'Spinco Rotor No 21' at 15,000 r p m for 42 minutes This treatment removes much extraneous material without depositing any appreciable quantity of virus From the clarified supernatant fluid virus was deposited by high speed centrifugation for 5 hours in the 'Spinco Rotor No 30' at 30,000 r p m The supernatant fluid containing small molecular constituents of the medium but only negligible amounts of virus was discarded, and the deposited pellet of each tube was resuspended in either 1 0 ml or 0 5 ml of saline solution Tube capacity was 38 5 ml , so the nominal virus concentration factor was either × 38 5 or × 77 Perfectly homogeneous suspension of the material in such small volumes of saline solution, however, was impossible Pooled virus concentrates were therefore given a final clarifying spin in the horizontal centrifuge at 1500 r p m for 15 minutes The resultant suspensions of virus were distinctly opalescent but entirely free from visible particles when viewed in a viewing box with the aid of a hand lens They were used as antigens both for the flocculation experiments and for the immunisation of rabbits They received no treatment for inactivation of the virus, nor was any preservative added

Preparation of Antisera

Rabbits were immunised by intravenous inoculation of the virus concentrates described above Two doses were given with an interval of 14 days Samples of blood were taken at various intervals thereafter Some rabbits were given a third dose of virus after a rest period of several weeks, followed again by bleeding at intervals The adoption of a uniform immunisation schedule was impossible because at that time nothing was known about the immunological responses of rabbits to poliomyelitis viruses , moreover, as the virus concentrates were used as soon as possible after their preparation, the amount of virus contained in each dose was not known until several days later, when the results of titrations in HeLa cell cultures were obtained The full range of sera will be used eventually for a more detailed study of the immunological responses of rabbits , but, for the flocculation experiments, only three of the samples, one against each virus type, were used They were obtained thus

Rabbit no	*Virus antigen*	*Day*	*Inoculation TCD/50 × 10^6*
4/55	Type 1 (Brunhilde)	0	1 60
		14	1 75
		24	Bled
1/56	Type 2 (Lansing)	0	0 003
		14	0 24
		24	Bled
3/56	Type 3 (Leon)	0	0 50
		14	0 63
		51	1 20
		58	Bled

Serum was separated from the clotted blood after overnight storage in the refrigerator, freed from cells by centrifugation, doubly inactivated by two separate heat treatments, each at 56°C for 30 minutes, and stored in the frozen state until required It is not known whether double inactivation is necessary, but it was adopted because of its importance in influenza virus flocculation (Belyavin 1956)

Flocculation Technique

Flocculation tests were done by the standard method of bacterial agglutination 0 3 ml quantities of each reagent, virus antigen and antiserum, were mixed in Dreyer agglutination tubes Dilutions of reagents were evidence from this and other countries to which he refers tends to show that mortality from cancer of the lung is twenty times greater amongst heavy smokers than amongst non-smokers The Government will take such steps as are necessary to ensure that the public are kept informed of all the relevant information as and when it becomes available.

Mr W. D. CHAPMAN While thanking the Minister for at last saying something very forthright on this issue may I first ask him what line of action he will take to inform the public about this danger? Has he in mind something as widespread as the campaign against diphtheria and in favour of diphtheria immunisation, and secondly, will he give us an assurance that the Government will take the initiative in such a campaign and will not leave it simply to the local authorities to do so if they wish?—Mr TURTON. In my view, in the present stage of our knowledge, a national publicity campaign would not be appropriate

Mr. VAUGHAN-MORGAN. Is there any evidence, particularly with regard to pipe-smoking, secondly, is there any evidence from the statistics as to how those who give up smoking are affected?—Mr. TURTON: It would appear that pipe-smokers face a heavier risk than non smokers, but the risk is substantially less than that incurred by heavy cigarette smokers There is some evidence that the risk of contracting cancer of the lung decreases when smoking is given up

Dr. EDITH SUMMERSKILL: In view of the fact that the Minister for the first time is informing the country that tobacco smoke has certain carcinogenic properties and has made an emphatic statement, would he not agree that it was rather unfortunate that this statement came after the statement by eminent authorities on the radio and on television? I understand that a film was even shown in this building last week. Is it not unfortunate that the Minister's statement should follow these statements and not precede them, and in view of the gravity of the present statement, will he say why he will not give us a periodic review of the situation?—Mr TURTON. Whenever any more knowledge becomes available, I shall deem it my duty to put it before the House at once That is what I have done in this case but I must first of all see what has been the increase in knowledge since the last statement made I did tell the House some time ago that two cancer-producing substances had been identified in tobacco smoke

Dr BARNETT STROSS. Will the Minister agree that there is now at least ample evidence to suggest that he should consult the Minister of Education and that all efforts should be made to bring this knowledge before school-leavers, boys and girls, in order that they at least may have some warning as to what may be the result of becoming as addicted to this habit, as so many of us are? Mr. TURTON I have given my decision regarding a national publicity campaign Any matter regarding what is done by the Minister of Education should be addressed to him. Mr ARTHUR BLENKINSOP Surely the Minister will review his statement with regard to a national campaign? Is it not highly important that any information that may become available should be reviewed from time to time?—Mr TURTON I quite agree. I certainly shall review it.

Housing of the Elderly

Replying to a question, Mr DUNCAN SANDYS, Minister of Housing and Local Government, said that he had decided to inquire into the arrangements that were being made for housing elderly persons. His object was to see whether, having regard to the requirements of other sections of the population, old people were receiving a reasonable share of the accommodation provided and whether this was of the kind best suited to their physical needs and financial circumstances. Accordingly, he proposed to ask all local authorities and certain voluntary organisations to send him particulars of what they had done to deal with this problem. While this information was being collected a qualified official of the Ministry would go and see schemes of various kinds in different parts of the country and make a report to him upon them. He also intended to seek the views of the Central Housing Advisory Committee. The problem of housing elderly people was in many respects connected with that of providing for their health and welfare His inquiries would therefore naturally be carried out in close collaboration with the Minister of Health.

Recruitment of Mental Nurses

Replying to a question, Mr TURTON, Minister of Health, said that the basic allowances of new entrant student mental nurses under twenty-one were being increased by amounts varying from £20 to £45 and of those over twenty-one by amounts varying from £80 to £110 per year The discontinuance of dependants' allowances would however mean that student mental nurses with a wife and one child would have these increases reduced by £72 16s. a year.

Replying to a further question, Miss HORNSBY SMITH said that the numbers of new entrants of male student nurses in mental deficiency were in 1954, 140 and in 1955 133, the numbers of readmissions were 34 and 25 respectively The numbers leaving while still students were in 1954, 174 and in 1955, 121

Nurses in Scottish Mental Hospitals

Replying to a question, Mr JAMES STUART said that at Sept 30 1955, the ratio of nurses to patients was less than 1 to 5 in twelve of Scotland's twenty-nine mental hospitals accommodating 42% of all patients in mental hospitals At the same date this ratio was less than 1 to 6 in two of the twelve mental-deficiency institutions, accommodating 18% of all patients in such institutions.

Colour of Milk Bottles

Replying to a question asking what consideration had been given to the deterioration of milk by the use of clear glass bottles, particularly when exposed to light and sun for long periods, Mr HEATHCOAT AMORY, Minister of Agriculture Fisheries and Food, said that there were no regulations about the colour of milk bottles The matter had been considered by the Milk and Milk Products Technical Advisory Committee and they had expressed the view, which he had accepted, that there were no adequate grounds for regulations

Replying to further questions Mr AMORY said he thought that it was true that milk retained its high food value better in coloured than in clear glass bottles Milk could retain its riboflavine and vitamin C content better, both of which suffered from long exposure to the sun. But there were practical considerations which made it difficult to deal with the matter by regulation. One of the considerations in the minds of the advisory committee was that with clear glass bottles purchasers could see more readily whether the milk was relatively clean or not.

Public Health

School Milk

CHANGES in the milk-in-schools scheme are announced. From Sept. 1 free milk will be available for schoolchildren only during term-time, and the limited arrangements for supplying milk at weekends and during the holidays will cease Children in nursery schools now receive $\frac{2}{3}$ pint daily, and those in nursery classes receive $\frac{1}{3}$ pint From Sept 1 all children will receive $\frac{1}{3}$ pint, with the exception of delicate children attending special schools who may be given $\frac{2}{3}$ pint. A saving of about £125,000 a year is expected.

In a circular to local education authorities the Ministry of Education asks that special care be taken in the ordering of milk, pointing out that the excessive purchasing of only 4 bottles in every 100 would involve the Exchequer in an extra expenditure of about £500 000 a year The amount of milk ordered should be based on the number of pupils taking milk regularly, allowing for the usual rate of absences.

From Sept. 1 local education authorities will be responsible for supplying milk to pupils in non-maintained schools as well as maintained schools. The terms under which local education authorities supply milk to non-maintained schools will be determined by agreement between the authority and the proprietor of the school, and should include provision by the proprietor of such information about ordering and consumption as the authority may require. The terms should also include a stipulation that no payment should be made by parents for milk supplied.

Slum Clearance

Speaking at Stoke-on-Trent on May 4 Mr Duncan Sandys Minister of Housing and Local Government, said that during last year some 25,000 slum houses were

TABLE III—CROSS-CHESS-BOARD TITRATIONS OF BRUNHILDE AND LEON REAGENTS

Antigens		Brunhilde serum						Leon serum					
		1/10	1/20	1/40	1/80	1/160	1/320	1/10	1/20	1/40	1/80	1/160	1/320
Brunhilde	1/1	+++	+++	++	+	op	−	op	op				
	1/2	+++	+++	+++	+	−	−	−	−				
	1/4	++	++	++	++	−	−	−	−				
	1/8	+	+	+	+	−	−	−	−				
	1/16	−	−	−	−	−	−	−	−				
Leon	1/1	op	−					+++	+++	+++	op	−	−
	1/2	−	−					+++	+++	+++	++	−	−
	1/4	−	−					+++	+++	+++	+++	−	−
	1/8	−	−					+	+	+	++	±	−
	1/16	−	−					−	−	−	−	−	−

Final reading at 4 hr. incubation.

from the HeLa cells but may equally well be an indication of an antigenic relationship between poliomyelitis viruses of different types similar to that which has been shown to exist between influenza viruses of types A and B (Smith et al. 1955).

Periodic readings from 30 minutes to the final reading at 4 hours showed progressive development and extension of flocculation with both virus types similar to the development illustrated by table II. In this experiment Leon reagents flocculated more rapidly than Brunhilde and gave a beautiful demonstration of inhibition in the zone of antibody excess in spite of the omission of serum dilutions lower than 1 in 10. Optimal flocculation tubes in each row were clearly recognisable at some stage of the observation period, shifting one tube to the right with each progressive twofold dilution of the antigen. Even so, except for a single tube, flocculation was confined to dilutions of antigen 1 in 8 or less. Also, with Leon reagents, very little extension of flocculation occurred after 2 hours, whereas with Brunhilde reagents the flocculation area at 2 hours was less than half that shown at 4 hours.

Flocculation of Type 2 Virus

All that it is possible to say at present is that the flocculation reaction does take place with type 2 virus and is likely to follow the same pattern as that with the viruses of types 1 and 3. The relatively poor growth of the Lansing strain in HeLa cell cultures led us to abandon it to concentrate on work with Brunhilde and Leon. Recently we have established cultures of the Y-SK strain of type-2 virus in HeLa cells and prepared antigens for rabbit immunisation, but a strain-specific homologous antiserum is not yet available. The Y-SK antigen, however, has been shown to flocculate with a rabbit antiserum against strain MEF1 kindly supplied by Dr. Tyrrell; it shows no sign of flocculation with our Brunhilde and Leon antisera.

Reactions with Human Sera

With the reagents so far available only a few preliminary tests of human sera have been possible, but these have clearly shown that poliomyelitis viruses may be flocculated by the type-specific antibodies which occur as a result of natural infection. Brunhilde antigen was flocculated by both acute and convalescent sera of a proved case of type 1 non-paralytic poliomyelitis in a child of 3 years, whereas neither serum showed any trace of reaction with Leon antigen. Conversely, the convalescent serum of a proved case of type 3 paralytic poliomyelitis in a child of 18 months flocculated the Leon antigen but not the Brunhilde antigen. The acute-stage serum of this patient did not flocculate either antigen. The tests were done with serum dilutions of 1 in 5 and 1 in 10.

Discussion

Discovery of a new phenomenon inevitably leads to speculation. It is therefore important to distinguish clearly between *what must be accepted as fact and what is merely possibility*. The essential facts definitely established by *our experiments may be stated in very simple terms*. An antigen-antibody reaction occurs in a mixture containing poliomyelitis virus and its homologous antiserum which under appropriate conditions and with suitable preparations of the virus antigen leads to macroscopic flocculation; furthermore, the reaction is strictly type-specific. It must be emphasised, however, that, so far, this flocculation phenomenon has been demonstrated only with antigens made from single strains of each virus type, with antisera from immunised rabbits, and with human sera from two cases of poliomyelitis in young children. Even so, it is quite certain that direct poliomyelitis virus flocculation can now be used as a research tool to explore the surface structure of these viruses and to investigate some of their biological *characteristics*.

One of the most urgent needs in current work on poliomyelitis is a simple and rapid in-vitro method of typing virus and of detecting and assaying the serum antibodies concerned in protection against infection. The value of such a method in the fields of serological diagnosis, production, and standardisation of vaccines, and epidemiology would be incalculable. There is obviously a possibility, perhaps even a probability, that the direct virus flocculation reaction may meet this need. If so, its simplicity and rapidity are such that tests could be made almost anywhere, because the only apparatus needed would be agglutination tubes, racks, graduated pipettes, and a water-bath. Results of a titration are as easy to read as those of a routine Widal test. But the possibility *can only* be determined by further work along several different lines. The number of relevant problems calling for investigation is too large to categorise, but those of particular urgency are the question of stability of the virus antigens, the correlation of flocculating antibodies with the neutralising and complement-fixing antibodies of various kinds of sera, the possibility that the reaction may be not only type-specific but also strain-specific, and the possible occurrence in sera of non-specific flocculation inhibitors. One essential for systematic attack on each of these problems is an adequate supply of antigens of all three types of virus from different strains. Though this would present no difficulty, given the equipment for virus culture on a really large scale, a microflocculation method would be advantageous for many kinds of test. Work to this end has already yielded very promising results which, if confirmed, will be published shortly.

Summary

A direct poliomyelitis virus flocculation reaction is described. This is type-specific and occurs in mixtures of concentrated suspensions of virus and homologous rabbit antisera. Flocculation has also been demonstrated with human sera from two cases of poliomyelitis in children.

Possible uses of the reaction and the relative problems requiring investigation are briefly outlined.

The *Encyclopædia Britannica* defines genius as "the highest conceivable form of original ability, something altogether extraordinary and beyond even supreme educational prowess", and in this definition one notes what is certainly a characteristic attitude of the beholder, that of astonishment, which gives rise to the notion of mystery. Of all the characteristics of genius Revesz selects *surprise* as being the most central, to which all others are accessory, and this seems to accord with the frequency with which geniuses receive their inspiration in a sudden flash that startles the recipient himself. In describing a recent discovery in physics Dr Gabor remarked: "This statement has that touch of offending common sense which is the hallmark of every truly important scientific discovery." Freud's discoveries, said Dr Jones, satisfied this criterion in full measure.

Allied to this feature of intuitive inspiration is the characteristic spontaneity with which the productions of genius appear. They can never be brought about by a deliberate effort of will, and nothing can ever force them. An attitude of passive surrender towards the flowing in of the valuable ideas must be significant for the psychology of the productive process.

Of the features characteristic rather of scientific production than of artistic inspiration the most obvious is the indispensable one of absolute honesty: "the first and last task required of genius," wrote Goethe, "is love of truth." Closely akin to this mysterious feeling for what is true seems to go a sense of what is significant. This enables, or compels, a genius to generalise a finding where a lesser mortal would cautiously go on collecting more evidence before venturing on a general statement. Freud, though he would be accounted a man of sober and reflective judgment, afforded several instances of this kind of superlative boldness and sureness.

A further attribute of genius is the power of concentration. Buffon held that *genius is nothing else than a greater aptitude* for patience than that possessed by other men, and Carlyle described it as "first of all a transcendent capacity of taking trouble." Another writer, referring to "the self-surrender so familiar to creative minds," says: "The concentration of such a state may be so extreme that the worker may seem to himself or to others to be in a trance"—as happened when Freud was composing the final chapter of *The Interpretation of Dreams* in 1899 and sometimes seemed oblivious of his surroundings.

"What is the significance of this extraordinary concentration and intensity?" Dr Jones asked. "What powerful impulses are driving their way at such moments? For there is every reason to suppose that men of genius are characterised by possessing exceptionally strong emotions and usually a correspondingly strong capacity for containing them. The tension induced by the preceding efforts to find a solution gradually mounts until it reaches a climax. The great mathematician of genius, Henri Poincaré, in describing how he made his own discoveries, said: 'One is struck by these appearances of sudden illumination, obvious indications of a long course of previous unconscious work. . . . These sudden inspirations are never produced except after some days of voluntary efforts which appeared absolutely fruitless.' Evidently there must be a special coincidence between the unconscious impulses and some essential feature of the objective problem. In the preliminary cogitation various shiftings and similar mechanisms are going on in the unconscious the purpose of which is to achieve a sufficient degree of harmony with the censoring functions of the super-ego by means of which the accompanying guilt is kept in abeyance. At the successful moment there must have been achieved a quite remarkable degree of integration between the ego, the super-ego, and the id. It is no doubt this successful degree of synthesis, the overcoming of all barriers, that accounts for the sense of elation at the final moment of triumph."

The lecturer believed that an essential prerequisite of the productivity of genius must lie in a particular scepticism. He must have refused to acquiesce in certain previously accepted conclusions. This argues a kind of imperviousness to the opinions of others, notably of authorities. Furthermore, he often has the capacity of seeing the existence of a problem where others have passed it by; he has refused to take something for granted as being either without meaning or too insignificant to bother about. This aloofness sets him free to speculate and investigate. But Freud himself once pointed out to Dr Jones that such freedom is always obtained under the condition that another aspect of mental functioning is inhibited. "It may well be that the compensatory inhibition of which Freud spoke is the explanation of a feature often remarked in men of genius—namely, a certain naïveté, marked simplicity, and ignorance of the ways of the world.

"The scepticism and imperviousness to opinion of which I have spoken were prominent features of Freud's personality and they extended over a wide field. Not long after getting to know him, however, I was struck by an exactly opposite feature, one which, it is true, operated in a far more limited field. I refer here to a curious credulity, a willingness to believe what he was told whether it was really likely or not. To it I would ascribe his well recognised difficulty in forming an accurate estimate of personal character, a deficiency of which he himself complained. . . . Pascal pointed out that greatness is never at one extreme but consists of the union between two extremes, an idea which Sainte Beuve later labelled the theory of the *entre-deux*. My own suggestion is a particular application of this."

Wondering whether his observation concerning Freud's personality could have any more general validity as a condition for the productivity of scientific men of genius, Dr Jones studied the characteristics of others among them. The reputation of Copernicus, he said, rests on his scepticism—on his doubting whether the sun revolves round the earth. But in questioning the views of Ptolemy, Copernicus was trying to justify Aristotle's dictum that all the heavenly orbs and orbits must have the form of a perfect circle; for in Aristotle's infallibility he had a credulous belief. In Sir Isaac Newton's personality both scepticism and credulity were prominent. His published work is marked by a rigid objectivity, and it was he who proudly proclaimed the famous sentence, *Hypotheses non fingo*; yet in earlier days he had spent much time in search for the philosopher's elixir and the means of transmuting metals into gold, and throughout his life theology was much more important to him than science—and, moreover, theology of a peculiarly arid and bigoted order. Faraday, the supreme physicist of the 19th century, had also his vein of credulousness: throughout his life he was an adherent of the obscure sect of Sandemanians, and for three years regularly preached sermons before them. In Darwin scepticism was tempered by a credulous attitude towards other authorities: even after his great discovery of the operation of evolution through natural selection he still believed in Lamarck's doctrine of evolution through the inheritance of acquired characters, a doctrine his own work had rendered superfluous. His friend and contemporary Huxley offers a very interesting contrast: he had a wider knowledge than Darwin, more originality, greater intellectual daring and any amount of scepticism; but there is no record in his life of any evidence of credulousness to match it and (according to Dr Jones's view) enable him to make really great discoveries. "Perhaps it is worth mentioning in the present connection the remarkable epidemic of belief in the cruder aspects of spiritism that infected several of the leading English physicists early this century: Sir William Barrett, Sir William Crookes, Sir Oliver Lodge, and Sir George Stokes. The number of times the mediums in whom they trusted were exposed as frauds made no difference to the tenacity of their beliefs."

After speaking, in psycho-analytical terms, of the possible correlation between credulousness and the characteristically receptive nature of genius, Dr Jones ended his lecture[1] by saying that it will probably be generations before all the implications of Freud's ideas are fully worked out and the stimuli he provided for us fully acted on. "Revolutions in thought such as he brought about do not happen very often in history, and it may well be long before another similar one takes place."

REMUNERATION OF SENIOR HOSPITAL MEDICAL OFFICERS

UNDER an Industrial Court award, the remuneration of the 2631 S.H.M.O.s in the National Health Service (including 1190 employed part time) is increased by £75 a year. Hitherto the scale has been £1500–£1950.

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[1] This will form one of a collection of essays to be published by Basic Books Inc., New York, and distributed in this country by Tavistock Publications.

TABLE II—BLOOD FLOW
(ml per 100 c cm of tissue a minute)

—	Normal heat exchange		Reflex vasodilatation		Reflex vasoconstriction	
	Operated side	Non operated side	Operated side	Non operated side	Operated side	Non operated side
Sympathectomised patients	9·0	3·1	12·4	19·0	11·8	13·0
Non sympathectomised patients		2·8		14·1		9·4
Healthy people		3·1		14·8		9·3

The technical quality of the operations was assessed by an independent examination of the operation notes without prior knowledge of the blood flow estimations The criteria used in this assessment were (1) the description of the operation in the notes, the difficulties of access, the amount of hæmorrhage, &c , (2) the surgeon's estimate of the amount of sympathetic tissue removed , and (3) histological evidence of the removal of sympathetic nervous tissue Although such an assessment is bound to be imprecise it nevertheless gives a reasonable idea of the technical efficiency of the operation, each being classified as " good," " bad," or " doubtful " Table III shows the results of this analysis together with the time between the operation and the blood-flow estimation, the presence or absence of the vasomotor reflexes, and the degree and duration of improvement in the patient's vascular symptoms after the operation A " t " test of the difference between the means of the blood flow of " good " and " bad " operations shows that this difference is statistically significant ($p<0·01$)

The comparison of the blood flow under conditions of normal heat exchange and the assessment of the quality of the operations are shown graphically in fig 2

Illustrative Case-reports

Patient 10—Female Born 1899 Attack of anterior poliomyelitis during infancy affecting mainly the right lower limb Coldness, cyanosis, and chilblains of the right leg since the age of 21

March, 1952 extensive right lumbar sympathectomy during which no technical difficulties were encountered In surgeon's opinion D12–L3 sympathetic ganglia were removed A total length of seven inches of sympathetic chain was removed, including a double chain between the L2 and L3 ganglia Histological examination confirmed the removal of sympathetic nervous tissue

Result—The patient's symptoms were considerably improved after sympathectomy, and this improvement has been maintained Blood flow of feet examined thirty five months after operation resting blood flow on operated side was 21·2 ml per 100 c cm of tissue per minute

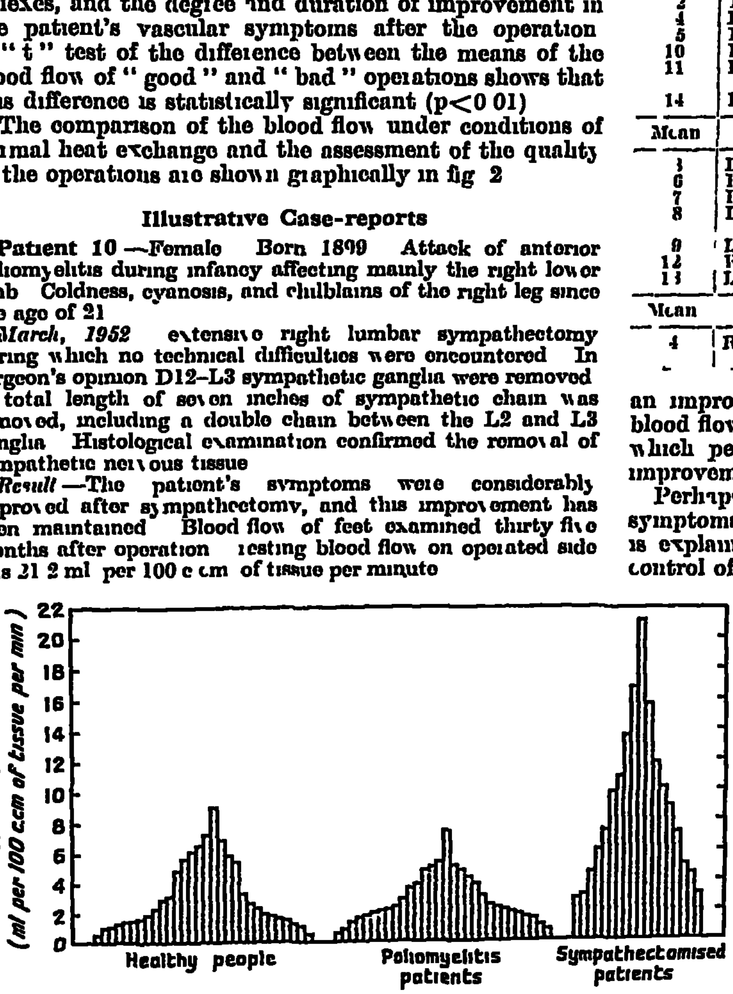

Fig 1—Blood flows of all persons studied

Patient 9—Female Born 1937 Attack of anterior poliomyelitis in 1942 affecting mainly the left lower limb Coldness, cyanosis, chilblains, and ulceration of the left leg since 1945

October, 1953 left lumbar sympathectomy during which there was moderate venous bleeding and the ganglia were difficult to identify In surgeon's opinion only L2 ganglion had been removed Histological examination confirmed the presence of sympathetic nervous tissue

Result—After the operation there was moderate improvement in the patient's vascular symptoms which lasted for only two months Blood flow of feet examined sixteen months after the operation resting blood flow on operated side was 7·2 ml per 100 c cm of tissue a minute

Discussion

An interesting feature of this investigation is that only one of the eighteen operations to remove sympathetic ganglia failed to produce some improvement, however short lived, in the patient's symptoms Of the 8 patients subjected to operations described as " bad " 2 showed an improvement which was still maintained when the blood flow was investigated , 5 showed an improvement which persisted for some months , and 1 showed no improvement

TABLE III—ANALYSIS OF RESULTS

Patient no	Operated side	Assessment of operation	Normal heat exchange blood flow (ml per 100 c cm per min)	Time since operation (mos)	Vasomotor reflexes	Symptomatic improvement	
						Quality	Duration (mo)
1	Both	Good	9·9	20	–	Good	20
		Good	10·2	20	–	Good	20
2	Right	Good	15·7	21	–	Good	21
4	Left	Good	10·9	17	–	Good	17
5	Right	Good	16·8	43	–	Good	43
10	Right	Good	21·2	35	–	Good	35
11	Both	Good	13·6	180	–	Good	180
		Good	11·8	22	–	Good	22
14	Right	Good	9·0	11	–	Good	11
Mean			13·2	41			41
3	Left	Bad	6·0	43	+	Good	30
6	Right	Bad	4·5	25	–	Good	25
7	Right	Bad	4·4	21	+	None	0
8	Both	Bad	2·8	67	+	Slight	[illegible]
		Bad	3·0	60	+	Slight	3
9	Left	Bad	7·2	16	–	Mod te	2
12	Right	Bad	5·0	26	+	Good	26
13	Left	Bad	3·0	25	–	Good	[illegible]
Mean			4·5	36			[illegible]
4	Right	Doubtful	7·3	17	–	Good	17

Perhaps the temporary amelioration of the vascular symptoms that follows a " bad " lumbar sympathectomy is explained by the temporary interruption of nervous control of the blood vessels and the subsequent recovery of local arterial tone, as described by other workers The temporary vasodilatation occurs, as can be shown by plethysmography even in cases in which there is no histological evidence of any sympathetic nervous tissue having been removed—e g , patient 8 Moreover the fact that, in this investigation, every patient whose vasodilatation was only temporary had a " bad " operation is unlikely to be explained merely by coincidence In our opinion it appears more likely that any attempt to remove sympathetic ganglia produces sufficient trauma of sympathetic nervous tissue to produce a temporary paresis of the sympathetic nerve supply to the blood vessels, even though no nervous tissue may have been resected The eventual recovery of arterial tone could then be

ON DIAGNOSING CANCER HISTOLOGICALLY*

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WHEN a pathologist makes a histological diagnosis of cancer he is doing two things He is giving a prognosis for the patient concerned, and he is also influencing the treatment of future patients, for his dictum inevitably forms part of the body of knowledge from which the ' facts " of incidence and curability of cancer will subsequently be deduced For those who deal with the problem of cancer—surgeons radiotherapists, statisticians, and others—it is clearly important that they should know just how closely histological diagnosis can approach absolute accuracy The pathologist himself is none the worse for studying the factors that influence his judgment

The pathologist giving a histological diagnosis of cancer is too often regarded as a dispenser of absolute truth The wide use of and faith in, the term " histologically proved " is evidence of this attitude In fact, it is not possible to make an absolute diagnosis of cancer by microscopy in that the causal agent, whatever it be, cannot at present be seen in the lesion The analogy with the histological diagnosis of tuberculosis or leprosy, where the causal agent can be seen, scarcely merits pressing here except as a contrast to the actual basis on which a histological diagnosis of cancer is founded

Basis of Histological Diagnosis

A histological diagnosis of cancer is, in practice, founded on three sources of evidence the gross specimen, the sections made from it, and the clinical data

Macroscopic Evidence

The appearance of the gross specimen is never the final arbiter in a borderline case It may, of course, raise suspicion, and, as has been said " suspicion is the beginning of diagnosis ' To the pathologist, and surgeon, of experience the naked-eye appearances usually indicate the zones that demand microscopic examination

Microscopic Evidence

The important evidence lies in the sections, stained in whatever ways may be appropriate As already mentioned, a causal agent cannot be seen All we can use as evidence are alterations from the normal in cell structure and in tissue architecture Diagnosis is then based upon an almost wholly empirical association—namely, the experience of pathologists in general has shown that such histological appearances are, in almost all cases, associated with increasing progression of the disease and shortening of the life of the untreated and even of many treated, patients In practice, of course, in straightforward cases the pathologist gives his outright diagnosis with confidence He does not set out his argument along these lines, but that is his reasoning, and that is what he implies

" Clinical Cancer " and " Histological Cancer "

We recognise a case as straightforward when the alterations in tissue pattern are obvious, and the correlation between these morphological alterations and subsequent death of a particular type is very high Diagnostic difficulties become progressively greater, the lower this correlation is, and it is because the level of the correlation is so low at what we call the early stages of cancer that our diagnostic criteria at that stage are so poorly defined. The best we can do is, as it were, to extrapolate the lethal tissue patterns backwards and try to visualise them at an earlier stage We do, however, use clinical correlations as long as we can When we give a diagnosis of early cancer we do so because we feel that this kind of histological appearance has in the past on some occasion been correlated with progression of the disease Diagnosis of cancer from the florid or straightforward case down to cases at this level is diagnosis of *clinical cancer*

There is, however, another school of thought prepared to extrapolate tissue patterns even further backwards—in fact beyond the point where a significantly positive correlation with the subsequent manifestation of clinical cancer virtually disappears This school argues that a histological pattern may be so atypical that only cancerous growth can explain it This is the type of cancer we are told is present in the prostate of some 30–40% of men over the age of 50 Yet nothing like 30–40% of men over the age of 50 die from prostatic cancer, so we can assume that cancer is being defined here in terms quite different from those used in defining clinical cancer This is, in fact *histological cancer* There is, possibly, no harm in using the term ' cancer of the prostate ' to describe these appearances as long as this kind of cancer is not equated with clinical cancer, and as long as it is understood that when a man has had such an organ removed he has been cured, not necessarily of a lethal disease, but of a certain histological appearance within his prostate Diagnoses made in this way, and such terms as ' histologically malignant but clinically benign," require to be regarded with caution if cancer pathology is to be treated as properly it should as a science

Histological " Criteria of Malignancy '

When we make the diagnosis of ' cancer " at a low level of clinical correlation it is extremely difficult to know how close to the truth we are approaching for the obvious reason that it is almost impossible to distinguish between *early* diagnosis and *wrong* diagnosis If a lesion, diagnosed as cancer, but wrongly diagnosed in that it is not a cancer, is completely removed the records will wrongly show that a cancer has been " cured " If on the other hand, the histologist has a high, perhaps unjustifiably high diagnostic threshold for cancer a truly malignant lesion may be diagnosed as " not cancer ' and the surgeon be cheated out of a genuine cure The pathologist's difficulty is that he must try to visualise the earliest stages of those abnormal tissue patterns which, when at their maximum in the " obvious " case, form unmistakable evidence of atypical and excessive growth of cells These patterns are manifest as (*a*) cell polymorphism accompanied by a varying degree of mitotic activity, and (*b*) the property which we call " invasiveness "

Neither of these properties can be depended upon absolutely *Cell polymorphism* is abundantly seen, for example, in granulation tissue, and indeed the distinction between active granulation tissue and sarcoma can at times be perplexingly difficult, especially as mitotic figures may be seen in both Polymorphism of cells is also prominent in many cases of Hashimoto's disease, so much so as to lead to an occasional wrong diagnosis of cancer difficulty may also be increased here by the presence of mitotic figures in the hyperplastic tissue Polymorphic growth is almost characteristic of proliferative trophoblast, such as is seen in some hydatidiform moles or even in simple placental polyps These are specific instances, but the same difficulty arises more generally because of the polymorphism and mitotic activity so often seen in ulceration of epithelial surfaces It is clear, therefore, that there are occasions in plenty when cell polymorphism and mitotic activity cannot be accepted as diagnostic criteria of malignancy

Invasiveness—This property of malignant growth becomes manifest sooner or later, but it is particularly

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* Based on a lecture delivered at the U S Armed Forces Institute of Pathology, Washington, D C, on Nov 1, 1955

MIXED STAPHYLOCOCCAL INFECTIONS

THE DEVELOPMENT OF PENICILLIN-RESISTANT STRAINS

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STAPHYLOCOCCAL infections constitute a major clinical problem, particularly in hospitals. They are relatively numerous (ranging from a mild superficial pustule to a fulminating pneumonia or enterocolitis) and an increasing proportion of them are caused by strains resistant to antibiotics, especially penicillin.

Barber and Rozwadowska-Dowzenko (1948) drew attention to the rising incidence of penicillin-resistant strains of *Staphylococcus aureus* by reporting that, in the same London hospital, the number had risen from 14% in 1946 to 59% in 1948. Many similar reports have since been published, and at present in the U.S.A. it is considered that 75–80% of staphylococcal infections in hospitals are caused by penicillin-resistant strains (Long 1955, Spink 1955). This high incidence is, so far, confined to inpatients, but there is some evidence that penicillin-resistant infections are also appearing with greater frequency among outpatients (Rees et al. 1955).

The origin of penicillin-resistant strains has not been satisfactorily explained. It has, however, been firmly established (1) that the resistance of naturally occurring strains of *Staph. aureus* to penicillin is due to the production of the enzyme penicillinase, and (2) that this enzyme is not produced by strains rendered resistant to penicillin in the laboratory. Thus there are two quite distinct mechanisms whereby resistance to penicillin is developed. I deal here with only the naturally occurring penicillin-resistant strains—i.e., the producers of penicillinase. It has been found that these strains are unstable. Barber (1949) obtained penicillin-sensitive variants from old cultures of penicillin-resistant strains of *Staph. aureus*, and Fairbrother et al. (1954) found that such variants readily appeared during the incubation of penicillin-resistant strains at 44°C. Penicillinase-producing variants have not, however, been obtained from cultures of penicillin-sensitive strains of *Staph. aureus*.

Investigations into the appearance of variants in infections have been few. Barber and Whitehead (1949) reported the isolation of both penicillin-sensitive and penicillin-resistant strains of *Staph. aureus* from the same patient, but from somewhat inconclusive phage-typing and serological tests they concluded that the strains were of different types and therefore had separate origins. Fairbrother et al. (1954) isolated penicillin-sensitive and penicillin-resistant colonies of *Staph. aureus* from the same cultures of infective material and found that, on six occasions, these had the same phage pattern, probably originating from the same parent strain.

The present investigation is a continuation of the study of the development of variant strains of *Staph. aureus* under natural and experimental conditions and provides a further explanation of the probable origin of the variant strains.

Methods

All material from infections was routinely seeded on to appropriate media, including blood-agar plates, and, after overnight incubation, plate cultures exhibiting colonies of *Staph. aureus* were selected for study. After careful examination with a hand lens representative colonies were selected for coagulase and sensitivity tests; if any variation in the colonial appearance was detected, 10–20 discrete colonies were investigated. The coagulase tests were done by the tube technique. The antibiotic sensitivity tests were initially made by the disc and strip techniques with pure cultures; but, where indicated, the serial dilution method was also used (Fairbrother and Martyn 1951). The penicillinase tests were done by the cylinder technique. The strains were phage-typed at the Public Health Laboratory, Manchester.

Throughout this work penicillin-sensitive strains of *Staph. aureus* proved to be coagulase-positive, were inhibited by $^{1}/_{16}$–$^{1}/_{32}$ unit per ml. of penicillin, gave a clear zone round the penicillin discs, and did not produce penicillinase. Penicillin-resistant strains of *Staph. aureus* were coagulase-positive, produced penicillinase, did not give a clear zone round the penicillin discs, and were not inhibited by at least 10 units per ml. of penicillin.

Results

The results fall conveniently into two main groups: those obtained in vivo from the examination of pus or other material from infections, and those produced in vitro with strains of *Staph. aureus* recently isolated from human infections.

ISOLATION FROM INFECTIVE PROCESSES

Incidence of Penicillin-resistant Strains

There are many reports, from different parts of the world, of the increase in penicillin-resistant strains isolated from hospital communities. Since the introduction of the disc technique in 1950 sensitivity tests have been made in this hospital as a routine, and analysis of consecutive samples of strains isolated at different times from the total hospital population (table I) shows an increasing incidence of penicillin resistance.

A more detailed analysis of the 1955 figures shows that 142 of the 550 strains were isolated from outpatients and 52 (37%) of these were penicillin-resistant, whereas 260 (64%) of the 408 strains isolated from inpatients were resistant. There was thus a much higher incidence of resistant strains among the inpatients, although the outpatient figures tended to be rather higher than those previously reported (Forbes 1949, Rees et al. 1955). The outpatient strains were collected largely from chronic and subacute infections, many of which had already been treated unsuccessfully with penicillin. Moreover among the strains from inpatients many were isolated from severe fulminating infections admitted as urgency cases; these are really representative of strains from the general population rather than the hospital.

TABLE I—INCIDENCE OF PENICILLIN-RESISTANT STRAINS OF *Staph. aureus*

Period	No. in sample	No. penicillin-resistant
1950–51	600	259 (43%)
1953–54	300	172 (57%)
1955	550	312 (57%)

During this period 60 strains of *Staph. aureus* were isolated from material sent by general practitioners from a health centre, and 20 (33%) were penicillin-resistant. There is thus disturbing evidence that the incidence of penicillin-resistant strains among the general community is also increasing.

Appearance of Variants in Infections

The possibility of staphylococcal variants developing in vivo has received little attention. Barber and Whitehead (1949) isolated penicillin-sensitive and penicillin-resistant strains of *Staph. aureus* from 11 patients, but in 8 of these patients one or both of the pairs of organisms were untypable; it was concluded that the organisms were probably of different origins. Fairbrother et al. (1954) found that 6 of 13 mixed cultures gave the same phage pattern and probably originated from the same parent strain.

Further investigations were made. Colonies were studied in many cultures; in the great majority the colonies appeared identical on examination with the hand lens, and sensitivity tests of a representative sample definition. A similar state of affairs—many other examples could be given—is afforded by the section of endometrial curettings showing hyperplastic trophoblast, and the suspicion is chorionepithelioma. It is probably true to say that given equally suspicious histological appearances a preceding history of hydatidiform mole is more likely to lead to a diagnosis of malignancy than a history of abortion or normal pregnancy. Chorionepithelioma certainly does follow hydatidiform mole with disproportionate frequency, but this fact clearly cannot alter the histological characters in a section. If the histologist, knowing the clinical data, gives the graver prognosis he is doing so, once again, by virtue of his clinical not his histological, knowledge.

The piece of clinical information which, known in advance, exceeds all others in warping one's histological judgment is knowledge of the patient's age. Foreknowledge of the sex is unlikely to cause bias in the diagnosis of malignancy—though it may delay the pathologist's own realisation of the close similarity shown by carcinomas of prostate and of ovary—but foreknowledge of the age of the patient can certainly do so. Few will deny that a borderline lesion—for example, a squamous cell overgrowth of lip—is much more likely to be diagnosed as carcinoma at age 50 than at age 15. The reasoning behind this practice is that since cancer of the lip (or other organ) is much commoner at age 50 than at age 15, a histologically borderline lesion at age 50 probably is cancerous but at age 15 probably is not cancerous. This reasoning is false, and based on a quite wrong use of probabilities. Cancer of the lip certainly is rare at age 15, but so are borderline appearances. The critical question is how often borderline appearances indicate malignancy irrespective of age. Largely because of lack of definition of what we call the borderline picture, there is as yet no exact answer to this question. The proper position at present is that if histological appearances are regarded as indicative of malignancy at age 50, then unless we propose to adopt different criteria of malignancy for every age-group (and how many groups should there be?), the same histological appearances are equally indicative of malignancy at age 15 or at any other age. If the pathologist, already knowing the age of the patient, is confronted by a borderline lesion of this kind, we can be fairly sure that he is unlikely to make a diagnosis of malignancy in the patient of 15. The pathologist would like to believe that he is immune to such a biasing influence, but this in effect is what happens to a greater or lesser extent in every report where the age and other data are studied in advance.

The self-discipline involved in "blind" examining has the additional valuable humbling effect of making the histologist realise how helpless he can be without information about site, age, and other clinical details. Current practice is such that, on proffering a section to a colleague, we are hesitant even to ask whether he would like to have the clinical data before or after his examination. We shrink from the thought of being charged with sharp practice, and are fearful lest we make our colleague appear foolish in diagnosing, say, carcinoma of the prostate in a woman, or glioblastoma multiforme in a pelvic mass; though, such are the limitations of histological technique, and so non-specific many of our criteria, that such diagnoses, in so far as they are purely histological interpretations, might not be so foolish at all.

It is only by examining sections and making up our minds on the question of malignancy or non-malignancy on histological evidence alone that we can hope to appreciate exactly what the limitations of histological interpretation are; and gradually, by this appreciation, to define more sharply the criteria by which we diagnose malignancy. The value of this procedure depends ultimately, of course, on knowledge of the fate of the patients whose sections we have diagnosed, and for this we are mainly dependent on the good offices of our surgical and radiotherapeutic colleagues. Our current criteria of malignancy would probably be less hazy at the edges and our standards of diagnosis of malignancy in marginal cases much higher, if follow-up departments had been initiated by departments of pathology forty or fifty years ago.

It is true that the habit of always examining sections "blind" at the outset adds a few minutes to the time required for reporting. To that extent it is a time consuming practice. That it is a time-wasting practice is, I consider, emphatically not the case.

Everyday Diagnostic Problems

These observations have application to everyday diagnostic problems, particularly in view of the double purpose we achieve in giving a diagnosis of cancer—prognosis for the individual patient, and provision of data for later studies on cancer in general. In order to see briefly how these observations do apply, we may divide neoplasms into three main groups.

CASES WITH PREDICTABLE BEHAVIOUR

The largest group comprises the straightforward cases—cases where as already mentioned, evidence of atypical cell behaviour is abundant, and the correlation of this with metastasis and a lethal outcome is high. Such cases may be "straightforward," but even here we may recall that diagnosis is not absolute. Our diagnosis which is prognosis is based, and for pragmatic reasons must be based, on the assumption that, in the absence of treatment, the lesion represented by the abnormal tissue pattern will progress and shorten life. In making this assumption we are not taking into account the fact that cancers vary greatly in their behaviour, not only in different organs but within the same organ. The recurrence of a cancer, locally or as a metastasis, ten years or more after its initial removal is well known and not infrequent. There is no method meanwhile whereby we can distinguish the original cancer of this type from any other in the same histogenetic family. A cancer which kills in six months may look quite similar to one which does not recur for ten years or more. Highly cellular cancers do, it is true, tend to grow more rapidly than less cellular ones, but all pathologists and surgeons are familiar with instances where a relatively poorly cellular densely scirrhous cancer, exhibiting, one would think, defensive fibrosis at its maximum kills within a matter of months. Handicapped by this inability to distinguish cancers of different growth-rates, the pathologist can only give the same diagnosis, or prognosis, to each. The ways in which this variability of growth-rate and behaviour may influence cure-rates are obvious.

CASES WITH UNPREDICTABLE BEHAVIOUR

This group is formed of neoplasms whose histological characters give no dependable clues to future behaviour. Past experience has shown that, in this group, tissue with a benign future may look just the same as tissue with a malignant future. The pathologist can thus supply little more than the rather unhelpful information that such neoplasms sometimes metastasise; he cannot predict the probability of this with useful accuracy. This is not a large group but it is, by its very nature, an interesting group histologically.

This peculiar difficulty—the lack of correlation between tissue patterns and likelihood of metastasis—arises in some forms of thyroid neoplasia. The extreme example would be the so-called benign metastasising goitre—a lesion which, to judge from reported cases, must be exceedingly rare nowadays. Some thyroid growths which are recognisably neoplastic but not obviously carcinoma do metastasise and kill; other

TABLE V—DEVELOPMENT OF PENICILLINASE PRODUCING VARIANTS FROM PENICILLIN SENSITIVE STRAINS OF *Staph aureus*

Source of original culture	No tested	Incidence of penicillinase producing variants
Infected material	8	0
Variant colonies from resistant strains	8	2

A further series was then tested, and in this the organism used for the test was a penicillin sensitive variant of an originally penicillin-resistant strain (table IV) The original inoculum was a discrete colony from a culture of the penicillin sensitive variant At all stages of isolation this organism proved to be sensitive to $^1/_{16}$–$^1/_{32}$ unit per ml of penicillin and did not produce penicillinase From 2 of 8 strains tested penicillinase producing variants were isolated (table V), one was isolated after 8 subcultures, and the other after 15 subcultures in broth at 33°C In one case the penicillin-sensitive variant could not establish itself in the culture, but in the other it became predominant At all stages the identity of the organism was checked by phage typing

Discussion

The high incidence, in this hospital, of staphylococcal infections caused by penicillin-resistant strains agrees with the general pattern in this and other countries, and evidence was also obtained of an increasing incidence of penicillin-resistant strains among the general population The relatively high rate (37%) in outpatient infections was not altogether surprising, because many of these were chronic or subacute lesions which had not responded to outside treatment, usually with penicillin It is not difficult to explain the prevalence of penicillin-resistant strains in hospitals where cross-infection is easy, and the personnel are often carriers, but the ultimate origin of these strains is uncertain

The main explanations offered for the appearance of naturally occurring penicillin-resistant strains of *Staph aureus* are (1) the acquisition of adaptive enzymes through some metabolic adjustment, (2) the spontaneous appearance of resistant mutants, (3) the survival of rare resistant mutants during penicillin therapy, and (4) a combination of these factors

It is generally accepted that the naturally occurring penicillin-resistant strains differ from penicillin sensitive strains mainly, if not solely, by their capacity to produce penicillinase Moreover it has been established that penicillin sensitive strains of *Staph aureus*, rendered resistant to penicillin by serial transfer in increasing concentrations of penicillin, do not form penicillinase, and that this type of acquired resistance tends to be temporary Little information is available about the possible appearance of mutants or variants in infections, Barber and Whitehead (1949) held that penicillin sensitive and penicillin resistant strains isolated from the same patient tended to belong to different phage types and thus had separate origins

It is generally assumed that the penicillin resistant organisms are the variant or mutant strains (Barber and Burston 1955) This, however, may not be so Another possibility is that the *Staph aureus*, in its original form, was resistant to penicillin, and that the penicillin sensitive strains are the variants or mutants *Staph aureus* is tough and hardy, differing considerably from most other pathogenic organisms of the upper respiratory tract, it is the only member to produce penicillinase or readily to develop resistance to penicillin Although the main reservoir of this organism is now the human nares, this may not always have been the case Probably *Staph aureus* existed formerly under relatively wild conditions in which the capacity to produce penicillinase would be a distinct asset for the survival of the species Penicillinase has little or no value in the cell economy it appears to be mainly concerned with the survival of the organism When the *Staph aureus* became established in the human nares, penicillinase was no longer needed as a defence mechanism, and the capacity to produce this enzyme gradually declined, as an evolutionary process

When penicillin was first introduced as a therapeutic agent, a few penicillin resistant strains were reported by different observers, although previous contact with penicillin was unlikely These strains represented the survivors of the original wild *Staph aureus*, they possessed some essential factors of the enzyme system which is probably controlled by some primitive form of genetic system and is hereditary Subsequent contact with penicillin stimulated the production of penicillinase and eliminated many penicillin-sensitive strains, hence the high incidence of penicillin resistant strains in hospital

Support for this hypothesis is obtained from the results of the present investigation, which has shown that penicillin-resistant strains of *Staph aureus* readily produced penicillin sensitive variants in vitro, whereas penicillin sensitive strains appeared to produce penicillinase-forming variants rarely and only then in special circumstances in which possibly some of the enzyme system was still present in the original culture This is not altogether unexpected, because it is easier to lose an enzyme system than to gain one

It is therefore probable that, when both penicillin sensitive and penicillin-resistant strains of *Staph aureus*, with an identical phage pattern, are isolated from the same lesion, the original infecting organisms were either penicillinase-producing strains readily forming penicillin sensitive variants during the course of the infection, or penicillin sensitive staphylococci still possessing essential traces of the enzyme factor

An increase in the number of penicillin resistant infections throughout the general community seems inevitable, particularly if the practice of using penicillin indiscriminately for all forms of trivial infection continues A serious development is the great increase of severe infections caused by penicillin resistant strains of *Staph aureus*, for which the use of penicillin is not only valueless but also may be dangerous because it delays the introduction of an effective antibiotic A stricter control of penicillin therapy is urgently required

Summary

Of 550 strains of *Staph aureus* recently isolated from infections 312 (57%) were penicillin resistant Previous figures for the same hospital were 42% in 1950–51 and 57% in 1953–54 The incidence of penicillin resistant strains among outpatients was 37%

Penicillin sensitive and penicillin resistant *Staph aureus* with the same phage pattern were isolated from the same lesion on 11 different occasions, this suggests a common origin for these organisms

Penicillin sensitive variants were readily obtained from penicillinase producing strains of *Staph aureus* by growth at 44°C

Attempts to obtain penicillinase producing strains from naturally occurring penicillin sensitive strains of *Staph aureus* were unsuccessful Such variants were, however, produced by 2 of 8 apparently penicillin sensitive strains obtained by growing penicillinase producing organisms at 44°C

It is suggested that *Staph aureus* formerly led a wild existence in which it produced penicillinase, and that this function was later largely, but not entirely, lost by prolonged adaptation to the human nares

It is a pleasure to thank Dr M T Parker for the phage typing results and my colleagues in the department for technical assistance

References at foot of next column

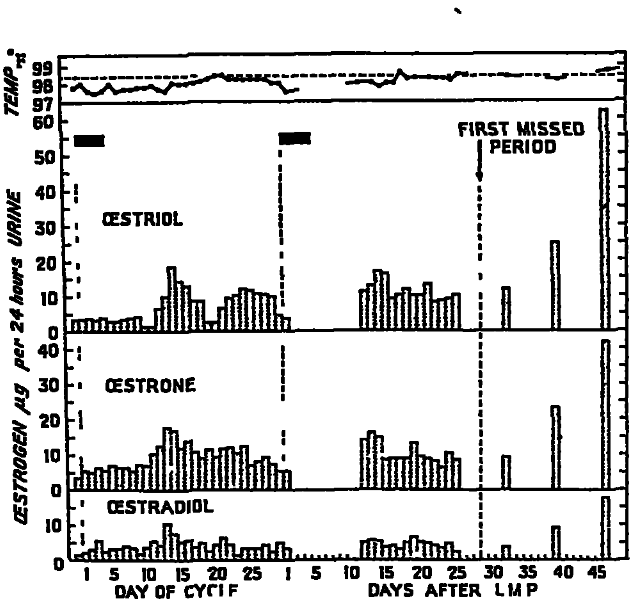

Fig 1

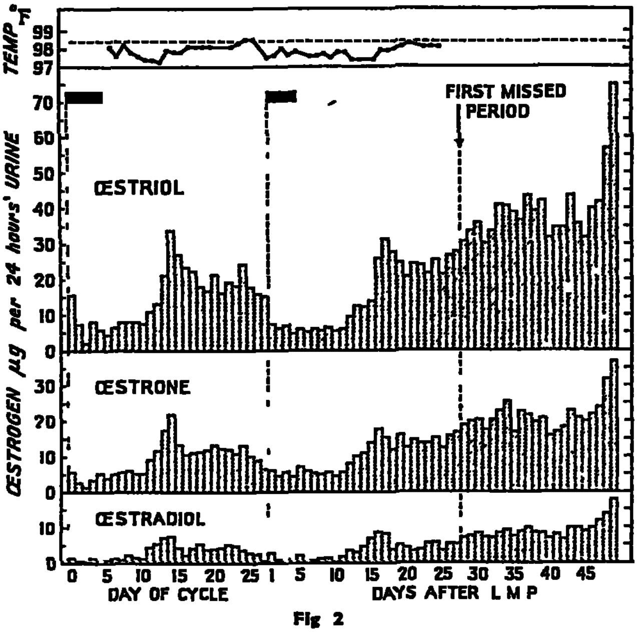

Fig 2

▪ Menstrual period

Fig 1 (subject 7) and fig 2 (subject 8) show the amounts of œstriol, œstrone, and œstradiol excreted per 24 hours and also the variations in basal temperature, during a normal cycle, the cycle in which pregnancy occurred and early pregnancy.

excreted rise from approximately 1 mg per day at 3 months (the smallest amount they could measure accurately) to 20 mg or more per day at 9 months. Later workers (Venning 1948, Clayton and Marrian 1950, Bradshaw and Jessop 1953) confirmed these findings and provided more information about the type and amounts of œstrogens excreted immediately preceding labour and delivery.

Recently a convenient, accurate, and apparently specific chemical method * for separately estimating œstriol, œstrone, and œstradiol-17β in human urine has been developed (Brown 1955a).

Material

Using this method, a study has been made of the daily urinary œstrogen excretion of a woman from before the beginning of a normal pregnancy, up to delivery, and then during the puerperium, lactation, and the recommencement of normal menstruation. The subject of this complete study was a woman (subject 8) who had already contributed urine for œstrogen determination throughout a menstrual cycle (Brown 1955b). A similar but less complete record from another woman previously studied (subject 7) is also included, together with the results obtained from two other women who were studied from the 16th weeks of their pregnancies until the onset of labour.

In all cases, the previous and present pregnancies were uncomplicated. Deliveries were spontaneous except in subject 10 for whom forceps were required. Lactation was established in all cases.

Subject 7, aged 33, para-2 (2 and 6 years ago). Delivery 276 days after last menstrual period (L M P). Baby's birth-weight 8 lb 12 oz (male).

Subject 8, aged 28, para-2 (2 and 3 years ago). Delivery 286 days after L M P. Baby's birth-weight 8 lb $3^1/_4$oz (male). Placental weight 1 lb 11 oz.

Subject 9, aged 27, para 1 (2 years ago). Delivery 289 days after L M P. Baby's birth-weight 8 lb 15 oz (female). Placental weight 1 lb 15 oz.

Subject 10, aged 29, para 0. Delivery 287 days after L M P. Baby's birth-weight 9 lb $3^1/_4$ oz (male). Placental weight 1 lb 12 oz.

Method

Complete 24-hour urine specimens were collected daily from subject 8 and approximately weekly from the others, until 2 weeks before the probable date of delivery, when daily collections were started. Subject 8 also collected all her urine during labour and delivery, 12-hourly for the next 4 days, and then daily until normal menstrual cycles were established.

The amounts of œstriol, œstrone, and œstradiol 17β in each specimen were determined by the method

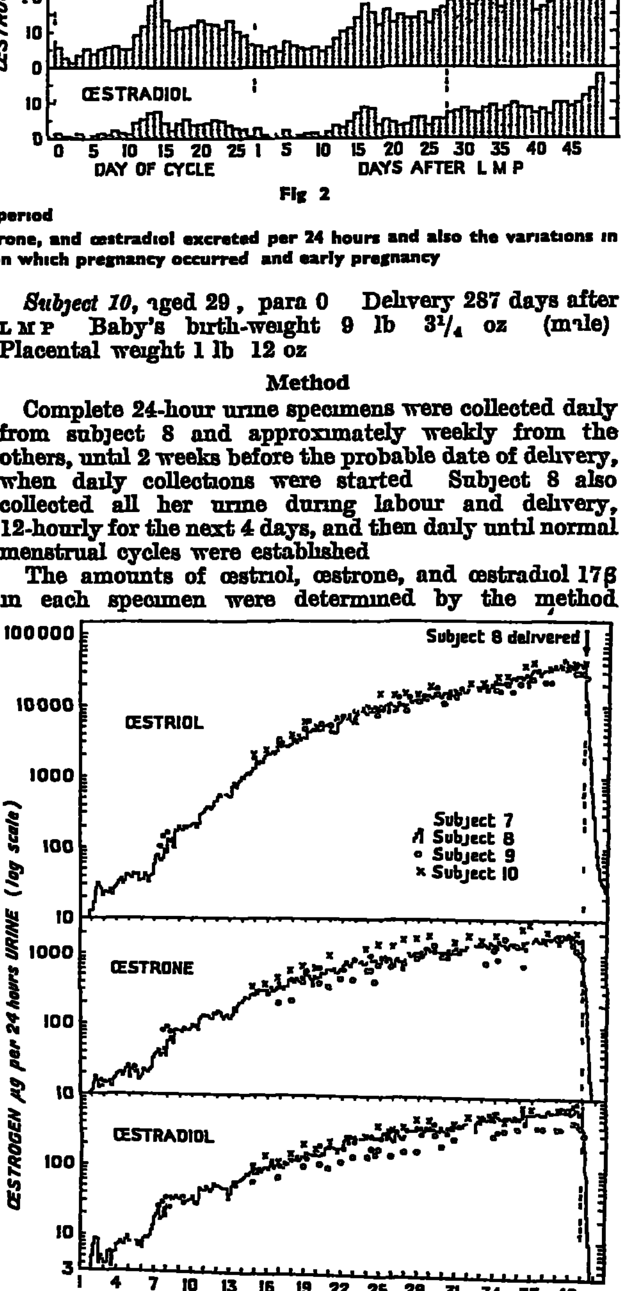

Fig 3—Excretion of œstriol, œstrone and œstradiol during pregnancy in the four subjects and during the puerperium in subject 8.

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* The two œstrogens 16 epi œstriol and the keto œstrogen recently found in human pregnancy urine (Marrian and Bauld 1955, Watson and Marrian 1955), are not determined by this method nor do they interfere with the results.

in this laboratory, where only 17 6% of 419 penicillin-sensitive strains isolated in 1954–55 from outpatients were not typable at the routine test dilution

Representatives of all four broad phage groups were found, but the number of strains isolated is too small for comparison of their frequency distribution with those found elsewhere

Where two or more strains were isolated from men living in the same locality the strains proved to be of different phage-patterns Although the total number of strains isolated was disappointingly low, the diversity of patterns found indicated that a fair sample of the pathogenic staphylococci present had been examined

Non pathogenic Staphylococci

110 strains of non-pathogenic (coagulase negative) staphylococci were examined for antibiotic sensitivity (table II)

87 of these strains conformed to the definition of *Staph saprophyticus* of Shaw et al (1951), all giving a positive Voges Proskauer reaction, 80 were white and 7 produced a yellow or golden pigment 6 (7%) of these strains were more resistant to penicillin than the control Oxford strain and produced penicillinase Using small inocula, they grew in concentrations of penicillin ranging from 0 075 to 0 6 unit per ml 2 of these strains were resistant also to chloramphenicol, growing in 125 µg per ml 1 strain grew in 2 mg per ml of streptomycin, in 250 µg per ml of chlortetracycline, and in 60 µg per ml of chloramphenicol In addition, 1 penicillin sensitive strain grew in 125 µg per ml of chlortetracycline

TABLE II—PENICILLIN SENSITIVITY OF COAGULASE NEGATIVE STAPHYLOCOCCI

Species	Pigment production	No of strains	Penicillin resistant	Penicillinase producers
Staph saprophyticus	White Yellow	80 7	6	6
Staph lactis	White Yellow	6 17	1 12	1 11
Total		110	19 (*17 3%*)	18

23 strains were classified as *Staph lactis* (Shaw et al 1951) since they fermented glucose but were acetoin negative 17 of these strains produced varying degrees of pigment, ranging from pale yellow to golden Their colonies were more opaque than those of *Staph aureus*, and confluent growth on agar displayed a metallic or iridescent sheen 12 such strains were penicillin resistant and 11 produced penicillinase None was resistant to any of the other antibiotics

Discussion

The low prevalence (19%) of nasal carriers of pathogenic staphylococci among the Wabaga, compared with that of 30–50% found in civilised communities, may be commented on It is tempting to correlate this finding with the small amount of clothing, ordinarily only a few leaves worn by these people, with the absence of communal bathing places (indeed, they wash but rarely), and with their relatively solitary manner of living in small groups These habits, together with their paucity of articles of material culture and the absence of indoor communal meeting places, suggest that they may have fewer opportunities to exchange their staphylococci than have urban communities It would be of some interest to compare their carrier rates with those in civilised but isolated agricultural communities

It is as yet undecided where these primitive people originated or for how long they have lived in the region, but it is likely that, until recently, they had been isolated for many centuries It is quite improbable that they could have acquired the variety of types of *Staph aureus* isolated from them by the limited contact that they have had with white people in recent years It is therefore of considerable interest that their strains of *Staph aureus* were similar to those found in civilised man The antiquity of man's association with the staphylococcus has been discussed elsewhere (Rountree 1955)

Finally, the presence of antibiotic resistant strains, although all were non pathogens, indicated that such strains can indeed occur naturally in the absence of antibiotics manufactured by man

Summary

23 of 120 people of the Wabag region of New Guinea were nasal carriers of *Staph aureus*

None of these strains was antibiotic resistant, but some non pathogenic staphylococci found in nasal swabs were resistant to antibiotics

Phage typing of the strains isolated from these primitive people showed that these were similar to those found in civilised man

This work was supported in part by the Australian National Health and Medical Research Council My thanks are due to members of the Nuffield Expedition, and in particular to Mr B Lockett who collected the swabs and to Prof N W G Macintosh Miss Judith Rheuben and Mr K Miller gave valuable laboratory assistance

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EFFECT OF VITAMIN-K DOSAGE ON PLASMA-BILIRUBIN LEVELS IN PREMATURE INFANTS

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THE effects of large and small doses of a water soluble vitamin K analogue ('Synkavit') on plasma bilirubin levels of premature babies on the fifth day of life are compared here

Investigation

In September, 1954, we began routine estimations of the fifth day plasma bilirubin levels in all surviving premature babies It was hoped that, by correlating these levels with the previous histories of the babies and their subsequent fate, criteria might be established for giving an exchange transfusion to prevent the development of kernicterus in premature babies showing no evidence of blood group incompatibility We were particularly interested in the number of infants attaining plasma bilirubin levels over 18 mg per 100 ml, which is perhaps the upper limit of safety as regards liability to develop kernicterus in hæmolytic disease of the newborn due to blood group incompatibility (Mollison and Cutbush 1951) The fifth day was chosen because it appeared that, preventive action would usually be required at that after this, measurable amounts of œstradiol-17β appeared in the urine and the levels of all three œstrogens rapidly increased and decreased in the manner characteristic of ovulation (Brown 1955b) However, the œstrogen levels did not rise again to a definite luteal maximum and menstrual bleeding began 8 days after the "ovulation" peak That ovulation followed by a shortened luteal phase had occurred was confirmed by morning basal temperature and urinary pregnanediol measurements † An ovulation peak followed by a somewhat shortened luteal phase of 10 days was seen during the next menstrual cycle, and during the third menstrual cycle there was a normal luteal maximum and the œstrogen levels throughout were almost identical with those during the menstrual cycle preceding pregnancy

Discussion

The results reported here are similar to those obtained by other workers, but they give a more detailed picture of some of the changes in urinary œstrogen levels during pregnancy, the puerperium, and lactation

Œstrogen Level During Pregnancy

The levels found during the menstrual cycle in which pregnancy occurred were very similar to those found during the preceding cycle up to the middle of the luteal phase, after which time they continued to rise slowly instead of falling as they do before menstruation At about 7 weeks after the last menstrual period, the urinary œstrogen levels began to increase rapidly, being soon outside the range found during a menstrual cycle, and thereafter they followed a smooth exponential curve which flattened somewhat towards the end of pregnancy

The abrupt change in the œstrogen excretion curve at about 7 weeks might well be due to the changeover from the corpus luteum to the placenta as the major producer of œstrogens This is earlier than the time suggested for this changeover by Venning (1948) who thought that it took place during the 2nd to 3rd months However, many workers have noted that the removal of the corpus luteum, even during the first month of pregnancy, does not necessarily cause abortion Koff and Tulsky (1953) concluded from this evidence, and from their own studies on eight women in whom they estimated urinary pregnanediol before and after removing the corpus luteum, that by the 35th day the placenta by itself secretes enough progesterone to maintain pregnancy This should apply equally to the œstrogens, and it would therefore seem that the rapid increase in œstrogen excretion observed at 7 weeks is caused mainly by placental production, and that even before this time the placenta is contributing increasingly to the œstrogen levels

Œstrogen Levels During and After Labour

My findings during late pregnancy and at the onset of labour are very similar to those reported by other workers, and support the conclusions of Bradshaw and Jessop (1953) that there is no correlation between œstrogen excretion and the onset of labour The considerable day-to-day variations in the excretion of œstrogens in the same woman and the variations in secretion between different women noted by Bradshaw and Jessop were also observed in my series These differences are masked in the logarithmic scale used in fig 3 but are shown more clearly in the table

The rapid decrease in the urinary œstrogen levels following delivery was consistent with sudden removal of the placental source and a continuous metabolism and renal excretion of the remaining œstrogens Œstriol was eliminated more slowly than œstrone and œstradiol-17β—an interesting difference observed following single intramuscular injections of these three œstrogens

Œstrogen Levels During Lactation and the Puerperium

The œstrogen levels during lactation were low and were within the range normally found during the early part of a menstrual cycle After lactation ceased, the œstrogen levels began to increase slowly until the regular rise and fall found during a menstrual cycle was observed It may be significant that, after the period of lactation amenorrhœa, slight menstrual bleeding occurred when the œstriol and œstrone levels were each approximately 7 µg per 24 hours Such levels, when maintained for a period, might represent the minimum amounts of œstrogens required for stimulating endometrial growth, and yet, being within the range normally found at menstruation (Brown 1955b), they might make the stimulated endometrium unstable and precipitate menstruation

During the first menstrual periods after delivery, ovulation took place, but during the first two periods the luteal phases were abnormally short (8 and 10 days) This is contrary to the belief that the luteal phase always lasts about 14 days It is possible to envisage a luteal phase so evanescent that it cannot be detected By all the usual criteria such a menstrual cycle would be considered anovular, and it may well be that brevity of the luteal phase is the explanation of some of the apparently anovular cycles following delivery The third menstrual cycle appeared to be normal in all respects, and during this cycle the urinary œstrogen levels were almost the same as those found during the menstrual cycle preceding pregnancy This is a further example of the constancy in the pattern and amounts of œstrogens excreted during different menstrual cycles

Summary

The urinary excretion of œstriol, œstrone, and œstradiol-17β during conception, pregnancy, the puerperium, lactation, and the recommencement of menstruation has been measured in women A new chemical method of estimation was employed The results are discussed

I wish to thank Prof G F Marrian, F.R.S, and Prof R J Kellar, for their interest in this work. I am also grateful to the wives of colleagues who contributed the urine specimens, and especially to the one who made possible the complete study over a period of 17 months I am also indebted to Mr H A F Blair and Miss Janet Mackie for their skilled technical assistance

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"General education is bound to differ according to the different lines of specialisation being followed It is no good whatever thinking that by laying on a course in literature and a course in current affairs it is possible to give both your scientists and your classics the general education which they need in addition to their special studies What you must try to do is to make them see their own line of study as one amongst many, and make them see where it stands in the general fabric of human knowledge You must persuade or cajole or force your scientists to write English coherently You must make them see that there are other approaches to reality than that of quantity and experiment, and get into their heads some appreciation of literary and artistic and moral values You must make them see how science has affected human life and give them enough history to enable them to do this general education in its profoundest sense is an essential part of specialist education"—H D P LEE, M.A., headmaster, Winchester College Report of Home Universities Conference, 1955 p 19 infants (Billing et al 1954) The action of large doses of vitamin K analogues may be to increase hæmolysis (Allison 1955), or to reduce further the liver's capacity to handle bilirubin

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† The pregnanediol measurements were kindly performed by Dr A Klopper using the method of Klopper, Michie, and Brown (1955)

Summary

Premature babies given a total of 30 mg of synkavit intramuscularly after birth showed a significantly greater hyperbilirubinæmia on the fifth day of life than those given a single injection of 1 mg

It is suggested that routine use of the smaller dose would reduce the incidence of kernicterus of prematurity

We wish to thank Dr B E Schlesinger for permission to publish Miss D Walker for the bilirubin estimations, and Sister E Edwards for her cooperation

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BONE-MARROW IN ANKYLOSING SPONDYLITIS *

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Patients with ankylosing spondylitis may be unusually susceptible to the development of leukæmia as a long term effect after X-ray treatment to the spine (Court Brown and Abbatt 1955, van Swaay 1955), but we have not been able to find any published description of the bone marrow in ankylosing spondylitis either before or after X ray treatment We therefore report here the bone marrow findings in 18 patients before treatment and 10 patients after one or more courses of irradiation of the spine

Methods

About 0 25 c cm of bone-marrow was aspirated with a Turkel needle from the manubrium sterni, and smears were made directly on to clean glass slides in the usual way and stained with Leishman's stain Differential counts of 1000 cells were made on each specimen of bone marrow

Material and Results

28 patients were diagnosed as having ankylosing spondylitis, with typical clinical criteria and radiological findings, and all responded well to X-ray therapy Their hæmoglobin was within normal limits except in case 7, who had mild anæmia (Hb 10 2 g per 100 ml) The clinical details, bone marrow findings, and previous radiotherapy are shown in tables I and II The erythrocyte sedimentation rate (E S R) (Wintrobe correction to 45% hæmatocrit) was also included when this investigation had been made The cellularity of the bone marrow smears, judged from the cell density of the stained specimens, was normal in 17 cases and hypercellular in 11 This increase in cellularity affected all the formed elements of the bone marrow, and the myeloid and erythroid cells both showed normal maturation Lymphocytes and megakaryocytes were present in normal proportions, and the myeloid/erythroid ratios were within normal limits The only abnormalities detected were plasmacytosis and eosinophilia in some of the bone marrow smears

TABLE I—BONE MARROW FINDINGS IN ANKYLOSING SPONDYLITIS NOT TREATED BY IRRADIATION

Case no	Age (yr)	Sex	Yr since 1st symptom	E S R	Cellularity	Eosinophils (%)	Plasma cells (%)	Myeloid/erythroid ratio
1	27	M	3		H	6 1	0 9	8 1/1
2	38	M	5		C	14 6	1 0	3 1/1
3	49	M	2	35	C	3 5	0 8	5 1/1
4	52	M	5	29	H	3 3	0 2	3 2/1
5	24	M	3/4	18	C	3 8	1 5	2 4/1
6	27	M	4	1	C	2 3	1 1	4 1/1
7	44	M	3	32	H	1 0	2 1	2 6/1
8	47	M	20	29	C	2 5	0 7	2 4/1
9	30	F	4	7	C	3 0	1 4	4 2/1
10	30	M	1/2	4	C	2 1	1 3	4 9/1
11	27	M	4	29	H	4 0	1 7	5 4/1
12	42	M	14	37	C	12 7	3 8	3 5/1
13	38	M	2	21	H	5 1	2 7	2 0/1
14	59	M	7	39	C	3 7	0 9	4 7/1
15	38	M	14	24	C	3 6	2 2	3 4/1
16	61	M	5	20	C	1 5	3 5	5 0/1
17	42	M	15	25	C	8 4	1 6	4 6/1
18	47	M	4	33	H	2 1	3 1	2 8/1

The results of the bone marrow findings are summarised in table III, which shows that 10 patients had an increase in plasma cells and 4 had an increase in eosinophils in the bone marrow

TABLE III—SUMMARY OF BONE MARROW FINDINGS

Group of patients	Plasma cells		Eosinophil	
	Normal	Increased	Normal	Increased
With previous X ray therapy (table II)	6	4	9	1
With no previous X ray therapy (table I)	12	6	15	3
Total	18	10	24	4

Discussion

Marrow hypercellularity was found in 5 of the 10 patients who had received previous X ray treatment and in 6 out of 18 patients who had had no previous irradiation, and thus bears no relationship to previous radio

TABLE II—BONE-MARROW FINDINGS IN ANKYLOSING SPONDYLITIS TREATED BY IRRADIATION

Case no	Age (yr)	Sex	Yr since 1st symptom	Previous X ray treatment No of courses and dates skin dose given × no of fields over spine and sacro iliac joints (220 kV)	E S R	Cellularity	Eosinophils (%)	Plasma cells (%)	Myeloid/erythroid ratio
19	47	M	20	1 1500r × 4 marrow at end of treatment		C	1 7	2 2	3 7/1
20	31	M	11	5 1944–51, last 3 yr ago 1800r × 2 900r 600r 300r × 2 (165 kV)	14	H	6 6	0 5	1 4/1
21	30	M	5	2 1951–53 last 14/12 ago 1400r × 4 1000r × 1		C	3 5	2 0	4 1/1
22	41	M	1/2	1, 10/12 ago 1500r × 4	10	H	12 9	2 3	3 1/1
23	36	M	12	1 in South Africa 11 yr ago	18	H	3 0	1 1	6 6/1
24	27	M	2	1 4/12 ago 1500r × 3		C	2 6	0 3	3 0/1
25	41	M	7	3 1946–53 last [illegible]/12 ago 2000r × 2 2000r × 1 1000r × 1		H	1 8	3 1	3 4/1
26	24	M	3/4	1 4 yr ago 1800r × 2	25	C	2 0	0 9	1 1/1
27	30	M	7	3 1949–52 last 10/12 ago 1500r × 3 1500r × 1 1500r × 1		C	2 4	1 2	4 0/1
28	35	M	7	2 1952–54 last 9/12 ago 2000r × 3 1200r × 2		H	4 0	1 5	4 0/1

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proposed by Morton and Wylie (1951), was shown by O'Mullane (1954) to be theoretically safe in the presence of passive regurgitation We induce anæsthesia with the patient lying flat on a tipping-table If the patient vomits she can be tipped into the Trendelenburg position Should regurgitation occur after the patient is completely paralysed, a similar position can be adopted Provided that the patient is completely paralysed and apnœic any regurgitated fluid will tend to drain out of the mouth, and since respiration has stopped such fluid will not be sucked into the chest The use of a laryngoscope and an efficient suction apparatus enables the pharynx to be cleared rapidly, and intubation is then performed

The equipment required is the standard anæsthetic equipment with a reliable mechanical sucker The labour-ward bed must be capable of being rapidly tipped into the head down position It is vital that, before anæsthesia is induced, the anæsthetist should check the machine, the laryngoscope, the suction apparatus, the inflatable cuff of the endotracheal tube, and the tipping mechanism of the table

Atropine sulphate gr $^1/_{100}$ (0 65 mg) is given intramuscularly twenty minutes before the operation is started In emergency it can be given intravenously

A Gordh needle is inserted into a vein on the dorsum of the hand and strapped into position, this is easily done since the veins are usually prominent owing to increased circulating blood-volume at term By means of this needle further doses of muscle relaxant can be quickly given should any difficulty in intubation arise Anæsthesia is induced with an oxygen rich mixture of cyclopropane, nitrous oxide, and oxygen, by a closed circuit with an intentional leak and with the absorber cut out As soon as the patient is unconscious succinylcholine chloride is given (5 mg per stone) through the Gordh needle At the onset of paralysis the lungs are gently inflated, adding extra oxygen to the gaseous mixture It is important to inflate gently, once in our experience vigorous inflation caused regurgitation of fluid into the pharynx O'Mullane (1954) has shown that any fluid present in the œsophagus after the crico pharyngeus muscle has been paralysed can, by vigorous movement of the lungs, be massaged from the œsophagus into the pharynx With the onset of full relaxation, laryngoscopy is performed and intubation carried out with a cuffed endotracheal tube The cuff of the tube is inflated to make a tight fit in the trachea, and artificial respiration is applied until spontaneous respiration has re established itself At this point gallamine triethiodide (5 mg per stone) is administered, and respiration is assisted as necessary, the carbon dioxide absorber being brought into the circuit

A light plane of anæsthesia is maintained with cyclo propane, nitrous oxide, and oxygen Additional doses of gallamine triethiodide may be required At the end of the operation the endotracheal tube is removed when the patient is becoming conscious, and tracheo bronchial toilet is performed On no account must the anæsthetist leave the patient until he is satisfied that she is fully awake and that her general condition is satisfactory

Discussion

To the anæsthetist a woman in labour presents problems similar to those in cases of intestinal obstruction All general-anæsthetic techniques in the latter cases are based on the use of a cuffed endotracheal tube to ensure a free airway, and it seems reasonable to use the same well-tried method in obstetric cases The advantages of using a tube are that once it is in position the anæsthetist has complete control of the airway for the remainder of the administration, that respiration can be easily assisted if required, and, most important of all, that gastric contents are prevented from reaching the trachea, bronchi, and lungs Further, as Mackenzie et al (1954) have shown, by this method a given plane of anæsthesia can be obtained with a smaller quantity of anæsthetic agent than otherwise In obstetric anæsthesia this is important

The mechanism whereby the fœtus obtains oxygen across the placenta is finely balanced, and any slight sub-oxygenation in the mother rapidly affects the fœtus At term, even under optimum conditions, mild anoxia may be present in the fœtus Any additional anoxia brought about by anæsthetic difficulties will tip the scale against the survival of the fœtus By the use of a cuffed endotracheal tube, adequate oxygenation can be provided at all times, and should fluid and debris appear in the pharynx the bronchial tree is protected

The danger of the technique described here arises during the induction of anæsthesia and before intubation By experienced, efficient, and gentle use of the laryngoscope and sucker, and by keeping a needle in one of the patient's veins, any difficulties that may arise can be overcome In a series of 100 cases (see table) trouble was experienced twice

100 CONSECUTIVE HOSPITAL CASES

Operation	No of cases
Mid-cavity forceps application	74
Cæsarean section	16
Antepartum hæmorrhage	3
Breach delivery	3
Eclampsia	1
Prolapse of cord	1
Extraction of dead fœtus	1
Delivery of anencephalic fœtus	1
Total	100

In the 1st of these 2 cases over vigorous inflation of the lungs in a paralysed patient squeezed fluid from the œsophagus into the pharynx This untoward event was treated by laryngoscopy and suction There were no ill results

In the 2nd case intubation proved difficult, and a further dose of muscle relaxant was necessary This case shows the value of the Gordh needle as a means of giving intravenous injections quickly

Criticism may be levelled against the introduction of a comparatively complicated technique But, like others (Gilliatt 1949, Jeffcoate 1953), we are certain that there is no place in the labour ward for the inexperienced anæsthetist

Conclusion

A cuffed endotracheal tube should be used in all cases where general anæsthesia is required for obstetric surgery

We wish to thank Dr G Edwards for encouragement and advice

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TABLE I—RESULTS OF TREATING 1474 PATIENTS WITH ORAL STREPTOMYCIN

Age (yr)	No of cases	No of cases cured with			
		1 course	2 courses	2 courses	
				plus chloram phenicol	plus oxy tetra cycline
0–1	155	122	24	4	5
1–2	340	282	47	1	10
2–3	272	229	37	1	5
3–4	166	145	19	0	2
4–5	135	121	11	0	3
5–6	70	62	6	1	1
	1138	961 (84 4%)	144 (12 6%)	7	26
Over 6	336	306 (91%)	25 (7 5%)	1	4
Total	1474	1267 (86%)	169 (11 5%)	8 (0 5%)	30 (2 0%)

4 patients (aged 5 weeks, 3 months, and 34 and 75 years) died within twenty-four hours of admission, and none of these received streptomycin Dysentery was a contributory cause of death in 3 other cases, but in only 1 case was streptomycin used

Streptomycin was given for five days in an unflavoured aqueous solution in equally divided doses at six-hourly intervals, patients younger than 10 years received 1 g daily and patients older than 10, 2 g daily Treatment was started as soon as the stool was known to be bacteriologically positive, usually within thirty-six hours of the patient's admission If the dysentery was severe or the diagnosis was almost certain on epidemiological grounds, treatment was started soon after admission and at least one specimen of fæces had been collected

During the acute phase of the illness, the patient was given a fluid and light diet which was regulated according to age, general condition, and severity of the illness, and this was followed by a low residue diet until discharge from hospital Carriers received a normal diet If more than one course of streptomycin (or any other antibiotic) was required, vitamin B_1 was added to the diet during the additional course and for a few days afterwards In only 12 cases was intravenous fluid replacement necessary

After treatment, the patients were kept under surveillance for a short period and were not discharged unless at least three consecutive bacteriological examinations of fæces in the week after treatment had proved negative For patients returning to other hospitals, institutions, or nurseries, the minimum requirement was six consecutive negative examinations

Results

Although no direct comparison is possible, table I shows that the results in the under 6 age-group, which accounts for more than three quarters of the total number of cases, are an improvement on the previous sulphonamide series Of the 1138 cases in this group, 961 (84 4%) were cured by one five-day course of streptomycin, whereas comparable success was obtained only after two seven-day courses of sulphonamide, when 84% of 170 cases were cured

Table II shows how the results varied throughout the five year period, the proportion of cures after one course of streptomycin dropped by about 10% in both age groups during this period, but the results in 1953–54 were still better than those of the sulphonamide treated series Furthermore in 1953–54 a second course continued to cure most of the cases which were not bacteriologically cured after one course This does not suggest that bacterial resistance is as formidable a problem as might be expected, indeed, the comparatively poor results in the under-6 age group in 1953–54 may well be due to the fact that a larger number of cases were dealt with in a shorter period (one year), leading to overcrowding of the dysentery wards and greater danger of reinfection In a few instances, after apparent cure there was direct evidence of reinfection, patients had exacerbation of symptoms, shigellæ reappeared in the stools, and, more positive proof, strains of the organism were isolated which had not been present previously

Effects of Treatment on Different Types of Shigellæ

Clinical distinction of the illnesses produced by the several types of shigellæ is well-nigh impossible, but, in this country at any rate, the more severe infections with greater constitutional upset and often meningism, are likely to be produced by *Sh flexneri* The clinical response to oral streptomycin was usually rapid irrespective of the type of organism, and indeed the results from the bacteriological viewpoint are equally satisfactory, as table III shows

TABLE II—VARIATION IN RESULTS OF TREATMENT DURING THE FIVE YEAR PERIOD 1949–54

Period	Age (yr)	No of cases	No of cases cured by streptomycin with		
			1 course	2 courses	2 courses plus C or O
1949–51 (2 yr)	Under 6	418	371 (89%)	42 (10%)	5 (1%)
	Over 6	132	128 (97%)	3 (3%)	1 (1%)
1951–53 (2 yr)	Under 6	243	209 (86%)	28 (11 5%)	6 (2 5%)
	Over 6	60	53 (89%)	7 (11%)	0
1953–54 (1 yr)	Under 6	477	381 (80%)	74 (15 5%)	22 (4 5%)
	Over 6	144	125 (87%)	15 (10%)	4 (3%)
Total		1474	1267 (86%)	169 (11 5%)	38 (2 5%)

C = chloramphenicol O = Oxytetracycline

In the first two year period (1949–51), there were few *Sh flexneri* infections (5%) Thereafter there was

TABLE III—EFFECT OF ORAL STREPTOMYCIN TREATMENT IN DIFFERENT TYPES OF INFECTION

Age (yr)	Period	*Sh sonnei* infections				*Sh flexneri* infections				Total
		No of cases	No of cases cured with			No of cases	No of cases cured with			
			1 course	2 courses	2 courses plus C or O		1 course	2 courses	2 courses plus C or O	
Under 6	1949–51	399	355	40	4	19	16	2	1	418
	1951–53	180	158	17	5	63	51	11	1	243
	1953–54	328	257	52	19	149	124	22	3	477
	Total	907	770 (85%)	109 (12%)	28 (3%)	231	191 (83%)	35 (15%)	5 (2%)	1138
Over 6	1949–51	129	126	2	1	3	2	1	0	132
	1951–53	46	40	6	0	14	13	1	0	60
	1953–54	95	81	10	4	49	44	5	0	144
	Total	270	247 (91%)	18 (7%)	5 (2%)	66	59 (89%)	7 (11%)		336
Grand total		1177	1017 (86%)	127 (11%)	33 (3%)	297	250 (84%)	42 (14%)	5 (2%)	1474

C = chloramphenicol O = oxytetracycline

made in physiological saline solution Racks were held in a 37°C water bath so that the columns of reaction mixtures were about two thirds submerged Readings were made at intervals against the black background of an agglutination viewing-box A hand lens (× 5) was used to extend the range of particle visibility

Recording of Results

An arbitrary choice of symbols for recording degrees of flocculation is unavoidable For our detailed records we used a range of plus signs from ++++, indicating complete flocculation with sedimentation to the bottom of the tube, down to ±, indicating fine particulation only just detectable with a hand lens In addition, various degrees of opalescence were noted For the sake of clarity records presented in tables I–III have been simplified, and the symbols have the following meanings

+++	Complete or almost complete flocculation
++	Floccules uniformly distributed and easily visible to naked eye
+	Fine particles visible with hand lens—includes particulation ranging from that on verge of naked eye visibility to that only just visible with lens
op	Opalescence of any degree greater than that of the antigen saline control mixture
–	No sign of any reaction

It should be emphasised that the flocculation is just as easy to read as a routine agglutination test with suspensions of bacteria, and that the adoption of a titration end point analogous with " standard agglutination " would present no difficulty

To avoid possible confusion dilutions of antigens and antisera shown in the tables represent the initial dilutions before mixing Actual dilutions in the reaction mixture were of course twofold higher

Experimental Results

The design and scope of the experiments recorded were necessarily conditioned by the rigorously limited capacity of our small laboratory to produce antigens The production of a few ml of a single virus type antigen utilises our full resources for a fortnight, and, as nothing is yet known about the effects of storage, it was considered unwise to accumulate batches for experiments on a more adequate scale

Cross test with Brunhilde and Lansing

The first flocculation of poliomyelitis virus took place in the experiment recorded in table I The speed of visible flocculation of Brunhilde antigen with the homologous serum at 1 in 5 dilution raised, at the time, serious doubt of its validity as a specific reaction, but it is now known to reflect the phenomenon of optimal proportions precipitation (Dean and Webb 1926) The Lansing reagents did not particulate, though the development of opalescence markedly in excess of that shown by antigen control mixtures was unequivocal There are two obvious reasons for this weak Lansing reaction Reference to the rabbit immunisation schedule shows that the amounts of Lansing virus inoculated were only a fraction of the amounts of Brunhilde and Leon viruses given, later experience has shown that such a small antigenic stimulus was unlikely to provoke a satisfactory antibody response Even with a very potent antiserum it is unlikely that the Lansing antigen would have flocculated Results of infectivity titrations on the two virus concentrates were

Brunhilde antigen TCD 50/ml = $10^{-7\cdot2}$
Lansing " = $10^{-4\cdot8}$

On the basis of tissue culture infectivity, therefore, the Brunhilde antigen was 250 times more concentrated than the Lansing antigen As all efforts to improve the yield of Lansing virus from HeLa cell cultures failed, it was decided to abandon this strain temporarily and to continue the investigation with Brunhilde and Leon viruses

TABLE I—CROSS TESTS WITH BRUNHILDE AND LANSING REAGENTS

Antigens	Period of incubation (37°C)	Brun serum 1/1	Brun serum 1/5	Lans serum 1/1	Lans serum 1/5	Antigen controls
Brunhilde	5 min	op	++	–	–	–
	2½ hr	++	+++	–	–	–
Lansing	5 min	–	–	op	op	–
	2½ hr	–	–	op	op	–
Serum controls		–	–	–	–	–

For explanation of symbols see text

Chess board Titration of Brunhilde Reagents

The titration recorded in table II was made to study the effects of dilution of reagents and the period of incubation of reaction mixtures Reactivity of the serum at dilutions greater than 1 in 40 was not expected, so the dilution range used was too limited to give the serum end-points The reaction showed the characteristics of precipitation such as occurs in many serum - antiserum systems rather than of bacterial agglutination It is clear that antigen concentration was the dominant and critical factor, beyond 1 in 8 dilution no trace even of opalescence was discernible, and for practical tests only the antigen undiluted or at 1 in 2 dilution would have been satisfactory The progression of the reaction throughout the four-hour period of observation emphasises the importance of the relative proportions of antigen and antibody Optimal-proportions precipitation was evident in each antigen dilution row with well marked inhibition in the region of antibody excess Indeed it is apparent that, even with a good antigen, flocculation may be absent with very potent sera unless the latter are diluted sufficiently to extend beyond the zone of inhibition The occurrence of flocculation through a wide range of serum dilutions indicates the possibility of comparative serum titrations by means of the reaction

TABLE II—CHESS BOARD TITRATION OF BRUNHILDE REAGENTS

Time of incubation at 37°C	Brunhilde antigen dilution	Brunhilde serum dilutions 1/1	1/5	1/10	1/20	1/40	Antigen controls
½ hr	1/1	op	+	+	+	+	–
	1/2	op	op	op	+	+	–
	1/4	–	–	–	–	–	–
	1/8	–	–	–	–	–	–
	1/16	–	–	–	–	–	–
2½ hr	1/1	+	+++	+++	+++	+++	–
	1/2	op	++	+++	++	++	–
	1/4	op	op	op	+	+	–
	1/8	op	op	op	op	+	–
	1/16	–	–	–	–	–	–
4 hr	1/1	+	+++	+++	+++	+++	–
	1/2	op	+++	+++	+++	+++	–
	1/4	op	op	++	++	++	–
	1/8	op	op	op	+	+	–
	1/16	–	–	–	–	–	–
	Serum controls	–	–	–	–	–	–

Cross-tests of Brunhilde and Leon by Chess board Titrations

Preliminary experiments with a Leon virus antigen showed that it was flocculated by various dilutions of the Leon antiserum and not at all by Brunhilde serum An extensive cross test using chess board titrations was therefore made

The results of the final reading after 4 hours' incubation at 37°C are presented in table III They afford a clear demonstration of the type specificity of the flocculation reaction The occurrence of opalescence, however, in the most concentrated cross type mixtures is interesting It may be due to contaminant antigenic material derived

RAPID TEST FOR HEPATOLENTICULAR DEGENERATION

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THE definitive diagnosis of hepatolenticular degeneration (Wilson's disease) rests upon the demonstration of the following specific biochemical or metabolic abnormalities: increased urinary excretion of copper (Cumings 1951) and amino-acids (Uzman and Denny-Brown 1948), a low serum-copper level (Cumings et al. 1955), a low serum cæruloplasmin level (Scheinberg and Gitlin 1952), and low serum-copper oxidase activity (Bearn and Kunkel 1952).

These determinations are so tedious, exacting, or costly that they are generally made only in special neurological or research centres and even then are usually reserved for cases where clinical suspicion is high. As a result the correct diagnosis of hepatolenticular degeneration is often deferred for many months, until the inexorable progression of signs and symptoms makes the diagnosis clear on clinical grounds alone. This is far too late for optimal results of therapy, however, since copper-complexing agents cannot be expected to reverse well established functional deficits, although they may arrest or significantly retard the progression of this disease.

Of the several characteristic biochemical findings in hepatolenticular degeneration the most consistently abnormal result, with the least overlap into the range of normal values, is the considerable decrease of serum-copper-oxidase activity (Bearn and Kunkel 1952). Apart from hepatolenticular degeneration, only an occasional case of frank nephrosis is associated with abnormally low serum-copper-oxidase activity (Markowitz et al. 1955). A simple, rapid, and accurate colorimetric estimation of this enzymatic activity, requiring only standard laboratory equipment, is briefly outlined here.

Reagents

Commercial paraphenylene diamine is dissolved in acetone and converted to a salt by adding concentrated hydrochloric acid drop by drop until no further precipitate forms. The precipitate is collected on filter paper, washed with either dry acetone or ether, and dried in a desiccator. A 0.5% stock solution of paraphenylene diamine hydrochloride is prepared for use in the test and should be stored in a stoppered container in the cold (4°C). An increasing brown colour of the stock solution indicates deterioration, but the stock solution can be safely stored for about a week under the conditions described.

0.1 N acetate buffer (pH 6.0) is prepared by adding 10 ml. of 0.1 N acetic acid to 200 ml. of 0.1 N sodium acetate and is stored in the cold (4°C).

A 0.1% solution of sodium azide is prepared as a stock solution to stop the enzymatic reaction at the desired time. This solution requires no special storage and keeps indefinitely.

A 3% solution of sodium chloride is used as the diluent of the reaction mixture for measuring colour density, to prevent the turbidity attendant on dilution of serum with water.

Fresh serum, free from hæmolysis and turbidity, is preferable for accurate results; but a minimal degree of hæmolysis or slight turbidity may be tolerated, and the serum paraphenylene diamine-oxidase activity remains intact for at least two weeks at 4°C.

Method

All the determinations are made in duplicate. The reagents are warmed to room-temperature (25–27°C) before use.

0.1 ml. of serum is transferred accurately into the bottom of a 15-ml. capacity test-tube with a blood pipette. 1 ml. of the 0.5% paraphenylene diamine stock solution and 2 ml. of 0.1 N acetate buffer are added. A control for non-enzymatic oxidation is prepared at the same time in the very same way (including 0.1 ml. of serum) but with the further addition of 1 ml. of the 0.1% sodium-azide solution to inhibit enzymatic activity. The test-tubes are shaken for a moment to mix the reagents and immersed in a water bath at 37°C. After an hour's incubation the test-tubes are removed, and 1 ml. of 0.1% sodium azide is added immediately to stop enzymatic activity, with a brief shaking to mix the reagents.

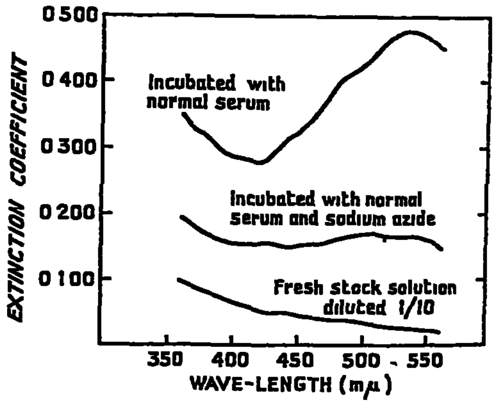

Fig. 1—Absorption spectra of solutions of paraphenylene diamine.

The colour density should be estimated within the first hour or two after completion of the incubation, because non-enzymatic oxidation of the substrate leads to gradual darkening of the solution. The reaction mixture is diluted to 10.1 ml., for quantitative estimation of colour density, by the addition of 6 ml. of 3% NaCl stock solution. The saline diluted solutions are analysed at 530 mμ (see fig. 1 for absorption spectrum) in cuvettes of 10 mm. optical path, with the sodium-azide inhibited control set at zero extinction.

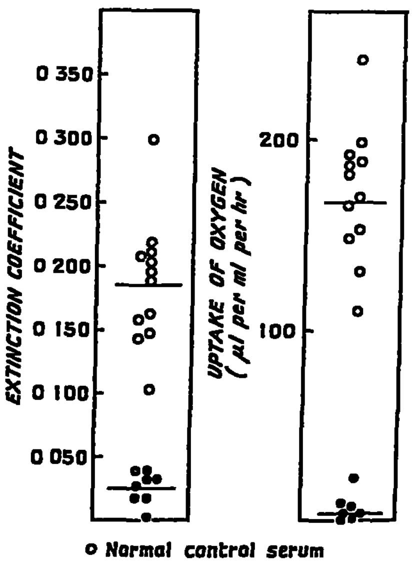

Fig. 2—Colorimetric and manometric measurements of copper-oxidase activity made in parallel on same samples of serum.

Results

The paraphenylene-diamine oxidase activity of serum is most readily expressed as the extinction coefficient of the diluted reaction mixture prepared and analysed under the standard conditions described above. Extinction readings and oxygen uptake obtained in 8 cases of hepatolenticular degeneration and in 14 unselected, control sera

We are greatly indebted to the National Fund for Poliomyelitis Research for a grant in support of Dr Churcher and a research expenses grant Expenses of the work have also been partially defrayed from financial support given to the department by the Medical Research Council Dr Lee is in receipt of a W H O fellowship Thanks are due to Dr Alistair Dudgeon for the sera from 2 cases of poliomyelitis, to Dr D A J Tyrrell for a sample of type 2 rabbit antiserum, and to Dr W Wood of Glaxo Laboratories Ltd, for supplies of 'Parker 199' medium

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DURATION OF VASODILATATION AFTER LUMBAR SYMPATHECTOMY

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In 1929 Lewis and Landis stated that in man the blood-vessels of the hand recovered their vasoconstrictor tone within four days after cervicodorsal sympathectomy They based their opinion on clinical observation, but since then many observers have investigated the blood-flow of the limbs after sympathectomy and have concluded that it returns to the preoperative level within weeks, or at most months, after operation Detailed plethysmographic studies have been made by Grant and Pearson (1938), Wilkins and Eichna (1941), Grayson (1948), Barcroft and Walker (1949), Lynn and Barcroft (1950), and Walker et al (1950), whose results confirm the transient nature of the vasodilatation in the persons they investigated

Many explanations for this recovery of tone after sympathectomy have been advanced, the more important of which may be summarised as follows

(1) The arteries become hypersensitive to adrenaline or to an unknown hormone (Meltzer and Auer 1904, Freeman et al 1934, Smithwick et al 1934, Grant 1935, White et al 1936, Ascroft 1936, Simmons and Sheehan 1939, LeCompte 1941)

(2) The muscle fibres of the arteries contract because of some "intrinsic property" of the muscle itself (Cannon 1937, Doupe 1943)

(3) Accessory sympathetic pathways which do not pass through the sympathetic trunk are left untouched by the operation (Richter and Woodruff 1945, Pick and Sheehan 1946, Skoog 1947, Boyd 1948, Ray and Console 1948, Boyd and Munro 1949, Wrete 1950)

(4) Regrowth of the damaged sympathetic axons may re establish connections with the blood-vessels (Lee 1930, Geohegan and Adair 1942)

A few investigators have stated that vasodilatation following sympathetic denervation may last a long time Adson and Brown (1929) reported persistently raised temperature of the toes after lumbar sympathectomy in man, and Ross (1946) wrote "The sympathetic denervation following a well-planned and correctly executed operation is permanent, as shown by sweating tests in addition to vasomotor reactions"

The present investigation of the blood flow and vasomotor reflexes of patients who had undergone lumbar sympathectomy for the relief of vascular symptoms (coldness, cyanosis, and chilblains) formed part of a larger investigation of the involvement of the autonomic nervous system in poliomyelitis (Kessel and McPherson 1953, McPherson and Kessel 1955)

Methods

The blood-flow in both feet of 14 patients (eighteen lumbar sympathectomies) was examined by venous-occlusion plethysmography Of the 14 sympathectomised patients 12 had poliomyelitis, 1 a birth palsy affecting the lower limbs, and 1 a hemiplegia during early childhood The sympathectomies were done by surgeons in several hospitals The controls consisted of 30 healthy people and 30 patients who had poliomyelitis but had not undergone sympathectomy The plethysmographs had volume recorders as described by Cooper and Kerslake (1951), and the investigations were made in a quiet draught-free, heat controlled room with the subject lying on a rubber mattress The lower limbs were immersed up to the thighs in water at a temperature of about 36°C for about thirty minutes before the insertion of the feet in the plethysmographs, to equalise their temperature as far as possible The investigations were made at room temperatures of 21–25°C, but in any one investigation the room temperature did not vary more than ±1°C The plethysmograph temperatures varied from 31 5 to 33 75°C, but in any one investigation did not vary more than ±0 25°C The difference in temperature between the two plethysmographs was never greater than 0 25°C Collecting pressures of 75–85 mm Hg were used throughout and were identical in both cuffs

Records were made at intervals of 5–15 seconds, and the investigation of each subject included measurements of blood-flow under three conditions (1) normal heat exchange (i e, the patient was covered by a light blanket at normal room temperature), (2) reflex vasodilatation (i e, after warming the arms in water-baths at 45°C and warming the body with a radiant-heat lamp until profuse sweating took place), and (3) reflex vasoconstriction (i e, while the warming was continuing, ice was suddenly placed on the forehead without warning)

The blood-flow was calculated from the average of twenty inflow curves except after reflex vasoconstriction, when it was calculated from the succeeding three inflow curves

The results of these tests are shown in table I

TABLE I—BLOOD FLOW OF SYMPATHECTOMISED PATIENTS
(ml per 100 c cm of tissue a minute)

Patient no	Normal heat exchange		Reflex vasodilatation		Reflex vasoconstriction	
	Operated side	Non operated side	Operated side	Non operated side	Operated side	Non operated side
1	9 9		6 7		6 7	
	10 2		7 2		7 5	
2	15 7	4 3	15 0	19 5	15 2	17 5
3	6 0	1 9	11 5	12 3	13 4	8 1
4	7 3		8 6		10 7	
	10 9		9 0		11 2	
5*	16 8	5 9	20 6	21 7	18 1	19 6
6†	4 5	1 4	5 6	17 3	4 3	6 7
7	4 4	5 1	36 8	37 9	25 9	35 9
8	3 8		17 2		15 4	
	3 0		14 1		9 3	
9	7 2	2 1	9 2	10 1	9 3	4 5
10	21 2	4 3	15 4	23 1	17 0	13 7
11	13 6		13 3		12 3	
	11 8		11 3		12 8	
12	5 0	2 0	15 7	24 0	10 0	11 7
13	3 0	2 2	5 9	16 9	4 8	12 1
14	9 0	2 0	10 4	16 9	8 9	10 2

* Hemiplegic † Birth palsy

The means of the controls are given in table II together with the mean blood-flows of the sympathectomised patients

The blood-flows of all the subjects studied are shown in fig 1 The reasons for the small differences in blood-flow of healthy people and non sympathectomised patients with poliomyelitis are analysed in detail elsewhere (McPherson and Kessel 1955) For our present purpose these differences are ignored a fair number of pepsinogen and oxyntic cells were present The mucosa was infiltrated throughout with lymphocytes and plasma cells, and occasional eosinophil and neutrophil leucocytes The picture was that of an atrophic gastritis of moderate severity, with survival of a fair number of specialised cells "

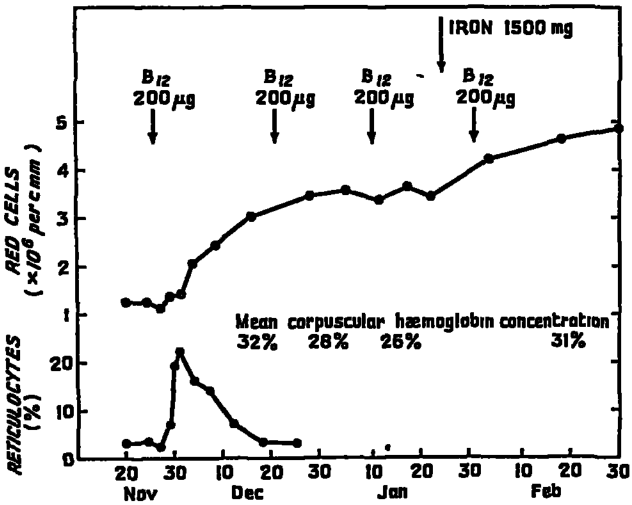
Fat balance —Normal 92% of the ingested fat was absorbed

Absorption of radioactive B_{12} —The patient absorbed 0 35 μg ^{58}Co labelled B_{12} from an oral dose of 0 6 μg given alone, and 0 39 μg from the same oral dose given fifteen minutes after the subcutaneous injection of 0 25 mg carbachol (carbamyl choline chloride) Similar amounts are absorbed by normal subjects (Mollin and Baker 1955)

Blood urea was 32 mg per 100 ml , and *serum proteins* 4 5 g per 100 ml (albumin 3 1 g , globulin 1 4 g)

Response to Treatment

The patient received an intramuscular injection of 200 μg vitamin B_{12} initially, and this was repeated on the 24th, 44th, and 75th days afterwards The response to this treatment is shown in the accompanying figure Three weeks after the first injection, the blood count showed signs of iron deficiency A course of 1500 mg saccharated iron was given intravenously The blood picture two months later was essentially normal (red cells 4,800,000 per c mm , hæmoglobin 14 0 g per 100 ml and P C V 46%)



The red cell and reticulocyte response to treatment with intramuscular vitamin B_{12} and intravenous iron 200 μg of vitamin B_{12} was given intramuscularly on each of the four occasions indicated

On admission to hospital on Nov 6 she ceased taking Glauber's salt but continued to pass four or five watery stools daily Four days after the first injection of vitamin B_{12}, the bowel action was normal Two weeks later her appetite had improved to the extent that she was able to take a full ward diet Her weight increased steadily and two and a half months after admission to hospital she had gained 1 st 4 lb The prolapse of her rectum was subsequently corrected surgically

Comment

These results indicate that the megaloblastic anæmia in this patient was due to vitamin-B_{12} deficiency, for her pretreatment serum-B_{12} concentration was low and her anæmia responded to treatment with B_{12} Deficiency of this vitamin may develop in patients after gastro-enterostomy who are taking an adequate diet (Mollin and Ross 1954) In these patients a blind antiperistaltic loop is usually present (Naish and Capper 1953) Such patients often have steatorrhœa and they are unable to absorb test doses of labelled B_{12}, excreting all or almost all of an oral dose of radioactive B_{12} in the fæces (Booth and Mollin 1955) In our patient, the gastro enterostomy functioned well, there was no steatorrhœa, and she was able to absorb normal amounts of test doses of labelled vitamin B_{12} This finding indicated that she had no intestinal lesion interfering with her ability to absorb vitamin B_{12} It also indicated that the patient was able to secrete normal amounts of intrinsic factor and was therefore not suffering from addisonian pernicious anæmia This was borne out by the gastric biopsy which did not show the gastric atrophy usually associated with this disorder

It is therefore clear that the deficiency of vitamin B_{12} in this patient was due to an inadequate dietary intake of the vitamin The patient's diet was, and had been for many years, grossly deficient in foods containing vitamin B_{12}, her sole source of vitamin B_{12} being her small daily allowance of milk, which did not exceed 200 ml per day, this is approximately equivalent to an intake of 0 4 μg of vitamin B_{12} (Gregory 1954) This proved to be quite inadequate to supply her requirements of this vitamin It seems unlikely that the constant intake of Glauber's salt interfered with intestinal absorption

Summary

A woman of 77 had lived on bread and margarine, tea, and potatoes for more than ten years She was found to have a megaloblastic anæmia which responded to vitamin B_{12} The B_{12} deficiency was due to the inadequate intake in the diet

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Preliminary Communication

IRRADIATION OF PITUITARY FOR ADVANCED MAMMARY CANCER

In a series of 80 bilateral adrenalectomies for cancer of the breast, despite the most careful preoperative and postoperative treatment we have found that this operation carries a mortality of 6% This figure is comparable with those reported by Huggins [1] and Cade [2]

We do not consider that adrenalectomy is justifiable unless it gives a clear remission of the disease with complete alleviation of pain for at least a year. In our series such remission has only been obtained in 35% of cases

Hypophysectomy, while giving a greater proportion of successful results (probably 50%), still subjects the seriously ill patient to a major operation with a mortality of approximately 5% For these reasons an attempt has been made to find a safe procedure which would not add further to the patient's suffering, and which would at the same time be of value in the treatment of advanced cancer of the breast

At this hospital we have tried to destroy the pituitary gland completely by implanting unscreened radioactive gold Unlike other workers we have relied on smaller and, if necessary, repeated doses of β irradiation The gold seeds are implanted in the anterior part of the pituitary gland through a fairly small bore needle which is introduced into the sella turcica via the nose and sphenoidal sinus Extremely accurate visual localisation of the sella turcica is obtained by means of an image intensifier working in two planes, and only the most accurate positioning of the gold grains is accepted

During the past eighteen months 50 patients have been treated in this way with full biochemical and partly explained by the recovery of the paretic sympathetic nerve fibres and/or transmission in sympathetic synopses

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[1] Huggins C Bergenstal D M *J Amer med Ass* 1951 147, 101 Huggins C Dao T L Y *Ibid* 1953 151 1388
[2] Cade S *Ann R Coll Surg Engl* 1954 15 71 Cade S *Brit med J* 1955 i 1

It is obvious that recovery from temporary injury to sympathetic nervous tissue cannot explain all the features of the recovery of arterial tone following some sympathectomies Some weeks or months after sympathectomy many patients have a blood-flow which is little different from the preoperative level, and in these patients it is often impossible to demonstrate any vasomotor reflexes Patients 6, 9, and 13, for example, had no vasomotor reflexes twenty five, sixteen, and twenty five months respectively after operation

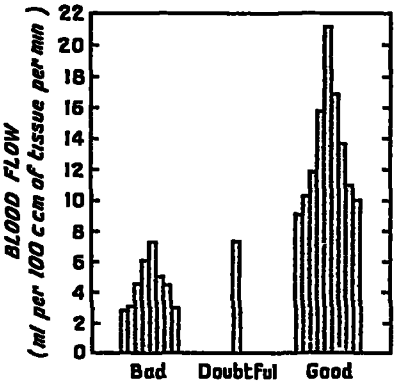

Fig 2—Comparison of blood flows and assessment of operations

Barcroft (1952) has suggested that the symptomatic improvement which follows sympathectomy, even though the arteries have regained their tone, can be explained by the protection of the blood vessels from vasoconstrictor stimuli which these sympathectomies provide The results of the present investigation suggest that the situation is more complex than this Patient 12, for example, had a considerable and long-lasting improvement in his vascular symptoms, even though the vasomotor reflexes were still present Conversely, patient 9 had only a moderate and transient improvement in his symptoms, although no vasomotor reflexes could be demonstrated sixteen months after his operation

It is usually assumed that the absence of vasomotor reflexes definitely indicates that the blood vessels have been deprived of their sympathetic innervation Hertzman (1954), however, has stated that, in his experience, a negative reflex vasodilatation test is uncertain evidence of sympathetic denervation, and Lynn (1954) has described patients whose vasomotor reflexes were absent but whose sudomotor activity was still present in the same limbs The fact that in the present investigation the vasomotor reflexes in the feet were sometimes absent regardless of the quality of the operation is, perhaps, supporting evidence for the conclusions of Hertzman although it is unlikely that this is the entire explanation of the phenomenon The results reported here suggest that both the absence of vasomotor reflexes and the resting blood flow level must be considered together as criteria for the adequacy of the sympathectomy

2 of the adequately sympathectomised patients (nos 1 and 10) showed a decrease in the level of blood-flow after reflex heating Patient 10 showed the larger decrease in blood flow on reflex vasodilatation (5 8 ml. per 100 c cm of tissue a minute), and this was the patient who had all ganglia resected from T12 to L3 inclusive

The results of this investigation suggest that the statement, sometimes made, that a patient has 'had a sympathectomy," merely because an operation was done with this intention, is likely to be misleading Sympathectomy may be difficult even in the most experienced and skilled hands, and its effects on the circulation may be extremely variable Table III shows that technically good operations for lumbar sympathectomy produce a considerable increase in the blood flow in the feet, and this vasodilatation may last for as long as fifteen years Such operations can produce a persistent vasodilatation which is almost as great (90%) as the "maximal" vasodilatation produced by heating the arms and body of healthy people On the other hand, technically poor operations for sympathectomy produce no persistent vasodilatation

The results obtained from the small series of patients investigated in this study indicate that, when an adequate sympathectomy is done, the denervated blood vessels do not regain their tone

It is difficult to suggest what constitutes a good lumbar sympathectomy, but the results reported here support the view of Hertzman (1954) "we feel that the surgeon must do a practically total lumbar ganglionectomy in order to increase the incidence of therapeutic gains" It is unfortunate that operations for sympathetic denervation have become less popular because of the reported recovery of vascular tone following the operation The present investigation supports the opinion of Ross (1946) that, when a sympathectomy is adequate, the results are long-lasting Further support for this point of view is provided by the fact that most of the sympathectomies producing a lasting vasodilatation were done by one surgeon who always removes, when possible, all the lumbar ganglia

Summary

The blood-flow in the feet of 14 patients with paralysed limbs who had had a lumbar sympathectomy (eighteen operations on 14 patients) was measured by venous occlusion plethysmography These blood-flows were compared with two control groups consisting of 30 poliomyelitis patients who had not had a sympathectomy and 30 healthy people

Those operations for sympathectomy which were technically good produced a lasting dilatation in the blood-vessels of the feet

Those operations which were technically bad did not produce a lasting vasodilatation

Our thanks are due to Mr H J Seddon for his continual advice and encouragement, and the surgeons of the various hospitals, particularly Mr G W L Bonney, of the Institute of Orthopædics, who made it possible for us to examine their patients

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Reviews of Books

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World Population and Resources

A report by Political and Economic Planning London P E P Distributed by Allen & Unwin 1955 Pp 339 30s

ACCORDING to the latest figures since 1930 the world's population has risen by a third Can this increasing population be supplied with adequate food, fuel, and raw materials ? Can the less fortunate of those now living be brought up to a decent minimum standard ? Can the hopes of advanced countries for still higher standards be satisfied ? Can the 30 million or so people added each year to world population be supplied with all their requirements ? Can all these things be done together and can they be done soon ? In particular, how nearly attainable is a balance between world population and world resources ? And if attainable, how can it be maintained ? It is the aim of P E P (Political and Economic Planning) to " study problems of public concern, to find out the facts to present them impartially, and to suggest ways in which knowledge can be applied ," and the organisation has produced an admirable report on these formidable questions

While much is being done and more can be done to increase the world's supply of foods, materials, and resources, there is obviously a limit to their production Unless some holocaust befalls or unless effective measures are applied to limit population, it will go on increasing for some time at least, and probably at a progressively more rapid rate Few people view with anything but horror the prospect of a third world war, yet there can be no doubt that ' population pressure " is one of the main factors that lead to war The problems of world population and resources must therefore be an urgent concern of all , and the report is intended particularly to provide the factual, quantative basis for frank discussion of the problem It demands the special attention of the medical profession, whose triumphs over disease have led to an increasing measure of death control and an upsurge in population One of the report's main points is that in future death control should not be pressed on in isolation but should go hand in hand with birth-control ' If programmes of death control and of economic development are to be thrust upon the people of underdeveloped countries, these peoples must be given corresponding opportunity to catch up with advanced Western countries in birth-control " " A major challenge to science is the supreme importance of finding a simple, generally acceptable, and low cost method of birth-control suitable for use by illiterates in difficult climatic or social conditions "

There are many difficult aspects to these problems, not the least of which is the attitude of religious bodies Many of these issues are boldly tackled in the report, and on the religious question some recent words of the Pope are quoted " The Church is not unaware of these problems she is not indifferent to their anguishing aspects We urge Catholics to take an active part in the research and in the efforts which are made in this domain "

Keratoplasty

R TOWNLEY PATON, M D F A C S , surgeon director, Manhattan Eye, Ear, and Throat Hospital New York and London McGraw Hill Book Co 1955 Pp 270 £10 14s

IT is fitting at this time that a surgeon of such international repute as Dr R Townley Paton should write a comprehensive book on keratoplasty for particularly during the past two decades, enthusiasm and interest in indications and contra-indications for this operation and in a variety of surgical techniques has become considerable To this difficult task Dr Paton has brought his valuable and large experience as a surgeon, a director of research a clinical professor of ophthalmology and an administrator of the eye bank, a superb organisation to which many patients and surgeons owe much

The book is admirably written and the author describes lucidly and thoroughly the surgical techniques which he has found most practicable and effective The procedures used by other surgeons are discussed and the vast literature is judiciously reviewed and sifted Throughout the work, Dr Paton has kept a fine balance between the scientific and clinical aspects, and has clearly shown where these are complementary to each other

There are 29 excellent colour plates as well as half tone photographs , and the drawings of the author s operations are well executed by Miss Daisy Stilwell

Die endogenen Psychosen

das delphische Orakel der Psychiatrie KURT KOLLE professor of psychiatry and neurology in the University of Munich Munich Lehmanns 1955 Pp 48 DM 3 [illegible]

THIS oration was delivered in memory of Emil Kraepelin by the present professor of psychiatry in Munich on the fiftieth anniversary of the opening of the clinic with Kraepelin as its director Professor Kolle is vehement in his opposition to current trends in psychiatry he belongs to the old school and demands more direct and convincing evidence before he will approve psycho-analytic interpretations or accept the claims made for psychotherapy by some and for insulin by others in the treatment of schizophrenia The psychogenesis of affective psychoses is no more plausible to him than it was to Kraepelin and even Kretschmer goes further than Kolle will follow There is, of course much for the sceptic to gird against in modern psychiatry but Professor Kolle seems to be certain that, with few exceptions, what we know of this subject is no more than we knew twenty-five or more years ago Like other sturdy diehards, he makes shrewd thrusts and picks off foolish adversaries while the main body moves past him possibly in the right direction

Scurvy as a Skeletal Disease

H J VAN WERSCH, M D Utrecht Dekker & van de Vegt N V 1955 Pp 365

THIS book came about in a curious way In 1935 the author saw as a patient a girl of 18 with a peculiar bone disease which had been variously diagnosed as sarcoma, von Recklinghausen's disease, and Paget's disease A shadow in the upper part of the femur, which had led to the first diagnosis turned out to be a calcified subperiosteal hæmatoma from scurvy The appropriate treatment was instituted—six years after the onset of the disease—and the patient made a gratifying recovery During the German invasion of 1940–45, Dr van Wersch lost touch with his patient, who had again developed scurvy , but after the war further treatment with vitamin C produced improvement Inspired by his study of this patient, he wrote this book on scurvy in its clinical and laboratory aspects There is little new work, but the subject is dealt with at length The book is rather like a large and slightly uncritical M D thesis

Standard Atlas of Human Anatomy (*Descriptive and Regional* Vols I and II 3rd ed London Butterworth Amsterdam Scientific Publishing Co 1955 Pp 11[illegible]4 *72s 6d* the set) —The third edition of Prof M W Woerdeman s atlas is the first in which the two volumes have been issued together, and in response to the author s wish ' to keep in mind the unhappy economical situation of so many students " the publishers have used again the blocks of the first edition This means that a few unimportant errors in the plates are retained, but the justification lies in the price which is indeed low for so well produced an atlas Vol I deals with the locomotor system in 512 plates the other systems are contained in vol II, which has 642 plates Each plate depicts an individual specimen and does not show features derived from several dissections , it is suggested that the student can thus obtain an idea of the range of the normal by comparing his own work with the plates There are many diagrams showing the lines of pull of the muscles most of these are helpful, but some might be a little confusing The central nervous system and the heart are dealt with in detail, and there are some rather complicated diagrams of neural pathways The peripheral vessels and nerves are shown in a semi diagrammatic fashion bereft of all but their largest and grandest relations Colour is sparingly used, it being contended that the student is forced to look more carefully at a monochrome picture than at a coloured one The plates are clear accurate, and well labelled The terminology used is the B N A and now that the anatomical world has adopted a unified system of terminology based on the B N A this excellent atlas should prove even more useful than before to British students

TABLE II—ISOLATION FROM SAME SPECIMEN OF PAIRS OF *Staph aureus* DIFFERING IN REACTION TO PENICILLIN

—	No of pairs	Phage pattern of pair		
		Same	Doubtful (one of pair untypable)	Different
Old series (Fairbrother et al 1954)	13	6	2	5
New series	12	5	3	4
Total	25	11	5	9

(10–50 colonies) gave uniform results Occasionally, however, slight differences among the colonies were detected in either production of pigment, size, or zone of hæmolysis on a blood-agar plate, on rare occasions a few colonies were found in the clear zone around an antibiotic disc Sensitivity tests often proved regular, but in a few cases differences in behaviour towards the various antibiotics were observed (tables II and III)

Despite the large number examined, differences in the reaction of individual colonies to penicillin were observed with only 12 cultures prepared from the same lesion Of these 12 pairs, 5 strains gave the same phage pattern, 4 proved to be quite different, and in 3 pairs one at least of the strains proved to be untypable

In the two series of investigations 25 pairs were isolated, and 11 of these gave the same phage pattern it is reasonable to assume that they had originated from the same parent strain in vivo In 5 of 25 pairs the typing results were inconclusive The reaction to penicillin of the organisms originally responsible for the infection could not be determined, and it was therefore impossible to identify the variant strains The pairs of *Staph aureus*, although reacting differently to penicillin, behaved consistently towards the other antibiotics

During this work a comparable variation in reaction of individual colonies to other antibiotics (chloramphenicol, tetracyclines, or streptomycin) was also observed on a few occasions (table III) In 6 of 15 infections variant strains seem to have developed in vivo This problem was, however, left for further study

IN-VITRO PRODUCTION OF VARIANT STRAINS

As there are serious practical limitations to the study of the mode of development of variant strains of *Staph aureus* under natural conditions, further investigations were made into the appearance, under experimental conditions, of (1) penicillin sensitive variants from apparently pure cultures of penicillinase-producing strains of *Staph aureus*, and (2) penicillinase producing variants from apparently pure cultures of penicillin-sensitive organisms

Development of Penicillin sensitive Variants from Penicillinase producing Strains

Although many workers have claimed that penicillinase-producing strains of *Staph aureus* are permanently resistant to penicillin, there is now much evidence that they are very unstable (Barber 1949, Fairbrother et al 1954) Further tests demonstrated the instability of penicillin resistant strains of *Staph aureus* grown in a water bath at 44°C

Penicillin resistant colonies of *Staph aureus* were selected from recent cultures of infected material, subcultures were prepared on agar plates, and, after overnight incubation, sensitivity tests were made on 10–20 discrete colonies If all proved resistant to penicillin, a subculture of a discrete colony from the first subculture was prepared and again sensitivity tests were made on individual colonies If these proved satisfactory one of these penicillin resistant colonies was seeded into 10 ml of broth and incubated in a water bath at 44°C, coagulase and penicillinase tests were done at the same time to ensure that a true penicillin resistant strain was being investigated Serial subcultures in broth were made usually every one to three days, to give a final total of 20, at intervals plate cultures were also prepared, by means of a large loop, for colony tests of penicillin sensitivity by the strip technique

TABLE III—ISOLATION FROM SAME SPECIMEN OF PAIRS OF *Staph aureus* DIFFERING IN REACTION TO STREPTOMYCIN, CHLORAMPHENICOL, OR TETRACYCLINES

Phage pattern of pair	No of pairs isolated
Same	6
Doubtful (one of pair untypable)	5
Different	4

14 penicillin resistant strains of *Staph aureus* were examined in this way (table IV) and 10 were found to produce penicillin sensitive variants Of the total of 21 strains so far examined, 14 produced variants In some cases the penicillin sensitive variants were detected after only one or two subcultures, but in the case of other strains the variants did not appear until later In some cases the penicillin sensitive variants exhibited definite colonial changes, the colonies being larger and less pigmented, but in other cases the colonies appeared to be identical with those of the penicillin resistant strains In all cases the phage patterns were either identical or showed only minor variations

TABLE IV—PRODUCTION OF PENICILLIN SENSITIVE VARIANTS FROM PENICILLINASE PRODUCING STRAINS OF *Staph aureus* BY INCUBATION AT 44°C

—	No of strains tested	Incidence of penicillin sensitive variants
Old series (Fairbrother et al 1954)	7	4
New series	14	10
Total	21	14

Thus it appears that penicillin sensitive organisms readily develop from apparently pure cultures of penicillinase-producing strains of *Staph aureus* during growth at 44°C, which is about the highest temperature allowing active growth of this organism The intermittent subculturing of a single loopful of a broth culture and the examination of about 100 colonies during 20 subcultures do not constitute particularly exacting tests for the detection of penicillin sensitive variants, so probably, if more rigorous methods had been used, penicillin sensitive variants might have been detected in every case

Appearance of Penicillinase producing Variants in Cultures of Penicillin sensitive Strains of Staph aureus

While there is no doubt about the instability of penicillinase producing strains of *Staph aureus*, there is as yet no unequivocal report of the isolation of penicillinase producing organisms from apparently pure cultures of sensitive strains

Initially abortive attempts were made to achieve this by growing penicillin-sensitive organisms in media containing small amounts of either penicillinase or penicillin Subsequent subculture on to agar plates and examination of discrete colonies failed to reveal any penicillinase-producing variants It was then decided to try serial subculture in broth at 33–35°C

Sensitive strains of *Staph aureus* which did not produce penicillinase were used, and a discrete colony from a plate, seeded with a discrete colony from the primary culture, was used as the original inoculum After inoculation of the broth an agar plate was seeded, and all the colonies tested from this proved to be penicillin sensitive In this way attempts were made to ensure that a pure penicillin sensitive culture was being investigated At least 20 serial subcultures were made, and at intervals colony tests were made

8 strains were thus tested, but on no occasion was a penicillin-resistant colony detected (table V)

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STAPHYLOCOCCI HARBOURED BY PEOPLE IN WESTERN HIGHLANDS OF NEW GUINEA

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NUMEROUS investigators have reported a steadily increasing prevalence of penicillin-resistant strains of *Staphylococcus aureus* in civilised communities (e.g., Barber and Burston 1955, Ternal and Chabbert 1955). Many of these strains appear to have been detected in hospital environments, but there is still some debate on their origin since penicillinase-producing strains may also be found in people who have not been admitted to hospital. There are fewer reports of the antibiotic resistances of coagulase-negative staphylococci, but 50% of a series of 444 strains of this kind isolated in this hospital in 1954–55 were penicillin-resistant.

Unfortunately few collections of staphylococci isolated before the introduction of penicillin are available for study. Anderson (1946), however, examined 396 strains; of these 281 were coagulase-positive and sensitive to penicillin, while of the remaining non-pathogens a few were penicillinase producers. Furthermore there are now few parts of the world where penicillin has not been freely used. Hopps et al. (1954) reported that 43 strains of *Staph. aureus* obtained from skin lesions of Dusuns of North Borneo were penicillin-sensitive, although 3 produced penicillinase. Similarly 14 strains from skin lesions in people indigenous to tropical Mexico were penicillin-sensitive, 5 being penicillinase producers. In both these groups of people antibiotic usage was minimal. It should be noted, however, that both groups have a long history of contact with white people.

In the Wabag region of the Western Highlands of New Guinea lives a group of people who have had very little contact with civilisation (Elkin 1953). Their existence was unknown before 1910; the area in which they live was first penetrated in 1934, and since that time no more than 30 white people have had contact with them—and even such contact has been slight (Macintosh 1955).

These Wabaga, numbering approximately 200 000, live in a mountainous region 85 by 100 miles in area in discrete family units, not in villages but in homesteads. They are exceedingly primitive and have a minimum of material culture. Ethnically, they appear to be distinct from their mountain neighbours and from the Papuans inhabiting the coastal regions, but their origin is still undecided. In 1946, after the area had been closed since 1938, administrative buildings and an airstrip were built in one locality (Wabag), and in 1949 a native hospital was established. However, as the Wabaga are free from yaws, there has been no mass campaign of penicillin therapy in the region.

The recent Nuffield expedition to the region provided an opportunity to take nasal swabs from some of these people. The 120 men swabbed were scattered throughout the area. So far as could be ascertained, none had ever received any antibiotics. Two groups of swabs were taken from men in areas where contact had been limited to the occasional passage of administrative patrols. The remainder of the swabs were taken from men in areas where there had been some contact with the administration and missionaries.

Methods

The swabs were inoculated immediately on to nutrient-agar slopes in screw-capped bottles and dispatched by air to Sydney for examination.

Representative inocula from the slopes were transferred to blood-agar plates. After incubation, single colonies of various degrees of pigmentation were picked for further study. Not more than three colonial types were isolated from any one swab.

Tests for sensitivity to penicillin, streptomycin, oxytetracycline, chlortetracycline (aureomycin), and chloramphenicol were carried out in the first place by a disc-plate method (Rountree and Thomson 1949, 1952). Strains showing the same amount of inhibition as the control Oxford H strain were regarded as sensitive. Strains showing less inhibition than the control were tested by a tube method. With penicillin small inocula of 0.02 ml. of a 10^{-4} dilution of an overnight broth-culture were used to inoculate serial dilutions of the antibiotic in 1 ml. broth. With the other antibiotics, 0.02 ml. of undiluted broth-cultures were used as inocula. Results were read after eighteen hours' incubation at 37°C.

Strains partially or completely resistant to penicillin by the plate method were tested for penicillinase production by the method of Voureka and Hughes (1949).

Certain strains were tested for ability to ferment glucose and to give the Voges-Proskauer reaction (Shaw et al. 1951).

Results

Pathogenic Staphylococci

Only 23 carriers of coagulase-positive *Staph. aureus* were found—a carrier-rate of 19.1%. However, the high proportion of cultures yielding coagulase-negative strains indicated that carriers of pathogens had not been missed because methods of collection or transport of the material were unsuitable for the survival of staphylococci. All strains produced α toxin, but no β-toxin was detected on 5% sheep-blood-agar plates. All strains were sensitive to the five antibiotics.

The strains were phage-typed with the results shown in table I. The seventeen patterns observed among the 23 strains are found in strains isolated from civilised communities. It was noted, however, that 8 of the strains reacted only when the phages were applied in high concentration, suggesting some minor difference in their behaviour compared with the strains normally examined

TABLE I—PHAGE-TYPE DISTRIBUTION OF STRAINS OF *Staph. aureus*

Phage group	Phage pattern	Number of strains reacting at: R.T.D.	Number of strains reacting at: 10^{-3}	No. in group
I	52/52A/79/80		1	7
	52A/80		1	
	79	1	1	
	79/80	1		
	80	1	1	
II	3A/3B/3C/55	2		4
	3B/3C/55	1		
	55	1		
III	6/31B/47/53/54/75/81	1		7
	7/47/54/77/81		1	
	7/77/81		1	
	31B	1		
	53	1		
	81		2	
IV	42D	1		1
Unclassifiable	42D/81	1		2
	7/29/42D/47/53/73/79/80/81	1		
Untypable				2
Total		13	8	23

R.T.D. = routine test dilution.

DR. FAIRBROTHER: REFERENCES

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that the risk of allergic reactions was too great Superficial burns cleaned and treated soon after the accident should not need prophylactic antibiotics but if inflammation spreads around the burn within the first few days it is often the work of the hæmolytic streptococcus, and usually responds rapidly to rest and penicillin Localised infection by *Staphylococcus aureus*, hæmolytic streptococci, and gram-negative organisms is also a hazard later on in cases in which sloughing and granulations supervene, but this is a problem better dealt with in hospital The advantages of the exposure method are greatest, probably, in treating superficial burns of the face—a site where dressings cannot easily be held in position, and where bandages require continual attention After careful cleansing of the burned areas, the corners of the nose, mouth, and eyelids are lubricated with soft paraffin, and the whole burn is allowed to dry as soon as possible These cases, in particular, should be referred for specialist treatment if at any time there is suspicion that the true skin is seriously involved

All our devices may fail to yield an accurate initial estimate of the severity, though accuracy increases with experience Few burns can be seen and assessed immediately by a plastic surgeon Those of us who see the moderate or severe burn only on rare occasions need not be embarrassed by having to modify our earlier views as the days go by and the slough becomes defined Where skin-grafting is necessary, the earlier it is done the better Nevertheless, in the present state of knowledge we must accept that the necessity cannot always be recognised at once In the doubtful cases an open mind for the first week or two allows a judicious change of policy without a recantation It will also obviate criticism of any particular method of treatment, where the reason for disappointment lies in the characteristics of the injury itself

Infantile Pyloric Stenosis

THE adoption of Rammstedt's operation of pyloromyotomy notably improved the results in infantile pyloric stenosis, and, with progress in the hospital care of infants, mortality-rates have sunk to about 2% in many clinics A discussion held at the Royal Society of Medicine[1] in 1951 revealed various preferences in the matter of preparation for operation, technique, and anæsthesia Some preferred medical management with atropine derivatives Nevertheless everyone reported good results, though DAVISON pointed out that the Registrar-General's figures still suggested a mortality for the country as a whole in the region of 10–15% He considered that treatment in a department where the nurses and doctors were accustomed to dealing with the condition was more important than the particular method used As family doctors now detect or suspect this not uncommon condition at a commendably early stage, its management seems to present few outstanding difficulties

Rammstedt's operation has now been in use long enough for some of the earlier patients to be having children This has stimulated interest in other facets of the natural history of the disease An increased liability to pyloric stenosis in the children of previously affected parents has been recognised for some time COCKAYNE and PENROSE[2] suggested inheritance by a recessive gene influenced by sex and birth order Further studies have shown that the ætiology may not be so simple MCKEOWN and MACMAHON[3] have examined the offspring of men and women who have recovered from infantile pyloric stenosis Adding the figures from CARTER and POWELL[4] and NEILSON'S[5] studies to their own Birmingham series, they found 14 "pylorics" amongst 203 children of affected parents—a high incidence of 6·9% Further search among records of their own and other centres revealed 33 instances of parent and child having this disease The affected parent was the mother in half of these, in spite of the well-known higher incidence in males Furthermore, examination of their fraternities showed that an even greater proportion of the children in these particular families suffered from the condition (42 out of 69 children) The conclusion drawn was that the increased risk of having affected children was not the same in all survivors, but was localised in certain families and was increased when the mother was the affected parent MACMAHON and MCKEOWN[6] have also studied the concordance in twins It used to be thought that identical twins would both be affected if either had the disease SHELDON[7] observed an exception, and others were described later by CARTER and POWELL[8] An environmental factor in the development of pyloric stenosis might account for this MACMAHON and MCKEOWN found in their series, which they believed to be more representative than earlier ones, that there was no increased concordance in monozygous twins compared with dizygous They support the suggestion of a postnatal environmental influence That the tumour itself usually develops after birth has been accepted for some time[9] GERRARD and his colleagues,[10] also working in Birmingham, have measured the size of the tumour in 51 cases and have confirmed an earlier finding of MCKEOWN et al[11] that its size is proportional to the age of the baby at operation The onset of symptoms was more rapid in the babies fed three-hourly than in those on a four hourly schedule The relative importance of inherited characteristics and postnatal influences can be assessed only by further inquiries along these promising lines

The number of particularly susceptible newborn children seems likely to increase as more survivors of infantile pyloric stenosis begin their families Prophylaxis of the condition by medical means may seem a wise course when the risk for each individual baby can be better assessed In this connection a paper by CRAIG[12] is timely He felt a contractile pyloric tumour in 17 out of 21 babies who were examined during the first two weeks of life for failure to thrive associated with possetting, regurgitation or vomiting Only 3 were operated on, and 2 had a typical hypertrophied pylorus All the others recovered promptly with gastric lavage Moreover, using precise time, since, in our experience, symptoms of kernicterus commonly develop on the sixth or seventh day and only occasionally on the fifth day

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Following reports by Allison (1955) and Laurance (1955) that the administration of large doses of vitamin-K analogues to premature infants was potentially dangerous in relation to the development of kernicterus, we reduced the routine dose of synkavit given after birth from a total of 30 mg in the first seventy-two hours to 1 mg on the first day The effect of this change of dosage on the plasma bilirubin levels forms the basis of this report

Materials and Methods

Plasma bilirubin levels were estimated in two groups of premature babies

Group A consists of the 55 survivors of 72 infants admitted to the premature baby unit from September, 1954, to April, 1955, inclusive, 17 having died before the fifth day of life They received 10 mg of synkavit daily by intramuscular injection for three days There were 26 males and 29 females, 17 were twins, their birth weights ranged from 2 lb 5 oz to 5 lb 7 oz

Group B consists of the 51 survivors of 60 infants admitted from May to November, 1955, 9 having died before the fifth day They received a single injection of 1 mg of synkavit on the first day of life There were 30 males and 21 females 10 were twins, and there was one set of triplets Their birth weights ranged from 2 lb 3 oz to 5 lb 8 oz

Cases of hæmolytic disease due to blood group incompatibility were excluded from both groups

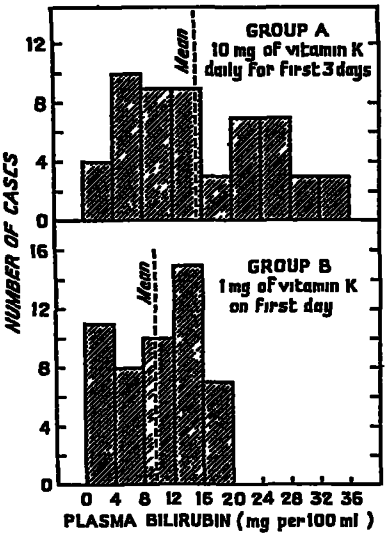
The two groups received the same routine care, apart from dosage of vitamin K

Plasma bilirubin levels were estimated in heparinised plasma by King's (1951) method Blood was obtained by puncture of a femoral vein

Results

The direct reaction with van den Bergh's reagent was negative in all the cases

The distribution of the plasma bilirubin levels in the two groups is shown in the accompanying figure The mean level in group A was 15 4 mg per 100 ml and in group B 9 7 mg per 100 ml The difference between the means (5 7) is four times the standard error of the difference (1 44) Thus there is a significant difference between the two groups



Distribution of fifth-day plasma bilirubin levels in premature babies according to dosage of vitamin K

The accompanying table compares the number of babies with a plasma-bilirubin level of 18 mg per 100 ml or higher in each group as a whole and when subdivided into standard birth weight ranges In group A the total is 21 of 55 (38%), whereas in group B it is 2 of 51 (4%) This difference is significant at the 0 1% level Further, it will be seen that the difference between groups A and B is reflected in each birth weight range

There were 2 deaths from kernicterus in group A one in a baby of birth weight 3 lb 10 oz and with a fifth day plasma bilirubin level of 34 mg per 100 ml, and the other in a baby of birth weight 4 lb 7 oz and with a plasma-bilirubin level of 22 mg per 100 ml 3 other babies had mild symptoms on the seventh day (lethargy and irritability when disturbed) which might have been due to kernicterus, their fifth-day plasma bilirubin levels were 24 4, 27 8, and 33 mg per 100 ml All 3 infants appeared normal at the age of 1 year

NUMBER OF PREMATURE BABIES WITH PLASMA-BILIRUBIN LEVELS OF 18 MG PER 100 ML OR HIGHER, ACCORDING TO WEIGHT AND DOSAGE OF VITAMIN K

Birth weight	Group A (30 mg vit K)		Group B (1 mg vit K)	
	No of cases	Plasma bilirubin 18 mg per 100 ml or higher	No of cases	Plasma bilirubin 18 mg per 100 ml or higher
3 lb 4 oz or less	9	5 (*55 5%*)	10	1 (*10 0%*)
Over 3 lb 4 oz to 4 lb 6 oz	23	10 (*43 5%*)	15	0
Over 4 lb 6 oz to 5 lb 8 oz	*23*	6 (*26 1%*)	26	1 (*3 8%*)
Total	55	*21* (*38 2%*)	51	2 (*3 9%*)

In group B there were no deaths and no baby developed symptoms suggesting kernicterus

Discussion

Premature babies tend to bleed in the first week of life (Smith 1954) It is usually advised that vitamin K be given to all premature babies after birth to prevent hypoprothrombinæmia, which is one factor producing the tendency to bleed Large doses of the vitamin (up to a total of 90 mg) have been used routinely in some centres

The present results show that the dose of synkavit given to premature babies after birth affects the degree of hyperbilirubinæmia on the fifth day of life The importance of this effect is shown by the fact that about 40% of the 55 infants given 30 mg of synkavit had plasma bilirubin levels of 18 mg per 100 ml or higher, and 2 died of kernicterus In hæmolytic disease of the newborn a plasma bilirubin level of 18 mg per 100 ml or higher is dangerous because of the possible development of kernicterus, and probably levels of this order are equally dangerous for all premature infants Certainly we have seen a small area of bile staining in the basal ganglia of a premature baby, not in this series, who died of an intercurrent illness and had a plasma bilirubin level of 17 8 mg per 100 ml a few hours before death

Only 2 of the babies given 1 mg of synkavit had a plasma bilirubin level of 18 mg per 100 ml or higher on the fifth day One of these babies had a birth weight of 4 lb 12 oz, and usually the reduction in the plasma-bilirubin levels in babies given the smaller dose of synkavit has been less marked in those with a birth weight over 4 lb 6 oz It must be remembered that fifth day plasma bilirubin levels are not necessarily maximal, and it is possible that a few babies given 1 mg of synkavit had levels above 18 mg per 100 ml either shortly before or after the fifth day

These findings indicate that a decrease in the incidence of kernicterus of prematurity could be anticipated if the practice of giving large doses of vitamin-K analogues to premature infants were abandoned Since it has been shown that one dose of 0 5–1 0 mg of vitamin K is as effective as larger doses in preventing postnatal hypoprothrombinæmia (Lehmann 1944), this dose might well be adopted universally for routine use

We have not investigated the mode of action of vitamin K in increasing hyperbilirubinæmia A reduced capacity of the liver to transform the indirect-reacting pigment, bilirubin, to direct reacting bile pigment is thought to be the major cause of the hyperbilirubinæmia of newborn

Among the 40 people who had stopped using their aids, the commonest reason given was noise and headache, 9 of them complained that the aid was too heavy Thus, the great majority of those who received the medresco aid were much better for it GETTES and TRACY remarked "Our general impression is that individuals who obtain employment and become deaf in the course of years usually retain their occupation and are helped to do so as the result of the provision of a hearing-aid On the other hand, deafness as such appears to make it difficult for some individuals to obtain employment, which difficulty is often overcome by the provision of a hearing-aid" They made no attempt to correlate the value of a hearing-aid with the causes of deafness From a medical rather than from a social point of view this information is, of course, of the utmost importance

KODICEK and GARRAD[3] have lately described a large survey of users of the medresco aid, and they included in their findings considerable detail about the relative values of the aid in different types and degrees of deafness They sent out 1459 questionaries to all patients who had been issued with an electrical hearing-aid by the ear, nose, and throat department at St Thomas's Hospital at least six months previously 964 replies were analysed The patients were placed in one of four main diagnostic groups according to the primary causes of deafness otitis media (29% were in this group), otosclerosis (41%), presbyacusis (senile deafness) (15%), and nerve deafness from other causes (15%) Thus, 70% suffered from conductive deafness, and the remaining 30% were about equally divided between cases of acquired nerve deafness and senile cochlear changes The otosclerotic group made the best use of the aid and seemed to get most help from it, wearing it both for work and pleasure The otitis media group was second best, as expected on clinical grounds These two groups accounted for more than two thirds of all the patients, yet only half of the 93 returned instruments came from patients in these groups An average loss of 60 decibels in the speech frequencies for both ears (by pure-tone audiometry) was taken as the dividing line between moderate and severe deafness, and it is interesting that those who were judged to be only moderately deaf were more critical of the aid, and used it less often and for fewer hours each day, than did patients with severe deafness Over half the employed people used their hearing-aids at work, but, from volunteered comments, it was clear that factors limiting the use of the aid at work were weight of batteries, background noise from clothes rub, and restriction of movement by the leads On the other hand, 19 patients volunteered the information that the aids had enabled them to stay at or return to work In reply to direct questions, over 90% said they found their aids helpful and that they had made their lives easier or more enjoyable The fact that 525 people failed to reply raises the question of the general applicability of the findings, and KODICEK and GARRAD think it probable that there was a larger proportion of satisfied patients among those who replied than among those who did not

However that may be, there are many thousands of people whose lives have been changed by the medresco hearing-aid When the National Health Service was introduced, the Government set out to produce an aid that would benefit the majority of deaf persons, at a reasonable cost they succeeded That is not to say there is no room for improvement there are very few hearing-aid users who would not welcome a less cumbersome "monopack" aid, and a preliminary trial has already been carried out with such a model It is only to be hoped that its general issue will not be too long delayed, although we are already warned that the earliest issues will be reserved, quite rightly, for children The transistor aids, with their lighter weight and longer battery life, offer attractive possibilities for the future, but they have yet to be put to the hard test of daily wear and tear, and it would be unreasonable to expect this latest modification to be applied to the Government aid until its rightful place has been carefully assessed As HELLER[4] puts it, "the advantages of transistor hearing aids lie in the realm of convenience and economy rather than in performance It is well to bear in mind that vacuum tubes have been used and studied for a much longer time than have transistors The latter are but recently developed and have considerable margin for change and improvement"

Annotations

PRINTING DISPUTE

SINCE work was provisionally resumed in the London printing-houses seven weeks ago, we have produced abnormally large issues of our journal so as to make up for some of its deficiencies in February and March But some obligations to subscribers and contributors inevitably remain unfulfilled, and, now that a settlement of the printing dispute has been announced, the Proprietors have decided to extend subscriptions to THE LANCET for four weeks beyond the present date of expiry To readers who obtain the journal through a bookseller or newsagent, and who were supplied with our token copies in February and March no charge will be made for the four issues of July

ANÆSTHESIA IN OBSTETRICS

THE benefits of new drugs and techniques in general anæsthesia are only slowly being brought into obstetric practice There can be few set operating lists in obstetrics and anæsthesia may be needed at any hour of the day or night Consequently the duty of giving the anæsthetic often falls to a junior and inexperienced resident But obstetric anæsthesia is seldom a simple matter, the patient may be unprepared and seriously ill, and there is usually a second life to consider Anæsthesia now holds an unenviably high place among the causes of maternal mortality,[5] and it therefore seems likely that a proportion of maternal morbidity and fœtal complications can also be attributed to it Yet modern methods, properly applied, have much to offer, not only by making conditions safer for operative obstetrics but by conferring advantages which, though less easily measured, can be found in such factors as a higher than normal maternal oxygen concentration and relaxation of skeletal muscle without uterine or fœtal depression

On another page Dr Coleman and Dr Day describe the use of a cuffed endotracheal tube in obstetric anæs-therapy The average myeloid erythroid ratio was 3 9/1 in both the treated and untreated groups Therefore in this series there is no evidence of stimulation of the bone-marrow by these dosages of radiation to the spine

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Plasmacytosis

The normal level of plasma cells in the bone marrow was discussed by Hayhoe and Smith (1951), who reviewed the findings of several other workers and concluded that 2% or more was above the normal maximum

In the 10 patients with an increase in plasma cells (2 0–3 8%) there seemed to be no relationship between the plasmacytosis and a history of previous irradiation Of the 18 patients who had not been treated with X rays 6 showed plasmacytosis Of the 6 patients who had received previous irradiation 4 showed plasmacytosis Although, when investigated the E S R was raised in patients showing plasmacytosis, the converse was not true

The plasmacytosis may be explained by some relationship between ankylosing spondylitis and rheumatoid arthritis Hayhoe and Smith (1951) reported 10 consecutive cases of rheumatoid arthritis showing an increase in bone-marrow plasma cells, which was usually associated with an increase in the plasma-globulin fraction The plasma-proteins, however, were not studied in the present patients with ankylosing spondylitis

Eosinophilia

The normal level of eosinophils (both mature and precursor forms) in the bone-marrow was considered to be up to 7 5% (Whitby and Britton 1953)

Among the 4 patients with eosinophilia (8 4–14 6%) in the present series 1 had received X-ray therapy, but the 3 others had not 2 of the patients with eosinophilia showed also plasmacytosis (1 had received X-ray therapy but the other had not)

Eosinophilia occurs in many diseases where there is a body reaction to foreign protein In all 4 patients with eosinophilia the E S R was raised

Summary

28 bone-marrow examinations are reported from patients with ankylosing spondylitis

The only significant abnormalities in the bone-marrow were plasmacytosis in 10 patients and eosinophilia in 4

These findings could not be correlated with previous X ray treatment

We are grateful to Prof J S Mitchell for advice and permission to publish

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ORAL STREPTOMYCIN IN BACILLARY DYSENTERY

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THE high prevalence of bacillary dysentery in the past fifteen years has apparently been uninfluenced by the introduction of chemotherapy and antibiotics, nevertheless the prevention of spread of dysentery may be aided by the successful treatment of acute cases and carriers

In recent years sulphonamides have produced fewer bacteriological cures in bacillary dysentery, this is generally held to be because resistant strains of shigellæ have appeared, and therefore the use of antibiotics must be considered seriously

Zintel et al (1945) showed that streptomycin administered orally produced a high concentration in the gut (particularly after four days treatment) and that absorption was negligible The earliest reports of its use in bacillary dysentery came from the United States, and good results were obtained by Hardy and Halbert (1948) in 37 cases of Flexner (Z) dysentery treated with 1 or 2 g daily for three days Ross et al (1949) gave a longer course for an average of 10 7 days to 34 cases with results which compared favourably with those in a control group treated with sulphadiazine In Shanghai, Chang and Su (1951) claimed a reduction in mortality from 14 to 4% using streptomycin. in their series of 110 cases they confirmed the rapid clinical response and the early disappearance of shigellæ from the stools, reported by the American workers

There are few reports from this country, and no large series has been published In a study of the sensitivity of *Shigella sonnei*, Forbes (1953) successfully treated 16 acute cases and 1 carrier with oral streptomycin, he gave 0 5 g *twice daily for two or three days with bacteriological* cure in all cases, although in 1 case the fæces proved bacteriologically positive on the sixth day after treatment 3 additional cases responded satisfactorily to streptomycin after sulphonamides and chloramphenicol had failed

More recently Abbott and Parry (1955), comparing the efficacy of tetracycline, phthalylsulphathiazole and oral streptomycin in Sonne dysentery, found that of 25 cases of all ages treated with streptomycin (0 5 g twice daily for three days) only 9 (36%) were cured by one course Similar results were obtained in the sulphonamide group of which 34% of 32 cases were cured by a seven-day course, but a high degree of success (96% of 27 cases cured) was achieved with tetracycline, again with a seven-day course

Previous Series

Of 200 consecutive patients (94% of whom were infected by *Sh sonnei*) treated in the City Hospital, Edinburgh, in 1948–49 with a seven-day course of succinylsulphathiazole or phthalylsulphathiazole or a combination of both drugs, all the 30 patients over 6 years old were cured by one course of treatment But of the 170 patients who were under 6 years old, only 106 (62%) were cleared by one course, 38 (22%) were cleared after two courses, and a further 8 (5%) after three courses, the remaining 18 (11%) were ultimately given streptomycin orally (1 g daily for five days) with good results, after four to six unsuccessful courses with several sulphonamides

The satisfactory *response in these 18 cases (they* were essentially convalescent carriers, having had positive stools for twenty nine to eighty-three days before streptomycin was started) *prompted me to use streptomycin* in acute cases In 13 such cases, the clinical response was entirely satisfactory, symptoms subsided in two to three days and all fæces were bacteriologically negative for periods ranging from thirty to fifty-eight days after the end of the five day course I therefore decided to adopt this form of treatment routinely for children, and later I extended it to patients of all ages

Present Series

The series comprises 1474 cases of proved bacillary dysentery treated with a five-day course of streptomycin at the City Hospital, Edinburgh, during the five years between November, 1949, and October, 1954 Cases of "clinical" dysentery and non-specific enterocolitis similarly treated are not included Most of the patients (1177) had *Sh sonnei* infections and the remainder (297) had *Sh flexneri* (type Z or X) infections, there were 1421 acute cases and 53 symptomless carriers The patients' ages ranged from 5 days to 79 years, most of them were under 10 years of age with chest pain there may be more in an advanced stage of the disease than there are among those who first have other symptoms." Taylor and Waterhouse[10] found that only 3% of 332 in whom the illness began with pain had a pneumonectomy, compared with 9% of those in whom the illness began with a cough and 13% of those in whom it began with hæmoptysis. Neumann et al., however, noted little difference in the proportion who underwent resection between patients under 40 and patients of all ages.

There is probably a greater danger in young people that the correct diagnosis will be missed, for in them lung cancer may not be so readily suspected. As we seem to be in the early stages of what has been termed a "pandemic" of lung cancer[11] this disease might well be put higher on the list for differential diagnosis even in those under 40.

SEMI-RETIREMENT

LAST week the National Insurance Advisory Committee recommended that the earnings rules for retirement pensions should be relaxed.[12] By their terms of reference they could suggest no radical changes, but their report has strengthened public interest in the principles on which our pension scheme is based. The committee recommended, and Parliament has now agreed, that retirement pensioners shall in future be allowed to earn 50*s* instead of 40*s* a week without loss of pension, and that pensioners earning over 50*s* a week shall have sixpence deducted from their pension for each shilling earned between 50*s* and 70*s* a week. This means that a pensioner can earn up to £5 a week before his pension is extinguished.

Probably these changes are as far as we can go without jettisoning the principle of pension on retirement rather than at a fixed age. Whether the principle is worth retaining is another matter. When unemployment was a national bugbear it was sensible to encourage elderly people to retire early and to give them some modest help to do so. But overemployment not underemployment is now our trouble, and today it might be equally sensible to encourage old people to remain at work as long as possible. Furthermore the proportion of old people in our population will rise steadily in the coming years. The help that they could give us will accordingly become more substantial, and, if need be, make it worth altering or adapting industrial traditions. In his reservation to the Phillips Committee's report Prof. A. K. Cairncross recast the problem. "Men of 65–70 (he said) should be free to choose not whether to retire but how much to retire." It is doubtful whether our present system of pensions gives them this freedom.

In defence of the principle of retirement and its bulwark the limitations of earnings, it is usually argued that employers would use the pensioner to cut wages, and that we cannot afford to pay full pensions irrespective of earnings. The advisory committee note that the abolition of the earnings rule would cost £76 million straight away. In his recent review of the subject Mr. Alan Peacock[13] was not greatly moved by either of these objections. The trade unions, he felt, might be relied on to defend the wage front. The Government Actuary on the other hand he thought might be overanxious. Had he not left out of account what the pensioners would bring to the Treasury by their effect on production and by their own increased expenditure? But Mr. Peacock agreed that the subject was difficult, for we are discussing the pensions problems "without any supporting inquiry into the economic resources of the aged."

Our nescience does not cover only the economic problems of the aged but extends to the intricacies of their pattern of employment. Here Mr. F. Le Gros Clark, with the backing of the Nuffield Foundation, is offering us a series of detailed reports on the kind of jobs that the elderly find for themselves. In his latest report[14] he has continued his inquiries among the employment exchanges and has discovered that many of the jobs found for the elderly are those that "have survived with us from the largely unmechanised world of the past." Perhaps this is a complementary problem to automation and one which in its way may prove as important.

POLIOMYELITIS FLOCCULATION REACTION

SPECIFIC flocculation reactions take place when a bacterial or viral antigen and its specific antibody are brought together under suitable conditions; macroscopically visible aggregates or clumps, appearing in antigen-antibody mixtures but not in controls, indicate a positive result. The term "flocculation" covers two phenomena: agglutination reactions, in which suspensions of large particles, such as bacteria, are clumped by specific antibody; and precipitin reactions in which very small particle antigens (often referred to loosely as soluble antigens) are precipitated by their specific antibody. Basically the reaction is the same in both cases. The term flocculation is sometimes used to cover them both, and also to describe the clumping of particles intermediate in size between bacteria and small particle antigens—for example, viruses. Antigens which flocculate with their specific sera usually fix complement under appropriate conditions, and flocculation and complement fixation have been useful techniques in investigating the antigenic properties of viruses and the serological responses of men and animals to infection. Flocculation reactions generally require the use of more concentrated and purified antigens than do complement-fixation tests, and for that reason the latter have been more often applied in virological investigations.

Recently Belyavin[15] showed that a specific flocculation reaction between influenza virus and antibody could be used for serological investigation of these viruses. Prof. Wilson Smith and his colleagues have followed this by applying the flocculation reaction to the poliomyelitis viruses, and on p. 710 they show very clearly that specific flocculation occurred when purified type 1 and type 3 poliomyelitis virus antigens were mixed with specific rabbit antisera. There is also preliminary evidence to suggest that specific flocculation may take place with sera of children convalescent from poliomyelitis. The test is likely to be useful in investigating the antigenic structure of the poliomyelitis viruses. On the other hand it is less likely that without substantial modifications the test will be much used in the routine laboratory diagnosis of poliomyelitis. This is because relatively large amounts of an antigen which has been previously concentrated 38.5 or 77 times are required, and it may be that complement fixation would be a more economical test to apply to this material. If not, however, the possibilities of a micro test seem well worth exploring. It would also be important to devise some method of inactivating the virus, if the test is to be used as a routine laboratory procedure.

THE next session of the General Medical Council will open on Tuesday, May 29, at 2.15 P.M., when Sir DAVID CAMPBELL, the president, will deliver an address. The Medical Disciplinary Committee will meet on Wednesday, May 30, at 2 P.M.

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[10] Taylor, A. B., Waterhouse, J. A. H. *Thorax*, 1950, 5, 257.

[11] Clemmesen, J. *Dan. med. Bull.* 1954, 1, 37.

[12] Cmd. 9752. H.M. Stationery Office, 1956. 2*s*.

[13] *Manchester Guardian*, May 4, 1956, p. 8.

[14] Le Gros Clark, F. Employment Problems of Elderly Men. 1956. Pp. 25. A limited number of free copies available from the Nuffield Foundation, Nuffield Lodge, Regent's Park, London, N.W.1.

[15] Belyavin, G. *Lancet*, 19[illegible], i, 698.

steady increase to approximately 25% in 1951–53, and by 1954 the proportion had risen to almost a third This increase was not responsible for the poorer results obtained latterly (table II) because, although the over all Flexner figures are slightly lower in the under-6 age-group, the chances of success after one course are more or less equal—i e , 4 out of 5 cases were cured, irrespective of the type of organism

TABLE IV—RESULTS OF TREATMENT WITH ORAL STREPTOMYCIN OR PHTHALYLSULPHACETAMIDE

Drug	No of cases	No of cases cured with			*Sh sonnei*	*Sh flexneri*
		1 course	2 courses	2 courses plus oxytetracycline		
Streptomycin	102	87	10	5	71	31
Phthalylsulphacetamide	102	53	28	21	73	29
Total	204	140	38	26	144	60

A Further Sulphonamide Trial

During 1953, sulphonamide was given a further trial Half the patients were given phthalylsulphacetamide ('Enterocid') in the recommended dosage for five days and half were given streptomycin (1 or 2 g according to age) for four days , all cases were treated as far as possible under similar conditions and the test of cure described above was employed Both groups were comparable as regards age and duration of symptoms The results are summarised in table IV

Better results might have been obtained with phthalylsulphacetamide if a longer course (seven days are recommended) and perhaps larger doses had been given Nevertheless it was clear that the sulphonamide results, which were similar to those obtained in 1948–49, did not compare favourably with those of the oral streptomycin group Although the four-day course of streptomycin was as effective as the five day course at that time, it was decided to continue with the latter to provide suitable comparison through the years

Discussion

The choice of dosage and duration of the course of oral streptomycin was influenced to a large extent by the experimental work of Zintel et al (1945), who suggested that 1 g of oral streptomycin daily would give a maximum concentration of streptomycin in the lower bowel of a healthy subject after four days Because the calculation of an optimum dose for each case was impossible owing to many variable and unpredictable factors and the absence of accurate fæcal estimations of streptomycin, I felt that a fixed amount, perhaps excessive in some cases, would be best, particularly as the effect of the streptomycin was almost entirely local Although the tests of cure in this series are not ideal, they were satisfactory in practice , in most cases which were still infected, confirmation was obtained from the first three clearance specimens

Forbes (1953) showed that, in vitro, streptomycin kills *Sh sonnei* in lower concentrations than aureomycin, chloramphenicol, or oxytetracycline, but that *Sh sonnei* acquires resistance to streptomycin earlier than to the others While this suggests that a short course of treatment is advisable, the speed of bacteriological cure is likely to be affected by the extent of the disease in the lower bowel and the accessibility of the organisms The five day course was considered sufficiently short to reduce the risk of resistance to negligible proportions , but, as a further precaution, if no sensitivity test had been done the course was repeated once only when indicated If the second course was unsuccessful another antibiotic (chloramphenicol or oxytetracycline) was given—with satisfactory results in all but a few cases Although the proportion of cases in the under-6 age group requiring more than one course of streptomycin increased from 11 to 20% during the survey, at least 95% of cases were cured by two courses throughout the five-year period (table II) This high degree of success attained by a second course does not suggest that the shigellæ soon acquire resistance but possibly in time this disadvantage will become more apparent

There were no toxic effects of the treatment , a few infants had a mild dermatitis in the napkin area, which may have been produced or aggravated by the streptomycin, but this subsided within a few days after the treatment was stopped

The results were equally satisfactory in acute cases irrespective of the duration of illness before treatment, and in carriers Moreover, the rapid control of symptoms (particularly diarrhœa) probably to some extent reduced the risks of auto-infection and cross infection A further benefit, of considerable importance to the patient as well as to the hospital, was the reduction of the patient's stay in hospital , this led to a considerable saving of time and beds Initially the cost of streptomycin treatment was relatively high, but this was offset by the advantages of a quicker turnover, and, with ever falling prices, streptomycin can now be used economically on a wide scale

It seems that streptomycin, administered orally, is useful and safe in the treatment of bacillary dysentery, and is to be preferred to sulphonamide That bacterial resistance will in time render it less effective is distinctly possible, but at present there is no strong indication for the routine use of newer antibiotics, some of which may have certain disadvantages

Summary

In 1949–54, 1474 cases of proved bacillary dysentery were treated with a five day course of streptomycin Although the percentage of first-time cures fell over the five years, the results in 1954 were still better than those previously obtained with sulphonamides , at least 80% of cases were cured by one course and 95% by two courses

A small trial (204 cases) in which phthalylsulphacetamide and streptomycin were compared showed that streptomycin was more effective and that the sulphonamide results were similar to those obtained before streptomycin was used

Oral streptomycin proved highly effective in clearing carriers who had been treated unsuccessfully with sulphonamide, as well as in acute cases

It is safe, reliable, and economical, but in time drug resistance may render it less effective

I am indebted to Dr A Joe, medical superintendent of the City Hospital, Edinburgh, for his support in this investigation The initial supply of 'Enterocid' was kindly provided by British Schering Ltd

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symptoms necessitated their recall. Where abnormalities had been found, a large film was taken and the patient was given a clinical examination and sputum tests (or, in the absence of sputum, a laryngeal swab). When other lesions were suspected—e.g., bronchiectasis or amœbic abscesses (which were frequent)—physical examination and special laboratory tests followed and the patient usually went to the tuberculosis hospital for bronchoscopy or bronchography. But, with all these diagnostic facilities, some cases remained undiagnosed. They were those with cavitation resembling tuberculosis but with negative cultures and equivocal histoplasmin and other skin tests. Though sputa were repeatedly examined for parasites and fungi, our facilities for and knowledge of, special methods were quite often insufficient for any firm diagnosis.

Sputum tests were based on the standard staining technique, followed by cultures to exclude acid-fast saprophytes. Owing to the shortage of incubator space only those positive sputa could be cultured which did not tally with the radiological appearances. Before the termination of the project amendments to such technical shortcomings had already been approved.

As a routine cultures were set up in two bottles, one containing Lowenstein-Jensen and the other Medlar-Sesano medium, which were prepared in the project's own laboratory. The processing of cultures was hindered by shortages of reagents unobtainable in Thailand, by electricity cuts which affected the running of the incubators, and above all by contamination with moulds, which during the rainy season abounded everywhere—in books, in shoes, in clothes, and (not surprisingly) in the laboratories too. Repeated revision, and strict observation, of sterility rules on which expert advice was sent from the Serum Institute in Copenhagen, reduced the contamination-rate to 3% at the time of the team's departure and after another year's experience it had come down to 1%.

The laboratory also undertook tests of sensitivity to streptomycin and drugs, blood grouping, and clinical blood examinations (for which a small room with separate entrance was set aside). It did routine examinations of excreta, especially for intestinal parasites and their ova.

Prevention

In the domain of prevention the public health nurses held the key position. As soon as the diagnosis of tuberculosis was made or suspected, the doctor referred the patient to them.

The general plan was directed towards:

(1) Prevention of primary infection.

(2) Prevention of breakdown of lesions seemingly healed.

PREVENTION OF PRIMARY INFECTION

Elimination of Source of Infection

As it was impossible to admit every patient to hospital the first subject of instruction was the collection and *disposal of sputum* and contaminated material. The standard practice was to use as sputum containers the cigarette tins so abundant in Thailand. They had to be placed on a charcoal fire until the contents turned black, and the nurses spent much time in explaining their correct use, recommending a no-touch technique in which the tins were handled with tongs. When it was discovered that little children—numerous in nearly every dwelling—played with the tins and upset their content patients were told to put them out of reach; but, since in hot countries people squat on floor mats, such counsel proved more theoretical than practical. A new plan was therefore adopted whereby rolls of toilet paper were used as handkerchiefs and were immediately slipped into paper bags, made from newspaper, which could easily be fixed on a chair or at the bedside and could be burned daily. This became also the routine method at the tuberculosis hospital, where a paper bag was attached to each bed—which was quite handy for the very sick and instructive to students. The nurses then advised on how to cleanse contaminated linen—by soaking it in soapy water before washing—and on how to make full use of the sunlight for the sterilisation of blankets, pillows, and the like. In tests made by W.H.O. bacteriologists in India the sun killed tubercle bacilli, in a layer 2 mm. deep, in two hours, and its sterilising action has earned it the title of "the most effective minister of health in the East."

The next important step was to impress on the patient the need for *segregation*, particularly at night. This was the most difficult preventive measure to put into practice. In Bangkok two types of dwelling were in use by the needy:

(1) Huts made of bamboo and atap palm, or of wooden planks built on stilts. Though sometimes there was space under the house, this was often flooded (the rainy season lasts five to six months) and full of refuse.

(2) Small one-storey houses in rows in narrow lanes with no space outside in which sleeping benches could be put up.

The average size of a room accommodating about 6 persons was 4–5 square metres. Ventilation was fairly good on the whole, and the rooms were generally kept clean; but sanitation was extremely poor, with primitive means of disposing of fæces and waste. Lighting was by kerosene lamps which were a fire hazard. Furniture was at a minimum, the chief item being a mosquito net under which five or six people slept on grass mats on the floor.

Desperate though this situation was in most of the dwellings, there were some more spacious habitations which even had a yard or some little extra ground where a separate bench could be erected. This had to be

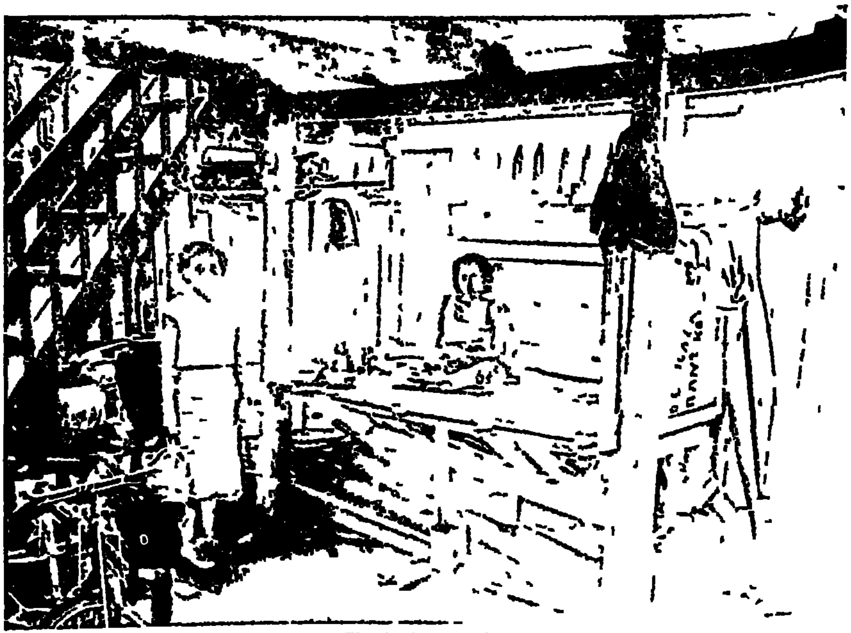

Fig. 1—Segregation.

Where some grounds or a yard were available, tuberculous patients were advised to use simple inexpensive sleeping benches made of wood from crates or remnants of wooden boxes. A mat was laid on the floor of the bench and a mosquito net affixed. The health visitor is seen on the left.

are presented in fig 2 Normal serum produces a dark lavender colour, whereas the serum in hepatolenticular degeneration produces a pale flesh colour The difference is so striking as to be recognised at a glance

Comment

The sequence of development of the characteristic biochemical abnormalities of hepatolenticular degeneration is unknown In several reported series the lowered serum copper-oxidase activity presented the most consistent and striking abnormality (Bearn and Kunkel 1952, Cumings et al 1955, Markowitz et al 1955) The lowered serum-copper-oxidase activity may be the most firmly established biochemical defect by reason of having been present longest—i e, the initial manifestation of hepatolenticular degeneration Reasoning on different grounds has led others (Bearn 1953, Scheinberg and Gitlin 1952) to suggest that deficient synthesis of cæruloplasmin (copper-oxidase) might be the primary defect If this hypothesis is correct, the use of this simple and inexpensive colorimetric technique in screening patients with obscure disease of basal ganglia or of the liver should detect those with incipient hepatolenticular degeneration far earlier than is at present practicable

It is not known whether the enzyme deficiency of the serum is always present from birth or has a gradual or abrupt onset before the development of clinical manifestations If the latter, a normal or near-normal oxidase activity could conceivably be found in someone who subsequently develops hepatolenticular degeneration Therefore, until evidence has accumulated on this point, it would be unwise to discount the possibility of early hepatolenticular degeneration on the basis of a single normal determination

Summary

A simple colorimetric technique is described for the estimation of serum-paraphenylene-diamine oxidase

Application of this test in cases of obscure liver or brain dysfunction may lead to the detection of early hepatolenticular degeneration and to earlier and more effective therapy

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VITAMIN-B_{12} DEFICIENCY DUE TO DEFECTIVE DIET

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It is now recognised that there is a deficiency of vitamin B_{12} in addisonian pernicious anæmia (Berk et al 1948) A similar deficiency may develop in patients who have undergone gastric operations (*Lancet* 1955) or who have intestinal anastomoses, strictures, or blind loops (Mollin and Ross 1954) It has also been described in about a third of the patients with a megaloblastic anæmia associated with "idiopathic steatorrhœa" (Mollin and Ross 1954)

Vitamin-B_{12} deficiency due to an inadequate intake of the vitamin is much rarer, at least in temperate zones Megaloblastic anæmia and neurological lesions responding to treatment with vitamin B_{12} have occasionally been observed in people who take a strictly vegetarian diet, from which all animal protein, including dairy produce, has been excluded (A G Badenoch 1952, J Badenoch 1954), in such persons low serum concentrations of vitamin B_{12} have been recorded (Mollin and Ross 1954, Wokes et al 1955)

This paper records details of a patient who was not a true vegetarian, but who had a megaloblastic anæmia associated with B_{12} deficiency which was due to inadequate intake of vitamin B_{12} in the diet

Methods

Hæmatological methods were those described by Dacie (1950)

Serum vitamin B_{12} assays were made with *Euglena gracilis* var *bacillaris* using the method described by Ross (1952)

Gastric biopsies were carried out using the tube designed by Wood et al (1949)

Fat balances were carried out over a continuous nine day period The patient was given a diet containing 50 g of fat daily After four days on this diet all stools were collected for five days and the fat content estimated

Absorption of vitamin B_{12} was estimated by determining the excretion of radioactivity in the fæces after the oral administration of a test dose of radioactive B_{12} labelled with cobalt 58 Details of the method employed have already been given (Bradley et al 1954, Baker and Mollin 1955)

Case-report

An old age pensioner aged 77 was admitted to hospital on Nov 6, 1954, complaining of weakness and fatigue of three months duration and of increasing swelling of her legs for one month

History

In 1919 she had a gastro enterostomy for relief of a duodenal ulcer After the operation pain persisted and she severely restricted her diet Since 1943 she had existed on a diet of bread and margarine tea and potatoes She had taken no meat or fish, and her only available source of animal protein was the small amount of milk with which she flavoured her tea For a year before her admission to hospital she had taken orange juice daily For many years she had taken about 2 oz of Glauber s salt daily and she passed about five or six watery motions a day For ten years she had suffered from distressing prolapse of the rectum There was no history of anæmia in her family

Examination

She was a thin poorly nourished woman (height 5 ft 3 in weight 6 st 1 lb) and she was too weak to stand She was obviously anæmic The skin was sallow but not icteric There was no finger clubbing, koilonychia, or purpura Her tongue was pale but there was no atrophy or glossitis There was moderate pitting œdema of the feet Pulse regular, 72 per min Blood pressure 100/70 mm Hg Jugular venous pressure not raised No cardiac enlargement Soft apical systolic murmur Respiratory system normal Old healed operation scar on the abdomen Liver and spleen not palpable Cranial nerves normal No weakness or wasting Tendon reflexes present and equal Plantar responses flexor No sensory impairment

Investigations

Blood picture —Red cells 1,200,000 per c mm Hæmoglobin 5 4 g per 100 ml Packed cell volume 18% Reticulocytes 2% Mean corpuscular volume 150 cμ Mean corpuscular hæmoglobin concentration 30% Leucocytes 5000 per c mm Stained blood-smears showed macrocytosis and marked anisocytosis and poikilocytosis Sternal marrow biopsy showed moderately severe megaloblastic change Serum-B_{12} concentration was 75 μμg per ml (normal range 100–900 μμg per ml)

Barium meal —The œsophagus was normal The barium passed immediately through the stoma of the gastro enterostomy into the jejunum and also, less rapidly, through the pyloric end of the stomach into the duodenum and afferent limb The afferent limb was short and peristalsis was satisfactory The stoma functioned well and no ulcer was seen

Gastric secretion —Histamine fast achlorhydria was shown on two occasions

Gastric biopsy —Three fragments were obtained at biopsy Dr I Doniach reported 'There was moderate reduction in the thickness of the gastric mucosa Though in some parts specialised cells were partly replaced by mucous neck cells, our doing this on a large scale, but the need for going on with such work was impressed upon our Thai colleagues

A B C G campaign—Parallel with these activities of the public-health nurse a B C G campaign was started at the outset of the project The first object was to test and vaccinate Bangkok school children, but machinery had to be created for an eventual all-Thailand campaign of teaching and propaganda, and medical, nursing, and lay personnel had to be trained in the technique of testing reading, and vaccinating In eighteen months all Bangkok school children were covered by this programme, though a proportion of children of school age who did not attend school were not at first included Over 90% of all the negative reactors accepted vaccination At the age of 15, 73% boys and 63% girls were already tuberculin-positive

After the establishment of our B C G team, in which lay vaccinators played an essential part, a mass campaign was launched, but when it had been in progress for over four months it was handed over to a newly appointed W H O senior medical officer At the time of transfer more than 233,500 children had been tested and nearly 84,000 vaccinated—i e, 90% of the negative reactors By June, 1955, this separate W H O /UNICEF unit had tested nearly 4 million persons, and vaccinated over $1^1/_2$ million They found a much higher proportion of positive reactors in Bangkok than in the smaller towns and the countryside

A small survey on the rate of conversion was undertaken by our project in September, 1952, on nearly 4500 children in the age group 5–18, who had been vaccinated six to ten months previously 81% were found to have converted to positive

Preventive activities had to be carried into the patient's home, but the large number of nurses needed for such a purpose were not to be had in fact, to recruit more nurses was a perpetual struggle Home visiting was a trying and tedious job Transport difficulties were enormous—buses overcrowded, *samlors* (the popular tricycle) dangerous, and the project's facilities wholly inadequate Most of the patients' dwellings were far away from the main roads, often they could be reached only by a quarter of an hour's walk over cat planks (fig 3) or through muddy lanes In the constantly hot and humid climate all this was bound to tire out any home visitor Then there were "the baffling masses of houses and shacks with no sequence or complete lack of numbering, forming a bewildering topography," to quote the W H O public health nurse's report Often the patient could be found only by mouth to mouth inquiry —which took a lot of time Yet, to make preventive work effective, repeated visiting was essential Nurses had to make friends with the patient and his family, who themselves were encouraged to spread the gospel of prevention Much help was given to our project by the W H O /UNICEF maternal and child health project, whose nurses looked after the tuberculous in their area

A monthly radiological survey of all pregnant women was made at the maternal and child health centre by our project's mobile X ray unit The tuberculous were given priority for admission to hospital

PREVENTING THE BREAKDOWN OF LESIONS SEEMINGLY HEALED

Whereas prevention of primary infection was chiefly the concern of the public health nurse and of the B C G team, prevention of breakdown in those already infected was that of the social services Among the patients attending the chest clinic, undernourishment and worry seemed to be the main causes of such breakdown Houses were overcrowded, and vitality and resistance were low, public assistance was still rudimentary, and there were no monetary grants or food supplements Because of financial stringency, our project was not granted an international social worker, but the medical social work expert of the maternal and child health project was able to tap a number of resources for tuberculous patients, thus affording material help to some of them This showed that funds were to be had if one looked for them, and led to fuller recognition of social needs

Treatment

Treatment was taught and practised under two main headings

1 Simple procedures for reducing cough and sputum and "cooling down" an active lesion, and for managing tuberculous meningitis

2 Major procedures for closing cavities and eradicating the tuberculous disease

The simple procedures have already been described they constituted the standard treatment for the out patients of the chest clinic The major procedures were confined to the Nonburi Tuberculosis Hospital, situated in the country, about 22 km from the clinic

By a happy chance an American thoracic surgeon Dr John Wilson,* had been assigned to the Washington University group attached to F O A, to teach in the Thai medical schools, and after several ward rounds with our team, he offered his help in alleviating some of the distressing complications

Within two weeks a blood transfusion service was organised with medically selected inmates of the Bangkok prisons enlisted as donors (No risks were taken with rubber tubings and bottles, new sets being employed every time, with the result that a few minor but no major reactions were recorded in our eighteen months' work) Similar arrangements were made for electrolyte and fluid replacement Instruments anæsthesia apparatus, and other requisites were borrowed from various hospitals and ordered abroad by the government The anæsthetist of Dr Wilson's team, and his operating room supervisor, gave the necessary assistance one of the two resident medical officers was trained in anæsthesia and one nurse in operating room technique

A number of empyemas were relieved by drainage, and within a few weeks the first thoracotomy was performed—on a very ill woman who had had pain and discomfort from a plombage plasty with pingpong balls placed in her chest two years previously This first major operation proved more difficult than was expected, but the result

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* Now head of the surgical department in the medical school of the American University of Beirut

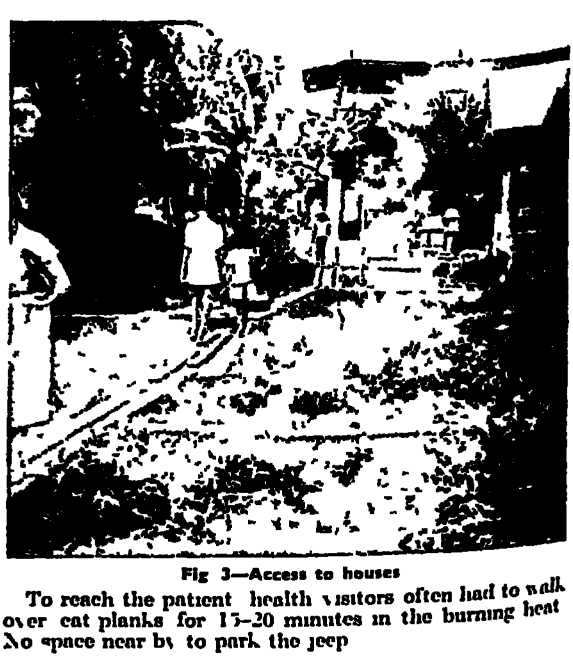

Fig 3—Access to houses

To reach the patient health visitors often had to walk over cat planks for 15–20 minutes in the burning heat No space near by to park the jeep pathological investigation. In this consecutive series there has been no mortality or complications, even though many of the patients were unfit for adrenalectomy. No evidence of any damage to the optic chiasma has been found. (In 2 cases with choroidal metastases vision has improved.) 1 patient, who has been in remission for a year, has a unilateral sixth-nerve palsy, the cause of which is as yet undetermined. There has not been a case of basal meningitis, or of cerebrospinal rhinorrhœa following this procedure.

Further careful assessment and follow-up of these cases is essential before any firm conclusion is reached, but apparently this method of accurate implantation and controlled dosage may prove a safe additional palliative measure in advanced carcinoma of the breast.

Royal Marsden Hospital,
London

W. P. Greening
F.R.C.S.

New Inventions

AN ARTICULATING ENTEROTOME

Since Paul first modestly described his method of colectomy with the formation of a spur in 1895, his operation has continued to be used by surgeons all over the world. In a bad risk case, or where, for a technical reason, colectomy with end-to-end anastomosis is dangerous, Paul's operation still offers a safe method of resection and approximation of the colon.

When restoration of continuity becomes necessary, various devices have been used. Some surgeons prefer formal end-to-end anastomosis, others use various techniques for destroying the spur. The success of the second stage of this operation depends on efficient destruction of the spur between the two loops, and numerous methods and instruments have been used to achieve this. Paul applied a pair of long dressing-forceps, tying the handles together with rubber tubing. Many kinds of enterotome have been used, including one devised by Dupuytren. All the instruments used for this purpose suffer from some defect, and it is difficult to devise one which is satisfactory in all respects. There are certain important points, however, which must be fulfilled if an enterotome is to be efficient.

(1) The blades must be sufficiently long to crush the whole spur, even in a patient with a fat abdominal wall.

(2) The blades should move parallel to one another and not, for example, as the blades of a pair of scissors, otherwise there is a tendency for the instrument to slip off, and for the deepest part of the spur to be uncrushed.

(3) The tips of the blades should meet first, though not so soon that they bite through the spur at the first tightening.

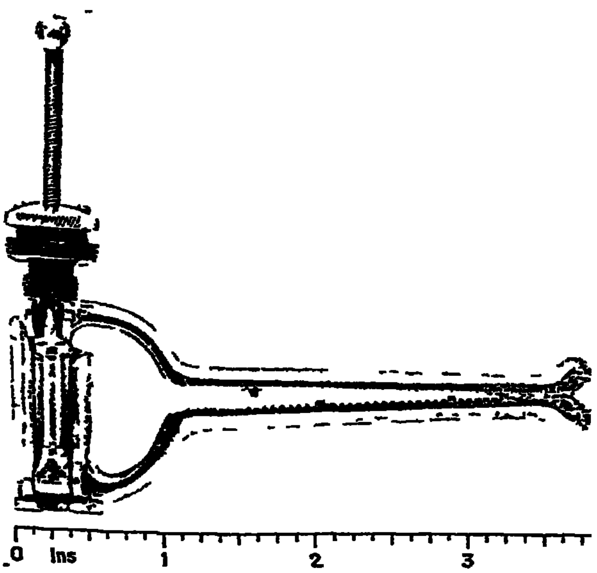

Fig 1

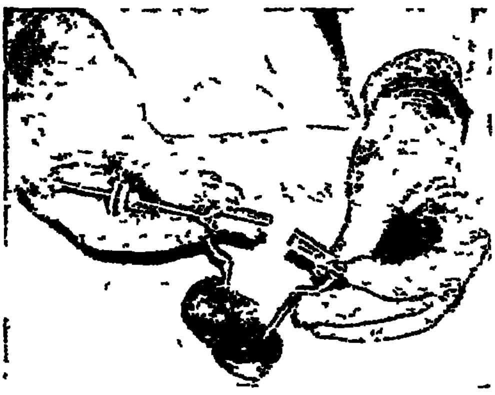

Fig 2

(4) There should be studs on the blades to stop them from slipping.

(5) The enterotome, when locked into place, should lie flush and snug against the abdominal wall.

(6) There must be a screw device which will approximate the blades and later separate them.

(7) If possible, the blades should be detachable one from the other, so that, when the colostomy lies awkwardly, each blade can be separately introduced into each loop of the colostomy and articulated when in position. They may then be screwed up tight.

I have used the instrument described below for five years and can honestly say that, on the whole, it has given satisfaction and does crush the spur right down to its base.

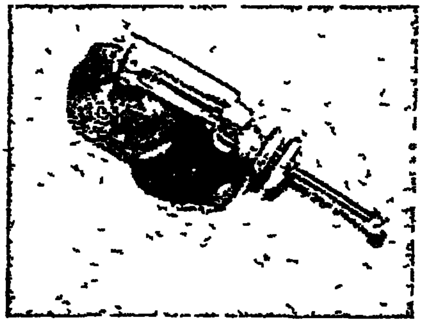

Fig 3

The instrument (fig 1) which is of stainless steel, consists of two serrated blades which "dovetail" like the blades of a pair of artery forceps. The female blade carries a hinged arm, which, when the male blade is slid into position, locks the blades together by means of a collar and knurled nut. The nut both approximates and (most important) separates the blades; it is double because a single nut tends to become unscrewed. The over-all length of the instrument is 4 inches, the blades are 3 inches long and $^1/_4$ inch wide. Each blade is studded to prevent slipping. The instrument is bowed outwards above each blade because, if the spur is crushed in its whole extent, there is a danger that the instrument may fall inside the bowel. Each blade is separately introduced (fig 2), and, when in position, as may be ascertained by passing a finger down alongside the blade, the two blades are locked together and screwed home. When the instrument is articulated and in place (fig 3) it lies fairly flat against the abdominal wall and does not protrude, and so does not tend to move as the patient moves. It is important to lock the blades fairly tightly on the first occasion, and they should be tightened at intervals until they can be tightened no further.

The Lloyd-Davies-Bond enterotome incorporates most of the features set out above, but the instrument described here can be disarticulated to enable the blades to be applied separately and then reassembled easily.

I wish to thank Mr Paul Dawson-Edwards for advice, Mr W Hanke, of Brierley Hill, Staffs, who made the prototype, Mr W E Smith, instrument mechanic of the Queen Elizabeth Hospital Birmingham, who modified it, and Messrs A L Hawkins & Co Ltd, 15, New Cavendish Street, London, W 1, who have made the existing instrument for me.

Queen Elizabeth Hospital
Birmingham

A. Gourevitch
M.C., M.B. Birm., F.R.C.S.

work between Thai, American, and W H O medical personnel

During two terms medical students, in groups of ten, were instructed on how to suspect, diagnose, and prevent tuberculosis, and on first-aid management of the emergencies of the chest It proved more difficult to impart modern knowledge on diagnosis and prevention to undergraduates than to postgraduates, since their professors still put their emphasis on physical signs, hardly considering prophylaxis at all They were also encouraged to spread the gospel of prevention among their own folk and to put it into practice by each taking an interest in three or four tuberculous families Unfortunately, the departure of the international team did not allow this important scheme to be pursued

Whereas most of the above responsibilities were carried by the team-leader, a large teaching programme was also covered by the W H O public health nurse Besides instructing the four to six nurses of her own office individually, she gave courses to student nurses of various hospitals, public-health supervisors of rural areas, municipal nurses, midwives, and sanitarians—with practical demonstrations at the clinic and during home visits The reading of 70 mm films was demonstrated to small groups of doctors by the W H O epidemiologist, who also organised a mass-radiographic survey, supervised the technique of B C G vaccination, helped to build up the B C G campaign, and evaluated the figures with his counterparts The statistician trained two young lay persons, with degrees in mathematics, in comprehensive charting and the principles of medical statistics

On the whole it proved rather difficult to impart theory to technical personnel For example, the local radiographers had not had schooling of a standard enabling them to comprehend elementary physics, and one had to be content with their technical skill and satisfactory photography

Results of Teaching and Training

Diagnosis —When we left, a medical staff of nine were skilled in the diagnosis of tuberculosis and other common chest conditions in so far as the potentialities of the laboratory allowed Four doctors were conversant with the interpretation of 70 mm films within the normal range of over reading and under-reading The bacteriological study of tuberculosis was in the competent hands of the bacteriologist in-charge and two reliable technicians, and several technicians were in training The routine examinations of sputa, taking laryngeal swabs, the preparation of media, the setting up of cultures, sensitivity tests, and (above all) the precautions for sterile handling of material, were under control Three technicians had become accomplished in radiographic technique and two doctors in bronchography and bronchoscopy

Prevention —All the medical staff and the small staff of nurses understood the meaning of prevention and the importance to that end, of combating cough and sputum

Treatment —More than ten doctors had full knowledge of routine procedures and of the diagnosis and management of the emergencies of the chest There was one fully trained surgeon with more than 60 major interventions, resections, and 'plasties (without any fatality) to his credit and a sufficient number of doctors to assist, including one acquainted with the principles of anaesthesia No major transfusion accidents had occurred and no postoperative abnormalities of posture On the medical side the following case histories may illustrate the standard of responsibility attained

(1) A tuberculous diabetic with ketonuria, tension pneumothorax and empyema left the hospital with his diabetes controlled his chest cleared of pus the lung almost re expanded and the residual pleural space obliterated by thoracoplasty His sputum had been freed from tuber bacilli and his weight increased by 7 kg

(2) A woman of 21, seven months pregnant and seriou ill with typical miliary tuberculosis, had complained of seve headache The cerebrospinal fluid was characteristic of tuber culous meningitis With standard treatment her sympto and her fever had long subsided, the cerebrospinal fluid h become normal, save for the number of cells (56 per c mm when she was delivered of a healthy child The baby wa immediately segregated and after four weeks was vaccinat with B C G Treatment of the mother continued until h condition was stabilised

In the past, the presence of a tuberculous lesion wa almost always regarded as an indication for endin pregnancy But when our Thai colleagues under tood that all children are born free of tuberculosis, and scheme for treating the mothers and segregating and vaccinating the newborn was put into operation, th previous policy was abandoned

Retrospect

Was this particular project in Thailand justified?

All three participants invested considerable fund UNICEF generously furnished a laboratory with modern apparatus, sent a mobile radiographic unit, a radioscope, and all the requisites for a mass B C G campaign (including a number of vehicles), and ensured a continuous flow of chemicals, radiographic film material, tuberculin, B C G vaccine, and a number of other items, even after our departure W H O provided the experts and repeatedly sent special advisers, also supplying some apparatus, instruments, and literature The Thai Government fulfilled all its obligations with regard to buildings with reasonable speed it completed a two storey laboratory, an extension to the chest clinic allowing separation of infectious and non infectiou patients, a new hospital block, and a nurses' home, and it commenced and planned a number of other buildings It procured high-quality radiodiagnostic apparatus and modern instruments for thoracic surgery The hospital wards were reconstructed and newly furnished The government also provided all the counterparts to the international personnel, and an additional staff of drivers, motor mechanics, technicians, doctors, and nurses

Among the Thai personnel there were able and talented doctors, nurses, and technicians, but salaries were generally low As a government division, the tuberculo i project could not create a precedent in this matter and the head of the tuberculosis division could certainly not be blamed for the failure to satisfy various social need of his staff But technicians—especially radiographer trained by W H O personnel—were in constant demand elsewhere, and many public health nurses and doctors had to do private practice to earn their living, particularly since most of them had large families This also accounted for a great deal of absenteeism of the nurse

Nevertheless a tuberculosis control project, with diagnostic, preventive, and curative sections, was established, and staff were trained sufficiently for each section to carry on the work indeed the facilities for diagnosi and prevention would have been the envy of many a Western tuberculosis service Moreover, interest in the fight against tuberculosis has been aroused, both in the population and in the medical profession This is reflected in the fact that, a year after the W H O team's departure attendance at the chest clinic had doubled, the chief of the tuberculosis division had been given a teaching appointment for tuberculosis at one of the medical schools, and frequent demonstrations on clinical and pathological chest material were being held by the Thai Medical Association Modern standards of diagnosis prevention, and treatment of tuberculosis are for the first time systematically attained in the country The project's laboratory has become the expert centre for

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J B Field and **De Witt Stetten** described studies on insulin resistance during diabetic acidosis They showed that the quantity of insulin required to save the patient was proportional to the concentration of a serum factor which inhibited the uptake of glucose by the isolated rat diaphragm Further observations on one case located this factor in the α globulin fraction, no adrenal or pituitary effect could be detected

K J Isselbacker, E A Anderson, and **H M Kalokar** demonstrated unequivocally that the essential lesion in galactosæmia is an absence of a specific intracellular enzyme, phosphogalactose transferase

R H Rosenman, S O Byers, and **M Friedman** reported work on anti kidney serum induced nephrosis in rats By preventing the external loss of urine they showed that hyperlipæmia and hypercholesterolæmia did not occur and, if urine loss was permitted, could be reversed by the continuous intravenous infusion of plasma albumin **R M Kark** supported this by reporting 3 patients in whom the intravenous administration of salt free albumin reduced the serum cholesterol and cholinesterase activity

At the meeting of the Association of American Physicians, **C A Janeway** described an arthritic syndrome in children with agammaglobulinæmia It was a polyarthritis, always involving and usually beginning in the knees, and going on to involve the middle sized joints Characterised by intermittent hydrarthrosis, it eventually led to chronic changes in the joints The syndrome was independent of any treatment received, and its ætiology was obscure

An interesting account was given by **I L Bennett** and his associates of an outbreak of pseudomembranous enterocolitis in chinchillas This was due to pathogenic staphylococci and promptly disappeared when aureomycin, which had been added as a growth promoting factor, was removed from the diet A section was shown from the bowel of a patient who died in 1893 from pseudomembranous enterocolitis Appropriately stained, groups of staphylococci and superficial necrosis, very similar to the chinchilla's lesions, were clearly visible

Data on a stilbene like compound (amphenone) were presented by **R Hertz** and his colleagues This substance was shown effectively to suppress adrenocortical activity, but was unfortunately a powerful narcotic Prolonged search has so far failed to reveal non-toxic analogues

W B Shelley and others described studies on the neurophysiological basis for itching They showed first that only certain spots on the skin can feel an itch They were about 1 mm in diameter, 1–2 mm apart, and localised in the dermis Further work showed that the sensation was caused by proteolytic enzymes, of which a number of examples, including trypsin, were given No structural changes were observed

J E Howard reported preliminary studies on a functional test for the detection of hypertension produced by one kidney The method used was to collect urine separately from each ureter, and to estimate its sodium content The concentration of sodium was lower in the urine from the affected kidney

Federation of Experimental Biologists

The Federation includes physiologists, biological chemists, pharmacologists, experimental pathologists, nutrition experts, and immunologists, and in the joint proceedings, also at Atlantic City last month, we were offered 2071 papers read in full (and a number of others by title only) in five days

The most significant papers were probably those recording synthesis of a virus by W M Stanley, H L Fraenkel Conrat, and R Williams,[1] of the California Institute of Technology They took two strains of the tobacco mosaic virus (a and b), broke them into two parts, one protein and one nucleic acid (a_1 and a_2, b_1 and b_2), and then reconstituted them as two new viruses (a_1 and b_2, b_1 and a_2) They went on to show that not only were the reconstituted viruses infective, whereas the fragments were not, but that many of the important qualities of the virus resided in the helical shaped nucleic acid

A series of joint sessions was devoted to atheroma J P Strong and his associates showed that subintimal fatty deposits were always present in human aortas by the age of 3 years, and that the rate of infiltration is greatest between 5 and 15 years T M Lin and his colleagues reported studies on 9 healthy subjects fed on standard diets supplemented by varying amounts of pure cholesterol They showed that, although absorption increased as the total dietary cholesterol increased, the blood-levels remained remarkably constant D W Petersons and his co-workers, however, showed that blood-cholesterol levels could be reduced by adding about 5 7 g of soy sterols daily to a normal diet, this could be concealed in butter, was quite tasteless, and produced falls, of 11% or greater in blood cholesterol J W Hahn and M A Nyman found that whole blood was capable of considerable synthesis of free cholesterol, phosphatides, and fatty acids when passed through a glass cannula, and that this effect was enhanced if a living aorta was substituted for the glass tube, implying some lipid synthesis by the aorta itself

Two papers with immediate clinical application are mentioned from the excellent series on blood clotting A J Quick reported a case of a woman of 22 with a history of mild bleeding since childhood and two severe postpartum hæmorrhages After the second, he found a normal platelet and prothrombin level, but clotting was indefinitely prolonged, and the thrombin time was 43 seconds (normal 3 seconds) He attributed these findings to hyperheparinæmia, and he was able to produce a similar picture by injecting papain into the rabbit D P Jackson and his colleagues reported severe abnormalities of blood coagulation after hæmolytic transfusion reactions in 2 patients In both there were hypofibrinogenæmia, hypoprothrombinæmia, and thrombocytopænia and in neither was there evidence of fibrinolysis One patient had reduced ac globulin activity and plasma thromboplastic component, and a circulating anticoagulant in low titre The picture could be reproduced in experimental animals by injecting thromboplastic substances, and it was suggested that the disorder followed the release of such a substance from lysed red cells

In the section on kidney diseases R C Mellors and L G Ortega gave a fascinating account of the localisation of γ-globulins in the kidney in human nephritis Using an ingenious technique they were able to show that, whereas there is no γ globulin in sections of normal kidneys, or in a variety of other conditions (e g, infarct, pyelonephritis), γ globulin is present in acute hæmorrhagic glomerulonephritis and in chronic membranous glomerulonephritis, but it is confined to the glomerulus

These and many other papers are summarised in the *Federation Proceedings*

Personal Papers

EYE-WITNESS AMONG THE EUGENISTS

The other day I turned up an early manuscript of my own, written some sixty years ago, which describes the first public meeting of the then embryo Eugenics Society As a medical student I enjoyed the meeting so much I lost no time in writing this detailed report For reasons that it may be evident it has not hitherto been published

A short time ago many learned people met together in London to discuss the "Improvement of the Race," or as the subject has recently been christened, the Science of Eugenics A casual enquirer after truth had inadvertently come into possession of a ticket of admission and was fortunate enough to be present at the meeting

The audience was composed of both sexes, and, in view of the subject under discussion, presented an interesting spectacle Healthy young men and women, parents of the next generation, in whose hands lay the immediate steps towards improvement, and to whom the meeting might be of some practical import, were singularly lacking In their place were the old and decrepit the halt the blind and the lame Hardly a

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[1] See *Lancet* April 21 1956 p 490

THE LANCET

LONDON SATURDAY, MAY 19, 1956

Burns and Scalds*

When the kettle is upset the first decision must be Do I treat this myself or do I call the doctor ? When the doctor arrives his first decision must be Do I treat this myself or do I send it to hospital ? In reaching these decisions the two most obvious guides are the extent of the injury and the degree of shock but a third factor which must be considered as soon as possible is the depth to which the damage has penetrated for failure to recognise that a burn or scald is a deep one is still responsible for long periods of disability Our correspondent whose letter appears on p 750 tells how his wife who is 80 years old, scalded her foot with half a pint of boiling water The exposure treatment was advised and for weeks the patient was confined to bed, suffering severe pain Treatment of burns by exposure [1] comes as a surprise to the many people who have been taught that the first thing to do for these injuries is to exclude the air immediately [2], and naturally our correspondent is doubtful of the value of a method which brought so much distress Probably in this case the scald went deeper than was at first appreciated Scalds, even when only a small area is involved, may be very deep and boiling water may entirely destroy the thin skin of an octogenarian, whereas in the same circumstances it would leave intact the deeper skin cells in the forearm of the baker After very similar accidents therefore, the baker s lesion may heal in fourteen days, and the old lady s may take months

From the days of Dupuytren doctors have recognised the significance of depth as well as the extent of damage, and his ' six degrees have been the accepted classification for over a hundred years

> " nous avons divise les brûlures en six degres ainsi caracterises 1° erytheme ou phlogose superficielle de la peau, sans formation de phlyctenes, 2° inflammation cutanee avec decollement de l epiderme et developpement de vesicules remplies de serosite 3° destruction d une partie de l epaisseur du corps papillaire, 4° desorganisation de la totalite du derme jusqu'au tissu cellulaire sous-cutane. 5° reduction en escarres de toutes les parties superficielles et des muscles jusqu'a une distance plus ou moins considerable des os 6° carbonisation de la totalite de l epaisseur de la partie brûlee " [3]

With advances in skin-grafting techniques, however, plastic surgeons have concentrated on distinguishing between two or perhaps three, groups—undoubted skin survival, undoubted full-thickness loss, and cases in which a period of waiting is necessary before it is certain that epithelium will grow over the area again The first 2 of Dupuytren s degrees belong to the first group, the last 3 to the second, and the 3rd degree (which provides most of the cases in hospitals and casualty departments) includes the ' uncertain " burns In the early stages the surface appearance of a burn is only a rough guide to its depth, for it can give no sure indication that the dermis has or has not, survived [4] Tests for circulation may be deceptive for pooling of blood in dead capillaries may produce reversible blanching on pressure when, nevertheless, coagulation necrosis will result in deep sloughing a week or two later Loss of sensitivity to pinprick in areas such as the trunk legs arms and backs of the hands (but not the face, scalp palms or soles), may indicate full-thickness destruction This is perhaps the only physical sign of much help in the first few days Sometimes a firm decision cannot be made until the eschar is beginning to separate, and this may not be until after the second or third week Electric burns in which the current has passed through the wound are particularly difficult to assess and their depth is very often underestimated

When the family doctor has decided to treat a burn or a scald at home, what can we regard as the modern treatment and what advantages can it claim over such simple remedies as ointments or picric acid ? The exposure method produces a hard coagulum within two or three days, but, as our correspondent makes plain, the pain may be considerable Local applications relieve the stinging and they have the added advantage of making it apparent that something is being done Moreover, doubt has recently been cast on the superiority of the exposure method by Lowbury et al [5] who showed that although the dry surface of the coagulum remains sterile the bacterial flora on its under side, where it is hoped that skin regeneration is taking place may be varied and prolific The probability is that when skin damage is only superficial, there is little to choose between the healing-times with any form of treatment If the initial estimate of depth is accurate, therefore those cases suitable for treatment at home should respond to any method and there seems to be no objection to the application of a soothing dressing and to the exclusion of air Before the development of blisters an anti-histamine ointment may minimise the reaction If blisters have appeared, the ' cleavage dressing ' [6] of two apposed pieces of tulle gras provides relief and allows a reassessment in four or five days without disturbing the surface of the burn itself The outer layer of tulle gras can be peeled off carrying with it caked gauze wool, and bandage This leaves the inner layer attached to the burn, which while still virtually undisturbed is painlessly displayed for inspection All burns should be gently cleaned with a detergent, and dried, before the first dressing is applied Opinion is divided on the use of antibiotic powders as a local application In giving their views on the management of burns,[7] the Association of Plastic Surgeons held and arteriovenous nipping are not dissimilar from those *found in man, the crocodile would seem to be an ideal* experimental animal, though minor technicalities remain to be overcome

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[1] Wallace A B *Lancet* 1951 i 501

[2] First Aid Manual British Red Cross Society London 1952 p 138

[3] Leçons de M Dupuytren Paris 1832 p 424

[4] Jackson D M *Brit J Surg* 1953 41, 588

[5] Lowbury E J C Crockett, D J Jackson D M. *Lancet* 1954 ii 1151

[6] Lowden T G The Casualty Department Edinburgh 1955 p 150

[7] *Lancet* 1954 i 39 See also The Management of Burns The Lancet Ltd, 1954

Meanwhile, at Barthomary's Hospital, clinical studies continue Two active principles have now been isolated, yenwupongine and venwupongeine, both of which, when suspended in vitriol and administered by surreptitious injection, produce perivascular cellular infiltration, necrosis, and refusal to submit to further treatment This phenomenon, known as Ducane's triple response, is thought to originate at some place in the craniotarsal axis, though some would dispute this hypothesis Other toxic side-effects may include leucocytosis, leucopenia, frequency, oliguria, depression, euphoria, wasting, obesity, diarrhœa, and constipation Clearly, the theoretical justification for the exhibition of yenwupongine and yenwupongeine has not yet been fully elucidated, nor are these measures free from hazard But the physician has acquired a remarkable chemical tool which, if used judiciously, may lead to a better understanding of a common disease of today

* * *

Parents and psychiatrists may be concerned because cowboys and Indians have lost their appeal Robin Hood is a back number, and all the current heroes are intrepid explorers of outer space and distant planets But for one anæsthetist it is a blessing The six-year-old spaceman never objects to the bathing-cap which is affixed preoperatively It is so like a space-helmet that it might have come straight from Dan Dare himself The anæsthetic face-piece holds no terrors for the modern nipper, for all the best space-men apparently breathe oxygen from a similar device Induction is carried out smoothly with appropriate asides—"Air-lock closed," "No two motor ready"—so that the roaring in the ears which heralds impending unconsciousness follows quite naturally The rocket motors are on (Somehow they never did seem to swallow that yarn about the workmen outside in the street)

This simple deception can be easily enhanced by the glittering paraphernalia on the average Boyle's machine A laryngoscope makes a very fair space-gun, an ethyl-chloride spray a convincing death-ray And Magill's forceps are just the job for removing meteorites from Martians' hooves

* * *

Lit-tle Gee-Pee is very hap-py be-cause his poorly pat-ients are all get-ting bet-ter on Sachets of Servo-assisted Senna, the new Wonder Drug "Ha-ha!" he laughs!

Lit-tle Gee-Pee reads all about Sachets of Servo-assisted Senna in the Fairy Tale Picture Books which the kind Uncles at the manu-fact-urers' of-fices send him ever-y morn-ing

But here comes Teacher! She is cross with Gee-Pee for pre-scribing Servo-assisted Senna in-stead of Bis-2 4 6 8 diethyleeni-meeni-amino-p'-benzaldehideho-dehyde of senna (90% u p) *N F* (Wasn't that a long word, Teeny-tinies? Be sure you get it right, or Jolly Uncle Jack at the Pric-ing Bur-eau will have to make you write out your pre-scrip-tions all over again!)

"You are a *naughty* boy, Gee-Pee!" scolds Teacher "Instead of play-ing golf this after-noon with the other lit-tle girls and boys, you will stay in after Surg-ery and write out fif-ty times, in your best hand-writing, 'The Standing Joint Committee on the Classification of Proprietary Preparations and the Joint Committee on Prescribing Know Best'"

"Boo-hoo!" cries poor Gee-Pee "*I will tell my* Psy-chiatrist about you!" But his lit-tle friends Sam-my Statist-ician and Rupert the Rep do lots of hard sums, and—what do you think! They find that Sachets of Servo assisted Senna cost ever so many less pennies than Bis- 2 4 6 8 diethyletcetc *of senna* (90% u p) *N F*!

Off they scam-per to tell Teacher, and now they are *all* staying in after Sur-gery *ever-y day this week* to write out one hun-dred times, in BLOCK CAPITALS, "I must not teach my Grand-mother to suck expensive medicaments" And there will be lots of pen-nies de-duct-ed from their quarter ly cheques!

(An-other teeny-tiny tale soon)

Letters to the Editor

SMOKING

SIR,—The Minister of Health's cautious pronounceme on the association of smoking with cancer and th tobacco firms' pontifical edict belittling the importa evidence to date[1] are disappointing but understandabl for the health service, for which the Minister is responsibl derives a substantial part of its financial nourishme from taxation on tobacco, while the tobacco compani have naturally to consider their employees and shar holders In the face of such powerful vested intere it is not easy for our profession to convince the publ of the dangers of smoking it is even more difficult f those of us who are already enslaved by the habit

The recent increase in tobacco duty suggests that th Government already have a guilty conscience, but wh did they not give a moral lead by increasing the ta on cigarettes only, for these represent the princip threat to health? They should have announced the intention of introducing legislation to prohibit the s of tobacco to persons under 18 and so educate the publ to adopt, as with alcohol, a responsible attitude towar its enjoyment At least they could have determined t warn National Servicemen, for whom they have a speci responsibility, of the insidious and costly nature of th cigarette habit

The tobacco companies' "smoke screen," to which yo referred in your annotation last week, is cleverly worded they speak of "a *possible* relationship" between lun cancer and smoking when the profession has accepte the association for some time, and "a *suggestion* tha smoking *may* be a *contributory* cause" (italics all mine They note that only a small proportion of smokers con tract this disease, which occurs also in non smoker What are they waiting for? Until every smoker contract cancer and until all atmospheric pollution has bee banished? Not everyone falls victim to smallpox o poliomyelitis in an epidemic, but this fact does not dete the State and the profession from doing their best t save as many lives as possible But even more perniciou is the firms' claim that smoking is a boon to million and that its benefits, both physiological and psychologica and as yet ill defined, might well be the subject o scientific research Such subtle propaganda as they hav put forth, directing the public's attention away fro the lethal facts, is calculated to stimulate the hardene but recently scared habitue to once more reach out fo a packet of his favourite blend of the drug and to incit others, including susceptible teenagers, to investigat for themselves these alleged benefits It would b salutary for the boards of certain tobacco companies wh actively encourage the growth of the cigarette habit t see the final stage of the grim tragedy, as do we, all to often, on the necropsy slab Their generosity in providin money for research was unquestionably activated b humanitarian interest, but at the same time it inspire the public's trust in their policy and judgment, the have therefore assumed a grave moral responsibility

As a profession it is our clear duty to be outspoke and broadcast the important truths which have *alread* been established We can vehemently discourage smokin in adolescence and warn against its habit-forming tend encies We can begin now to speak of "tobacc *bronchitis,*" "*smoker's cancer of the lung,*" "smoker cancer in the liver (or in the brain)," so that the publi will the more quickly learn to associate cause with effect Finally, we who enjoy a smoke can ourselves se an example by keeping the habit under control

W H McMENEMEY

London

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[1] *Times* May 8 1956

criteria for physical signs a tumour was also found in a considerable proportion of well babies of this age (25 of 115 babies under two weeks old). A barium meal was given to 62 of the babies, and hurry seemed more common than delay in emptying of the stomach. Post-mortem examination of the pylorus in 138 newborn or stillborn babies did not reveal any muscular hypertrophy corresponding to this frequent clinical finding of a palpable tumour. CRAIG's important conclusion was that a palpable tumour in the first two weeks of life is not evidence of an organic change in the pylorus: it seems rather to indicate a dysfunction which can resolve rapidly. It is comforting, however, to note that these tumours, although similar to those of hypertrophic pyloric stenosis in rather older babies, were not usually identical. They were not so firm, well defined, or rapidly contractile, and they did not fit so aptly the classical description of the tumour of pyloric stenosis as resembling an olive suddenly appearing beneath the examining finger. It seems that attention to detail must be even stricter in assessing a palpable tumour in the newborn than in the slightly older baby suspected of having hypertrophic pyloric stenosis.

CRAIG discusses the condition of pylorospasm as an entity causing vomiting in the absence of organic pyloric hypertrophy. On the other hand THOMPSON and GAISFORD[13] believed it "exists more in the mind of the pædiatrician than in the abdomen of the child". WOOD and ASTLEY,[14] however, when they were studying a group of babies with vomiting of uncertain origin, considered that they had radiological confirmation of pylorospasm in some of their rather older "non-persistent vomiting babies". Clinically their cases bore some resemblance to those described by CRAIG. In a contrasting group, there were persistent vomiters, some of whom later showed evidence of gastro-œsophageal abnormalities. These conditions, such as œsophageal hiatus hernia, must also be borne in mind in the diagnosis of vomiting in these younger babies. Perhaps the term pylorospasm should be retained as a convenient label suggesting a reversible upset of function rather than as an exact diagnosis. CRAIG agrees with THOMSON's view[15] that such babies often empty their stomachs by repeated small vomits rather than by one copious vomit as in typical hypertrophic pyloric stenosis. The affected babies in CRAIG's series stopped vomiting with no more treatment than gastric lavage, but he mentions the possibility of giving antispasmodics. Some people may feel that this might confuse the issue and lead to difficulty and delay in diagnosis when there is in fact an organic cause.

CRAIG's investigation is modestly described as a pilot study showing that a palpable tumour is not evidence of organic hypertrophy of the pylorus in babies under two weeks of age. Further research along these lines should increase our knowledge of gastric function in the newborn. Moreover this knowledge may become of increasing practical importance in the examination of babies who are shown by such ætiological studies as those undertaken in Birmingham, to have a greatly increased risk of developing true hypertrophic pyloric stenosis.

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[13] Thompson, W. A., Gaisford, W. F. *Brit. med. J.* 1935, ii, 1037.
[14] Wood, B. S. B., Astley, P. *Arch. Dis. Childh.* 1952, 27, 562.
[15] Thomson, J. The Clinical Study and Treatment of Sick Children. Edinburgh, 1921, p. 291.

The Medresco Hearing-aid

THE Medresco hearing-aid was introduced with the National Health Service in 1948 and it remains one of the very few appliances that can still be obtained entirely free of charge, on the recommendation of a consultant otologist. That it is one of the most widely appreciated amenities of the health service has long been apparent to those working in hearing-aid clinics. What is perhaps not quite so fully recognised is the type of case likely to benefit from the use of a hearing-aid. Deafness can be classified into three broad categories: conductive deafness, from deficiencies in the sound-conducting apparatus; perceptive or nerve deafness, from affections of the neural apparatus of hearing; and mixed deafness, by which is commonly understood a combination of conductive and perceptive deafness. Many causes of conductive deafness, such as otosclerosis and inflammations of the middle-ear cleft, can be treated by medical or surgical means with varying degrees of success. When these measures are unsuccessful or the patient declines them, nearly all patients with conductive deafness can derive very real benefit from the use of a hearing-aid. The problem of perceptive deafness is much more difficult and the results less happy; for perceptive deafness is essentially untreatable and the hearing obtained through an electrical aid is less satisfactory. But fortunately most deaf people fall into the conductive group; and even in nerve deafness modern developments in construction and design have produced hearing-aids that can bring relief to many who were previously thought to be beyond their help.

The requirements of an ideal aid are "high amplification, high fidelity, small size and weight, low power consumption and low cost. Not all of these qualities can be achieved in practice. Objectives of low cost and light weight are directly opposed to the objectives of high fidelity, high amplification and long battery life".[1] This is certainly true of valve aids, and all models of the medresco are at present valve aids. It is also partially true of the newer transistor aids now being manufactured, but these do in fact combine lightness of weight with high fidelity, high amplification and long battery life. But a transistor aid costs considerably more than a valve aid. With increasing experience in the development of the transistor aid, costs should fall.

Last year GEFFEN and TRACY[2] recorded an investigation into the distribution and use of medresco aids supplied by the Royal National Throat, Nose and Ear Hospital in London to residents of St. Pancras. 419 aids were issued between June 1948 and May 1953, the period covered by the survey. 330 of these patients were visited and interviewed by one of the borough's sanitary inspectors. The object of the questionary was to determine how much the aid was used and how valuable it was. 31% used their aid all the time, 57% used it only part of the time, and 12% had ceased to use it altogether. In other words 88% derived some benefit from the aid. In almost half the cases the aid had never caused any trouble, and in a further third very little trouble; in the remainder the instrument had failed frequently

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[1] Fisch, L. *Med. ill.* 1954, 8, 302.
[2] Geffen, D., Tracy, S. M. *Med. Offr*, 1955, 93, 261.

In (*a*) and (*b*), which are likely to be of long standing particularly in mitral disease, thickening of the alveolar basement membrane prevents the easy access of interstitial fluid into the alveoli [10]

It is fundamentally important to interpret radiographic signs logically (hence radi ology) in terms of anatomical site, disordered physiology, and pathological processes This valuable radiographic sign, appreciated years ago by Kerley,[11] should be regarded as indicating œdema of the peripheral interlobular pulmonary septa and *not* necessarily as indicating pulmonary hypertension The anatomical site is the interlobular septa ; the disordered physiology is œdema ; and the pathogenesis is either pulmonary capillary hypertension, lymphatic obstruction, or, less commonly, increased permeability of capillary membrane or hypoproteinæmia, depending on the particular clinical associations

Now that the basic mechanisms responsible for these lines are better appreciated, we are no longer justified in naming them in purely visual (and verbose) terms (e g , " basal horizontal lines on chest radiographs ") or by eponymous reference This valuable radiological sign should be given an anatomical designation (e g , " peripheral or [basal] interlobular septal lines ") or should be described in pathological terms (e g , " lines of interstitial pulmonary œdema ") When described in such terms, their significance will become more widely appreciated they represent the only objective evidence of waterlogging of the pulmonary interstitial tissue and its lymphatics

St Thomas's Hospital
London S E 1

RONALD G GRAINGER

SIR,—We were most interested to read the paper by Dr Rossall and Mr Gunning The findings agree substantially with our own [12] As we stated, " when lines B were absent the pulmonary capillary pressures were usually well below 30 mm Hg When present the pressures were almost invariably above 30 mm Hg " We agree with Rossall and Gunning on ætiology also " It appears likely that when the pulmonary capillary pressure approaches plasma osmotic pressure, there is exudation of fluid with deficient reabsorption "

We, too, found at first some difficulty in seeing basal lines in patients with heavy breast shadows, but this was overcome by taking an additional postero-anterior chest film of the bases with the mammary tissue well elevated by the patient's own hands The film, however, is likely to be too dark for diagnostic purposes unless some reduction is made in exposure—usually of the order of 3 kV

Our present studies suggest that, although the raised pulmonary capillary pressure plays a major part in the production of basal horizontal lines in mitral valve disease, in the other conditions in which the lines occur there are other factors of greater importance

J H E CARMICHAEL
D G JULIAN

Liverpool

TREATMENT OF BURNS AND SCALDS

SIR,—Last November my wife who is 80, scalded her foot very badly, although it was the result of upsetting only half a pint of boiling water Her doctor said that no ointment or oil should be applied, and the foot must be exposed to the air, even to the extent of keeping it out of bed for two nights, in none too warm weather

For weeks my wife was confined to bed, with severe pain for which no soothing substance was applied Later on penicillin injections were given It is only within the past two or three weeks that she has been able to get about while the foot has been, and still is very painful There is a large scab of wrinkled flesh right across the toes, from the stretching of which, during walking, blood has appeared in two places

Can this be considered a successful example of the modern method for dealing with burns and scalds? In contrast, I would instance the case of a local baker who badly burned his arms He was treated in the old-fashioned way, by applying ointment and covering the arms Within a fortnight he was back at work

UNCONVINCED

CYSTIC PNEUMATOSIS

SIR,—Cystic pneumatosis, although comparatively uncommon, cannot be so rare as is imagined Since 1951 two cases have occurred in this hospital Both were detected during routine barium meals and were subsequently proved at operation

Most workers agree that this condition occurs in association with intestinal obstruction

Nitch [1] described 85 cases and stated that 50% of the cases were associated with gastric or duodenal ulcer and in 83% of these pyloric stenosis was present

Mathews [2] reported a case of enteric pneumatosis in which the pelvic colon was mainly affected, the cysts being submucous and subserous

Griffiths and Ellison Nash [3] report a case of gastric ulcer with associated ileal pneumatosis, the affected loop being under the diaphragm and in a suprahepatic position and leading to a diagnosis of peptic perforation

The commonest complications are pneumoperitoneum and intestinal obstruction, including intussusception Nitch is of the opinion that the cysts and the affected portion of the intestine are best left alone unless causing obstruction by pressure, adhesions, or projection into the lumen of the bowel The cysts disappear in the majority of cases after the cure of the coexisting lesion

Jones [4] described a case in which a chronic volvulus of the sigmoid colon was associated with cystic pneumatosis of the large gut However, I am unable to find a reported case in which chronic volvulus of the jejunum was the obstructing lesion

CASE 1 —A man, age 49, was admitted to this hospital on Dec 6, 1951, with a two year history of intermittent dragging pain on the left side of the abdomen, associated with attacks of diarrhœa and constipation Subsequent barium enema revealed no abnormality, but straight radiographs of the abdomen showed mild pneumoperitoneum and several fluid levels in moderately distended loops of small intestine in the left upper quadrant Barium meal and follow through showed partial obstruction of the upper small gut but no abnormality in the stomach and duodenum

Laparotomy on Dec 23 1951, revealed volvulus of the upper jejunum The mesenteric border of the affected jejunum contained multiple large diverticula ranging in diameter from $^{1}/_{2}$ to 2 in The terminal ileum was affected by cystic pneumatosis, the cysts being subserous and situated both on the mesenteric and the antemesenteric borders All were small (about $^{3}/_{8}$ to $^{3}/_{16}$ in in diameter) and sessile The volvulus was reduced and the affected jejunum resected continuity being restored by end to end anastomosis

Convalescence was marred by a burst abdomen, but the patient was finally discharged as an inpatient on Feb 5, 1952

CASE 2 — A woman age 60, was admitted to this hospital on April 6, 1954 with a two year history of vomiting and indigestion indicative of pyloric stenosis The patient was thin and had a vague, tender, small epigastric mass Radiographic examination on April 14, 1954, showed free gas under both halves of the diaphragm and evidence of a small pyloric ulcer with severe spasm

Laparotomy was undertaken on April 20, 1954 when a firm hypertrophied pylorus was found in association with cystic pneumatosis of the terminal ileum, involving two isolated lengths 6 in and 9 in long The cysts which were about thesia primarily to prevent the aspiration of gastric contents The essence of their technique is to induce anæsthesia with a mixture of cyclopropane nitrous oxide, and a high concentration of oxygen, and then to use the short acting muscle relaxant, succinylcholine chloride to produce favourable conditions for intubation When the tube is in the trachea and the cuff inflated, they maintain anæsthesia on a light plane with a similar mixture of gases, and once the succinylcholine has worn off relaxation is produced by intravenous gallamine triethiodide Respiration is assisted or controlled as necessary Many people will protest that this seems to be an unnecessarily complicated technique for obstetric practice and that it introduces the potential hazards of muscle paralysis while not entirely excluding those of aspiration until the cuffed tube is in position Yet in its essentials this is a method with which many anæsthetists are familiar in the operating-theatres of general hospitals, and which, in its ultimate results, has been shown to be of considerable value Moreover the use of an endotracheal tube not only eliminates the risks of aspiration but also ensures adequate oxygenation at all times and satisfactory conditions for operation with the minimum of depressant anæsthesia Paradoxically, should it be desirable or necessary to deepen anæsthesia, this can be done easily and quickly All in all the obstetrician is not called upon to hurry because of the anæsthesia

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[10] Parker F Weiss S *Amer J Path* 1936 12 573
[11] Kerley P J *Brit med J* 1933 ii 594
[12] Carmichael J H E Julian D G Penrhyn Jones G Wren E M *Brit J Radiol* 1954 27 393

[1] Nitch, C A R *Brit J Surg* 1923, 11 714
[2] Mathews F J C *Brit med J* 1951 i, 851
[3] Griffiths J D Nash D F E *Ibid* 1955 ii, 1602
[4] Jones J D T *Brit J Surg* 1948, 36, 49

With such a method dangers are most likely at induction and during the period before intubation is complete During induction there is a risk of vomiting, but with the onset of paralysis this is superseded by that of passive reflux In considering the prevention of these complications, not all anæsthetists would agree with Coleman and Day's method of induction with cyclopropane and nitrous oxide, which is relatively slow, followed by inflation of the lungs before intubation and with the patient horizontal Quicker loss of consciousness can be achieved by a 50% mixture of cyclopropane and oxygen inhaled from a 6 litre bag[6], and a head-up tilt will help to prevent reflux from the œsophagus when the patient is paralysed With this technique the mother's oxygen saturation remains high enough for intubation to be performed without prior inflation of the lungs, but the tube must be passed without delay

The success and safety of these and similar types of anæsthesia depend upon two essentials—an experienced anæsthetist and adequate equipment Indeed the standard of labour-ward anæsthesia—whatever the technique—will be raised only when both are freely available Coleman and Day are at pains to emphasise this and they point to the need for an efficient suction apparatus and a labour-ward bed that can be quickly tilted

If these methods of anæsthesia become generally acceptable in hospital practice, what should be done in domiciliary work? There is little to recommend them for use in the home even in the hands of an anæsthetist of experience There is a problem here, especially for the teaching hospitals What are students to be taught about obstetric anæsthesia and how are they to be equipped to deal with an emergency in domiciliary practice?

BRAND-NEW SHAMBLES

ALLOCATIONS to hospitals for capital expenditure still lag behind real needs, and we should all like to believe that any money which the country spares for this purpose is prudently used A few months ago a new operating-theatre suite was opened at a hospital in the Home Counties The following were among the defects which came to light

In the *theatre* eleven floor blocks were loose, when stepped on, they went down at one end and up at the other Four of the encased radiators leaked and every day rags had to be placed here and there on the floor to absorb the water

In the *sterilising room* the steriliser itself leaked and some of its taps leaked and could not be used It had been so installed that it could not be serviced without complete disconnection The hood above it, to collect the steam came no farther forward than the front of the steriliser Accordingly steam condensed on the ceiling from which water fell impartially on the sterile and the non sterile Subsequently the paint on the ceilings of the sterilising room and the sluice room peeled off

The *swing-doors* warped and dropped catching against each other

Most of the faults might perhaps have been averted by closer supervision of the building work, and one or two by consulting accounts of the design of other operating-theatre suites—this, after all is not the first to have been erected in Britain A harassed staff has for the past month been working in the theatre which they had hopefully discarded, while the new theatre is being put in order We hope that their unhappy experience may, by example help to avert such happenings elsewhere

LUNG CANCER IN YOUNG PERSONS

IN England and Wales during 1954 308 persons under 40 years of age were certified dead from lung cancer[1] This was only a small proportion—less than 2%—of the total lung-cancer certifications, but the disease in young patients has some interesting features For instance, the ratio of men to women—3 to 1—is lower than in older people and the squamous type of cancer is much less common Neuman et al,[2] at the Mayo Clinic, have studied 51 patients under 40 and found only 4 (8%) with squamous tumours compared with 34% among patients of all ages at the same hospital[3] On the other hand there were 37% with adenocarcinomas (the type believed to be less commonly related to cigarette-smoking[4-6]) whereas there were only 13% in the whole group In the young the disease runs a more rapid course In one series only 31% of patients under 50 who were not treated surgically or by radiotherapy survived for a year compared with 46% of those over 70[7] Neuman et al state that the survival-rate after resection is "definitely lower" in young patients But their conclusions are based on only 13 resections, and Bignall and Moon[8] found that in 77 patients under 45 who survived operation the five-year-survival rate—45%—was in fact higher than that of patients aged 45–59, and the distribution of histological types among their young patients was much the same as that in older patients There seems to be insufficient evidence at present to conclude that in young people the outlook after resection is necessarily bad.

Anderson et al[9] found that chest or shoulder pain was the commonest presenting symptom in 30 young men, this symptom was recorded in almost three-quarters of them In most large series of patients of all ages cough is the commonest early complaint There is some indication that among those whose illness begins amounts of ordinary alcoholic drinks for about ten years They then turned to methylated spirit for economic reasons and at a time of "heightened loss of morale"[1] However, as Dr MacDougall remarks, methylated-spirit drinking is by no means the last stage of alcoholic excess On the average a further five years of excessive drinking followed before these addicts reached what they themselves regarded as their "lowest point"

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[6] Bourne J G *Brit med J* 1956 i 984

[1] Registrar General's Statistical Review of England and Wales Part 1 Medical. 1954 H.M Stationery Office

[2] Neuman H W Ellis F H McDonald, J P *New Engl J Med* 1956 254 502

[3] Kirklin, J W McDonald J R Clagett O T Moersch, H J Gage R P *Surg Gynec Obstet* 1955 100 429

[4] Doll R., Hill A B *Brit med J* 1952 ii 1271

[5] Breslow L Hoaglin L, Rasmussen G Abrams H K *Amer J publ Hlth* 1954 44 171

[6] Wynder E L *Penn med J* 1954 57 1073

[7] Bignall J R *Lancet* 1955 ii 210

[8] Bignall J R. Moon A J *Thorax*, 1955, 10 183

[9] Anderson, A. E Buechner H A., Yager I, Ziskind M M *Amer J Med* 1954 16 404

Compared with the majority of our alcoholic patients, the methylated-spirit drinkers were slightly lower in occupational status, intelligence, and rates of recovery and improvement Thus most of them belonged to social class III and were of average or just above average intelligence (compared with a large proportion in social classes I and II and of superior intelligence among our alcoholics in general) Methylated spirit drinkers were also found among small recent samples of homeless excessive drinkers (3 out of 40)[2] and of alcoholics admitted to a London observation ward (4 out of 56)

Drinking of methylated spirit was held responsible for the condition of the offender in approximately 0 9–1 8% of "proved offences of drunkenness" in England and Wales over the past fifteen years[3]

Warlingham, Surrey M M GLATT

ARTIFICIAL RESPIRATION

SIR,—I am writing on behalf of the chief medical officers of the area gas boards

Artificial respiration should be carried out immediately and uninterruptedly on people who have been partly asphyxiated by drowning, gassing, or electrical shock It is well recognised that a delay of even a few seconds may be fatal Nevertheless it appears to be common practice to move patients undergoing artificial respiration into an ambulance and to attempt to carry out artificial respiration on the way to hospital

It is highly improbable that satisfactory artificial respiration can be carried out in a moving ambulance, and it therefore follows that a patient who needs artificial respiration should have it on the spot This must be well known to all doctors who have considered the matter, but the fact that such patients are still put into ambulances indicates that the ambulance attendants are not aware of the correct practice We therefore suggest that all doctors who have to do with the instruction of ambulance attendants should emphasise and re emphasise this point

South Eastern Gas Board,
Medical Department,
589 Old Kent Road, London S E 15

R E W FISHER
Chief medical officer

CLOSED TRAUMATIC LESIONS OF THE AXILLARY AND BRACHIAL ARTERIES

SIR,—I read with interest the successful results of sympathectomy for occlusion of the axillary artery described by Professor Rob and Mr Standeven (May 5) The following case responded to intravenous procaine

A woman, aged 67, was referred by Dr Curtis Bain, with thrombosis of the right axillary artery of seven weeks' duration The right hand and forearm were cold and pale the pallor increasing on raising the arm and on immersion in hot water Movements were weak and inhibited by pain No pulsation was palpable in the right brachial, radial, and ulnar arteries A feeble pulse was felt at the apex of the axilla The pulses of the left arm and both legs were normal

Intravenous infusions of 1 g of procaine hydrochloride in one pint of physiological saline solution were given at a slow rate daily for four days in the outpatient department Thereafter, procainamide 0 75 g daily in three doses was taken by mouth for one week Improvement began at once and after the third infusion was maintained Four to five hours after the third infusion the patient felt a wave of warmth steal down her arm, and she saw the veins of her hand fill up Pain on movement was reduced to a dull ache On the sixth day the stellate ganglion was blocked The hand warmed still further within five minutes—an effect similar to that at the end of an infusion of procaine hydrochloride This effect lasted four to five hours Eight days after the beginning of treatment she spent all the morning sewing with her right hand and complained of only a slight ache The right hand was now only slightly paler and colder than the left It became red and comfortable on immersion in hot water Sympathectomy now seemed unnecessary Six months later the brachial and radial pulses had returned

The vasodilating properties of procaine hydrochloride are cumulative and independent of the speed of infusion Unpleasant side effects can be prevented by slow administration The procainamide may or may not have been beneficial

General Hospital, Harrogate JANE PEARCE

PERFORATED ACUTE AND CHRONIC PEPTIC ULCER

SIR,—We owe a considerable debt to Mr Hermon Taylor for proving, beyond all doubt, that a diagnosis of perforated peptic ulcer does not necessarily demand immediate operation

However, I am a little confused by the recent report by Mr Taylor and Mr Warren of their treatment of 200 cases of perforation (April 14) Part of the confusion may be due to their published data having been limited by considerations of space

1 What proof is there that all these 200 cases had a perforated ulcer? The authors do not pretend that clinical diagnosis is very reliable, and indeed they admit to 17 proven errors in 108 cases Is it possible that there were other, unrecognised, mistakes? May we know how many unoperated cases showed no radiological evidence of gas in the peritoneal cavity?

2 They remark "it seems clear that partial gastrectomy is the treatment of choice" for perforated chronic ulcers which do not respond to conservative treatment With the utmost respect, it is not clear to me How many emergency gastrectomies were, in fact, performed, and was the number large enough to justify such a dogmatic opinion, from so authoritative a source, on a matter of such far reaching importance?

Why is it better to stop the leak by an operation lasting an hour and a half on a patient in rather a delicate state of health, when it can be stopped quite easily by an operation lasting fifteen minutes? It beats me

South Mimms, Herts V J DOWNIE

MEPACRINE FOR PETIT MAL

SIR,—Arellano and Alejandro[1] described long continued benefit in cases of petit mal epilepsy from mepacrine in a dosage, for patients over 7 years of age, of 100 mg every six hours to a total of 1 3–3 3 g In the two following cases I gave 100 mg six-hourly for four days to a total of 1 6 g

CASE 1 —An imbecile boy, aged 7 years, had had severe petit mal despite many different drugs The best regimen was phenobarbitone gr $^1/_2$ thrice daily and dexamphetamine 5 mg twice daily, but even with this the average number of petit mal attacks observed was 300 a month To his normal routine was added a course of mepacrine Fits immediately ceased for two weeks, they then returned in their former intensity but slowly decreased over the next month to a level of 2–3 a day, and this level has been maintained for the past three months This boy has improved as a whole and can now take a greater part in the games of his friends and walk to the occupation centre (about 200 yards) without falling Before treatment with mepacrine he had had to be taken in a chair —

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[1] Expert Committee on Mental Health Alcoholism Subcommittee Second Report *Tech Rep Wld Hlth Org* 1952 48 37

[2] Glatt M M Whiteley J S *Mschr Psychiat Neurol* (in the press)

[3] Offences of Drunkenness, 1953 H M Stationery Office 1954 p 3

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[1] Arellano A Alejandro P *Int neurol Congr* 1954 p 253

The Wider World

TUBERCULOSIS IN THAILAND

The Story of a Venture

A J BENATT
M D
FORMERLY W H O SENIOR MEDICAL OFFICER,
TUBERCULOSIS CONTROL PROJECT, THAILAND

IN many Eastern countries, though immunisation of large numbers of children with B C G may be feasible, there are grave difficulties in introducing other Western methods of controlling tuberculosis Is it, in fact, worth trying to introduce them until social and economic circumstances change? In particular is it worth establishing a "tuberculosis control project" like the one in which I worked in Thailand? Since the answer to these questions is important for people in the East, I shall describe what we tried to do and what we did

Unlike its neighbours Burma, Indo China, and Malaya, the kingdom of Thailand has never been under foreign rule Its population of nearly 20 million are Siamese and Chinese—the latter mostly immigrants Poverty is wide spread Bad housing, overcrowding, and malnutrition—particularly in the capital, Bangkok, a city of over a million—provide all the conditions favouring a rapid spread of infections, including tuberculosis Tuberculin testing of school-children showed in 1951–52 a positive Mantoux reaction in 70% at the age of 15, suggesting that children are much exposed to the disease A random-sampling radiographic survey in 1954 revealed a tuberculosis prevalence of at least 5% in the capital, and the figure was probably higher in the poorer quarters Tuberculous meningitis and miliary lesions were common

The General Plan

Confronted with tuberculosis in a country where modern measures of control have hardly been attempted, a W H O team-leader will think it his principal task to prevent the spread of the disease, especially to the young The first essentials, when a case is recognised, are to make the sputum free from tubercle bacilli, by the simplest means, and to safeguard possible contacts Compared with the control of infection the further treatment of patients is a secondary objective

But, however correct this may be in theory, it did not prove workable in practice In Thailand we found a small tuberculosis hospital, of 75 beds, in which patients had been kept for years with little hope of recovery or discharge—a picture of gloom This hospital, having lately come under the jurisdiction of the tuberculosis division of the government, was the main concern of the chief of that division, and he asked our help in alleviating some of its worst features Our activities in the hospital were evidently to be the acid test of the usefulness of the international team—a *hic Rhodus, hic salta* So, without neglecting preventive duties, we had to give a certain priority to amending as well as preventing therapeutic disasters, and it was not long before we found that, in point of fact, understanding of the importance of the social aspects of tuberculosis or other diseases could be imparted to the national staff more effectively if relief to the physically distressed could be demonstrated In the two medical schools of Thailand, preventive and social medicine were not part of the curriculum With its discussions on ward rounds and clinical conferences the tuberculosis hospital offered a golden opportunity to inculcate and encourage thinking in terms of prevention, social needs, and rehabilitation

The Team and Its Language

Since 1949 a tuberculosis service of the Thai health department had gradually developed, with a physician in charge who had had several years' training in the United States A chest clinic had been established with a small laboratory radiological apparatus, and a small nursing service Under an agreement with W H O, an international team was to be sent to Bangkok to set up a demonstration centre and to teach and train local staff The government had promised to provide for each international member a suitable counterpart, preferably with previous experience in his field, the counterpart to the team leader being the director of the tuberculosis division Parts of the project were to be equipped by UNICEF

The international personnel, who were sent to Thailand one by one during the latter part of 1951, consisted of a British trained laboratory technician, a British public-health nurse, a Dutch radiographer, a Chilean epidemiologist, an Indian statistician, and a British team leader—this last replacing, in June, 1952, a Swiss physician who had initiated the project Two British laboratory experts came for short periods to give advice, and a Danish laboratory technician to revise the sputum culture technique A Swedish technician assisted for a few months in improving the radiological technique

The language was to be English As only a few of the Thai team, of whom some had held fellowships abroad, knew much English, the language barrier was (and remained) a difficulty, especially with the technicians, who had seldom learnt English at school However, the Thais got to know English far more rapidly than the international team got to know Thai To have to acquire a difficult language imposes a serious additional strain on people tired by a day's work in great heat and humidity, and I would urge the need for teams, *before* they go abroad, to get acquainted with the fundamentals of the language of the country to which they are assigned The language barrier is also important in relation to clerical assistance In Thailand, anyone proficient in English could earn from commercial firms high salaries with which the government could not compete Thus the international staff had to spend on clerical work much time that should have been spent in other ways

The Central Chest Clinic

The chest clinic lay in the heart of a congested middle-class shopping area in the centre of Bangkok In 1952, a few months after the project began, there was a monthly attendance of 2800 of whom more than 500 were new patients Two years later, when the project ended, the corresponding figures were 3500 and 750 Of those attending for the first time half were found to have tuberculosis

More than three quarters of those who came to the clinic sought advice of their own accord, others were referred by the mass X-ray survey of the project, while a few were sent by their doctors or by other organisations About 40% lived far outside the Bangkok area, and, in hope of getting effective treatment, many had to make long journeys by boat and train, not infrequently taking two or three days, or even longer, to reach Bangkok

A new patient entered the chest clinic by a special entrance which was also used by sputum negative patients Entrances and waiting rooms were put at the two opposite ends of the building so as to minimise the mixing of the tuberculous and non tuberculous When the team left, an entirely separate small block only for contacts was under construction

Facilities for Diagnosis

Every patient seeking advice had a 70 mm film taken by a static mass radiography unit At the same time the tuberculin test with 5 units P P D was applied If he was very ill, a clinical examination followed immediately, but otherwise he was asked to return in three days for the results of the miniature X ray and for the reading of his tuberculin test Patients without radiographic abnormalities were then discharged, unless special tions owing to intolerance and 22 4% owing to inadequate response Some may have failed to respond because they were suffering from a megaloblastic anæmia of pregnancy, which does not appear to have been excluded by examination of the bone-marrow

Dudley Road Hospital
Birmingham

R O GILLHESPY

PRODUCTION OF CODEINE

SIR,—The enzymatic dehydroxylation of phenols, which Mr L M Spalton (March 24) claims is non-existent, is not an uncommon reaction Burton [1] has shown that dopa melanin is formed by the elimination of water between phenolic hydroxy groups A large number of analogous reactions have been reported [2]

Winnipeg Canada

E P EVANS

CARRAGEEN

SIR,—In your issue of April 14 a Peripatetic Correspondent says that he often wonders what chondrus or carrageen is

Carrageen is familiar to most people in Ireland and often is consumed as a sweet there It is a small seaweed, which has curly, branching fronds It is harvested on the shore and is washed and then dried and bleached in the open

It may be purchased loose from sacks in grocers' shops in towns near where it is harvested and elsewhere in packets in which it may be inspected through a transparent window It is packed loosely and is very light for its bulk

Nowadays its commonest use is for making a sweet which is a cross between jelly and blancmange, with a delicate flavour It is soaked for some hours in water and then discarded, the decanted liquid being heated with milk, which may be coloured at will and which some misguided persons also flavour artificially The agar like gel extracted by soaking causes the milk when cooled to set The resulting dish is light and readily taken in large quantity Hence it has a place in the diet of invalids

Its other medical interest lies in the fact that from ancient times it has been thought to have a value in the treatment of cough, being so used by the public to some extent even now and being incorporated in some commercial cough remedies widely sold at present in Ireland I doubt if it has any effect on cough apart from its soothing of the throat, but who am I to say that another Fleming may not at some later time say otherwise ?

If your correspondent or others not familiar with this weed would like to try some, I should be happy to oblige

Uarán Mór
Gaillimh Éire

SEAGHAN UA CONCHUBHAIR

THE PATTERN OF GENERAL PRACTICE

SIR,—I should like to thank Dr Richards (May 5) for telling us something of his experience of general practice and its relationship to medical education Though he said little that was new he presented many of the important facts and feelings in a connected and convincing way

For those who work and teach in hospital this kind of communication is most helpful, and I hope that other family doctors in differing types of practice will be encouraged to follow Dr Richards's example All medical practice, including general practice, requires both general professional education and specialised training In planning this for the undergraduate and early graduate stages we need to know more precisely than we do at present what are the proper functions of a family doctor today This is essential if the doctor in training is to make serious contact at appropriate points with the attitudes and experiences of family practice

I hope myself that at the undergraduate stage this contact will be limited, that in the preregistration stage we shall one day find time for a substantial apprenticeship for all in general practice, and that during the years of established professional activity we shall step out beyond the occasional "round" and the afternoon "course" into more imaginative forms of contact between the general practitioner and the specialist

Newcastle upon Tyne

DONALD COURT

RESEARCH DEFENCE SOCIETY

DR W LANE-PETTER, hon secretary of the Research Defence Society (11, Chandos Street, London, W 1), writes

On more than one occasion recently there have been broadcast programmes on the subject of animal experiments in which doctors have taken part May we, through the courtesy of your columns, invite any doctors or scientists who may be asked to take part in future programmes of this kind to remember that the Research Defence Society exists to help them in just this sort of activity

DAPHNE AND THE GREENFINCHES

MR MAX PETTERSSON, PH D (Linnean Society, Burlington House, Piccadilly, London, W 1), writes

In the classical myth Daphne was persecuted by Apollo, while in contemporary gardens her namesake, *Daphne mezereum* L , is newly set upon by greenfinches (This daphne species is the small shrub covered with a profusion of pink and fragrant blossom about March) A pair of greenfinches will gouge out every single seed, in May or June, and before the fruit is mature—to feed themselves and their nestlings To study the origin and spread of this new habit, I should be glad to hear of cases where this does, or does not, happen and, if it does, about how many years ago the first despoliation took place Further details are given in *Nature* (April 14 1956, p 709)

Public Health

Contaminated Flour ?

AT Pontardawe, Glamorgan, over 100 people were affected in an outbreak thought to be due to contaminated flour The first to be taken ill were those who had had bread rolls in a canteen Later, cases became more general in the village The illness began one to three hours after eating the bread Those most severely affected had epileptiform fits, sometimes accompanied by violent muscular contractions and followed by unconsciousness for up to one hour In milder cases there was weakness, twitching, nausea, and confusion of thought Some people became aggressive They all recovered, but a number were injured when they fell Inquiries suggest that 3 sacks of flour out of a consignment of 100 were contaminated—perhaps by coming in contact with some toxic substance Samples are being analysed

Help for the Family

Kent County Council recently completed the first year of a family-help service to households where there was temporary difficulty in looking after the children in their mothers' absence The aims of the service were to avoid breaking up the family and to reduce the cost of taking the children into the care of the county council It was limited to families of 2 or more children, with an initial term of not more than three months, and a contribution was assessed on the parents' means

The helpers were recruited mainly from the council's domestic help service, and they either lived in or visited daily 1000 children in 302 families were helped in that way during the year, with an average of twenty four days per family The cost of £5400 was estimated to be less than half the expense of taking them into the council's care

94% of the cases were the result of confinements or treatment in hospitals and convalescent homes, and the remainder were due to deaths or desertions 126 further applications for the service were not granted, most of those families made their own arrangements, and only 12 children had to be taken into care by institutions or foster parents Although it was intended that help should be withdrawn when the mother returned home, it proved necessary to extend it in some cases until she was able to cope with her children's needs constructed in the simplest possible way with the least possible expense to the patients most of whom were living below subsistence level The wood of crates or boxes was used for the basic structure to which a mosquito net was affixed (fig 1)

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[1] Burton H *Nature Lond* 1948 161 725

[2] Mason H S *Advanc Enzymol* 1955 16 121

Because segregation was so difficult, other ways of preventing the spread of infection had to be found The *combating of cough and sputum* became one of the project's main objectives One of the recognised means of diminishing cough is rest, but this rule was hard to observe in the hot and humid climate of Bangkok moreover, most of the people had to go out daily to earn their living, whatever their physical condition—the more so since there was no system of financial assistance for the sick Streptomycin, with the two cover drugs, is usually effective against cough and sputum, but in order to get it the patient had to go to the chest clinic at a sacrifice of time working hours, fares, or rest We were considering, therefore, whether we could recruit and organise a flying squad of nurses who would go out in jeeps to the various districts to give streptomycin injections But when the first results of a Medical Research Council trial on isoniazid and *p* aminosalicylate treatment by mouth were published[1] this plan was abandoned The M R C workers had found combined use of these two drugs almost as efficacious as the use of streptomycin plus one of them, and since administration of isoniazid and P A S is a relatively simple matter, we hoped that the introduction of this combination might prove to be the *turning-point in the control of tuberculosis* in countries *en cours de développement*

Between January, 1954, and May, 1954, a total of 550 patients were treated by this method at the Bangkok chest clinic, and *at least* half of the patients receiving the two drugs for two or three months (including those who continued physical work) said that cough and sputum had become slight or had disappeared The recommended dose of 20 g P A S daily proved impracticable and had to be reduced to 16 g, or (in most cases) 12 g, but the subsequent M R C report[2] justified this smaller dosage One could be pretty sure that the drugs supplied were taken, since, once he accepted medical advice, a poor Siamese or Chinese would follow it strictly

Where isoniazid and P A S did not fully control cough and sputum, and in the few cases where P A S could not be tolerated, artificial pneumoperitoneum was induced at the chest clinic, provided that suitable arrangements could be made—e g, if a car or ambulance could get near enough to the patient's dwelling to take him home, and if he could receive a certain amount of care at home Though in Britain the use of artificial pneumoperitoneum has latterly declined, in areas such as Thailand, where the tuberculous patient can seldom rest for any length of time, it can still be an important adjunct to drug therapy, reducing cough, and a useful means of preventing extension of the disease after drug treatment has ceased In the second year of the project 275 patients had an artificial pneumoperitoneum

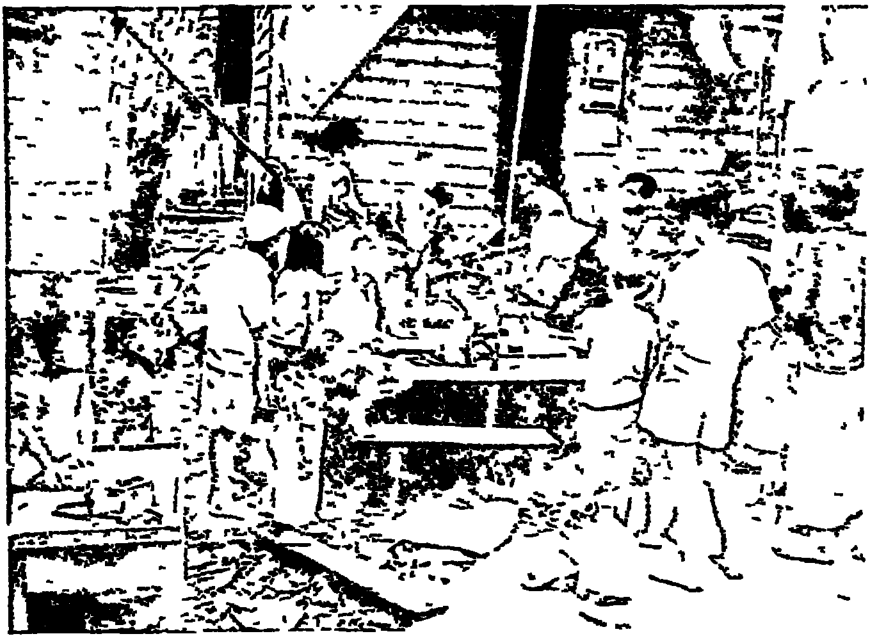

Fig 2—Contacts

"Where a younger patient is immobilised he becomes the focus of attraction for the neighbour's children They are considered as contacts and vaccinated with B C G on the spot"

The patient is the young man in a white shirt, squatting

Note the close proximity of huts, and the cleanliness of the children in contrast to the amount of rubbish characteristic everywhere

Few cases failed to respond to isoniazid and P A S by mouth, or to these drugs supplemented by pneumoperitoneum Unfortunately the time limit set on our project prevented any statistical assessment of the value of these measures, but it was evident that patients receiving this treatment no longer required sputum-containers or toilet-paper handkerchiefs in increasing numbers

Prevention by Conferring Immunity

The contact clinic—This clinic, organised by the W H O public-health nurse, was the first of its kind in Thailand All contacts were tuberculin-tested, and (once the test proved unequivocal) negative reactors were vaccinated with B C G positive reactors under the age of 12 with clinical suspicion of abnormality, and those over the age of 12, were radiographed with a 70 mm film

In trying to ensure satisfactory attendance the nurse encountered many obstacles The elderly could hardly be persuaded to leave their homes for radiography, and as the very old customarily looked after the very young, they were often a source of particular danger Also distances were great in Bangkok a city of bizarre lay out intersected by numerous *klongs* (canals) which made short cuts impossible and caused congestion of traffic Families were usually large and could not afford the fares to the clinic—especially when (as often) the mother was the breadwinner Disruption of communications, by floods and quagmires, during the rainy season was another difficulty Yet with all this the number of contacts attending the clinic steadily rose

Where the contacts could not attend, we sometimes undertook tuberculin testing and B C G vaccination in the patient's home Any tuberculous person who was partially immobilised usually attracted a crowd of the neighbours' children and regarding these as contacts, we sought their parents' consent, and then tested and vaccinated them with the household members (fig 2) Unfortunately, shortage of nurses and transport prevented

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[1] *Brit med J* 1953 i 521

[2] *Ibid* 1955 i 435

CUTHBERT ALLAN SPRAWSON

Kt, C I E, M D Lond, D Litt Lucknow, F R C P

Sir Cuthbert Sprawson, whose death on May 7 at the age of 79 we announced last week, held high administrative and university appointments in India at a time which was important for the future of the medical profession there As director-general of the Indian Medical Service, as professor of medicine in the University of Lucknow, and as the first president of the Medical Council of India he made a lasting contribution to the land which he served for nearly forty years

[Stoneman

He was born at Wimbledon and educated at King's College School and King's College Hospital, qualifying in 1898 Two years later he joined the I M S and at Netley he won the Herbert prize and the Montefiore medal and prize He held posts as deputy sanitary commissioner in the United Provinces and as civil surgeon at Jhansi before he was appointed professor of physiology at Lucknow Medical College in 1911 In 1913 he became professor of medicine at the college During the 1914–18 war he left India to serve as a consulting physician with the Mesopotamia Expeditionary Force In 1919 he was elected F R C P and appointed C I E

In 1920 he returned to his work at Lucknow, and on the formation of the university there he was appointed professor of medicine and dean of the medical faculty The university conferred on him the honorary degree of D LITT, and J W D M writes

"The award of this distinction by an Indian University to an I M S officer may well have been to some extent a tribute to his remarkable personality which ensured for him the friendship and confidence of people of every race and class This power of inspiring trust and affection was also the secret of his ability to maintain harmony among the students of different classes and communities who were living together in the hostel of the college His example of disinterested friendship was far more effective in this respect than disciplinary measures would have been He was an accomplished physician and teacher of medicine, he never ceased to be also a student and a seeker after fresh knowledge '

In 1930 he was promoted major-general and became inspector-general of civil hospitals in the United Provinces and surgeon-general with the government of Madras Three years later he was appointed director-general of the I M S During his term of office the Medical Council of India was set up to establish a uniform standard of higher qualification in medicine for all provinces For the first four years the president of the council was nominated by the governor-general, and Sprawson became the first president He retired in 1937, but his interest and his influence continued He published an important survey of the teaching standards and of the facilities at Indian medical schools which was the basis of an All-India conference in 1938 This conference recommended the gradual abolition of the inferior licentiate medical qualification throughout India, and the upgrading, by stages, of the schools to college status These proposals became effective in one province before the late war interrupted progress, and to some extent paved the way to the commissioning of licentiates as medical officers in the I A M C which was created in 1913

G R McR writes

"Throughout his service it happened that Sprawson occupied posts at a time when events of importance were taking place His appointment to Lucknow University gave him an opportunity to make his influence felt during its critical formative years, in Mesopotamia his experience of the nutritional needs of Indian soldiers and his knowledge of their reactions to disease was complementary to the wider experience of diseases of temperate climates possessed by his British Service colleague, W H Willcox the pair made an admirable consulting team When surgeon general with the Government of Madras he succeeded in opening the teaching hospital to highly qualified members of the independent medical profession as honorary members of the consulting and teaching staffs As director general it was fitting that he was the first president of the All India Medical Council He strove hard to put the new council on a strong foundation before the first non official president, Dr. B C Roy, took charge At all times Sprawson bore in mind the main objective—to prepare for the eventual hand over to Indian successors His work as professor, principal, inspector, and director general was steadfastly directed to that end .

"The pulmonary infection which laid him low from time to time might have daunted a lesser man He carried on resolutely in his own determined fashion—sometimes at odds with those in high places In addition to his official work he was greatly interested in tuberculosis and leprosy work He was a valiant campaigner in both causes while in India After retirement he was an active member of the medical committee of the British Empire Leprosy Relief Association until his death"

Sir Cuthbert married in 1901 Miss Theodora Mary Burton, who died in 1912 He is survived by a son and a daughter

ROBERT PAUL SCOTT MASON

M C, F R C S

Robert Paul Scott Mason, surgeon to the United Birmingham Hospitals, died on May 3, only two days after his 63rd birthday His origins were cosmopolitan, for he was born in Brest of a French mother, and spent his early years in the Far East It was even said that he could speak Japanese before his native tongue These early vicissitudes were due to his father's peripatetic profession, that of a naval officer who had been a wrangler and whose mathematical talents were bent to the science of gunnery Tradition did not dictate that Scott Mason should follow his father's career, after leaving Portsmouth Grammar School he turned to medicine, entering Middlesex Hospital Medical School in 1910, where he came under the influence of Bland-Sutton, Pearce Gould, and Sir Gordon Gordon-Taylor Soon after he qualified in 1915 he joined the R A M C, and as regimental officer to the artillery in the 18th division early proved his remarkable courage, for which he later received an immediate award of the M C His courage was manifest again during the last eighteen months of his life when, though he was seriously ailing, he continued to fulfil his duties both as senior surgeon and adviser within his own hospital, and as vice-president of the Royal College of Surgeons

After the first world war he returned to Middlesex Hospital to work under Sir Gordon Gordon-Taylor then went to Bradford General Infirmary as resident surgical officer before holding a similar position at the Birmingham General Hospital Here his surgical skill soon won the respect of his discerning seniors such as Seymour Barling From the time of his election to the honorary staff of that hospital, and the Children's Hospital in 1925, his reputation as a general surgeon with thoracic interests and a particular facility in gastro intestinal work grew until in his maturity he was recognised in the Midlands as an outstanding abdominal surgeon He was elected to the council of the Royal College of Surgeons in 1946 and in 1955 became a vice-president

B N B writes ' Scott Mason's operating was a delight to behold, being the acme of gentleness, there were never any histrionic flourishes, no alarums and excursions and each was encouraging. Two weeks later a pneumonectomy was done on a male teacher, with unilaterally advanced disease, in whom a previous thoracoplasty had failed. Both patients did well and were back at work long before our team departed. In the subsequent sixteen months other resections, as well as thoracoplasties, were undertaken—106 interventions in all, with 2 postoperative deaths.

Dr Wilson completed the training of a Thai surgeon who had qualified in England and studied thoracic surgery for a brief period in the United States. By the time the American team left after ten months' work the latter was proficient in all major operations. The resident medical officer who had become familiar with the basic principles of anæsthesia prepared himself to go to the United Kingdom on a British Council scholarship. Postoperative adjustment of posture was practised by one of the Thai doctors following the manual of the British Association of Physiotherapists.

When our team began its spade work at the hospital, where it was soon assisted by the American surgical group, there were only two Thai doctors in attendance. But their devotion skill and cooperation was exemplary. Besides taking part in the preparations for building up a surgical unit, attending to all the preoperative and postoperative care, and assisting with operations anæsthesia, and transfusions, they carried a heavy load of nursing duties. Gradually, however, the medical staff increased from two to nine. More nurses were employed, especially aides, since well-qualified nurses were few and far between. A nurses' home was built. The small operating theatre received modern equipment, the wards new beds and nursing requisites. A new two storey hospital block for female patients was added to the bed space, now 130. A small hospital laboratory increased its scope. A modest electrocardiographic department was set up and a doctor was trained in the technique and in the common abnormalities, especially those associated with thoracic surgery. In short, the previous gloom gave way to cheerfulness hope replaced despair and resignation. Coughing was rarely heard on the wards. Patients no longer wore masks—a depressing sight at first. The infection scare was dispelled and the "plague" stigma removed. Instead of wearing their daily clothing in hospital beds, as is common in the East, the patients now had light white garments.

Unfortunately, as there was no provision for rehabilitation, or for social assistance, only those with reasonable home conditions could be considered for major surgery. The Thai team recognised this shortcoming and agreed to set up a convalescent home, with retraining facilities, which would have had the additional advantage of relieving the pressure on hospital beds. Before the international team left, a convalescent home beside the hospital was being planned, but sudden budget restrictions imposed delay.

The Mass-radiographic Survey Near Failure

"Random sampling" was the method chosen to investigate the prevalence of tuberculosis in Bangkok, and the United Nations statistician assigned to the Thai National Economic Council provided the samples. For this purpose, Bangkok was divided into several hundred areas. Of these twenty-four were selected at random for the radiological survey, which was to be combined with tuberculin testing and sputum examination (or laryngeal-swab cultures in the absence of sputum). House to-house propaganda was prepared by sanitarians who explained that in no circumstances would the results be communicated to the employer. But, when an attempt was made to register names, difficulties at once arose. A large proportion of the population were Chinese, who lived under certain legal restrictions, and, fearing political implications, many of them resented an inquiry. It was then proposed to enlist Chinese helpers to explain, but the Chinese comprised at least three groups whose dialects were unintelligible to each other. Tuberculin tests and laryngeal swabs soon became unpopular, and had to be confined to the radiologically suspect. Finally—one of the greatest disappointments—the demographic information arrived rather late. However, before this sampling scheme was undertaken, group surveys had been made frequently in factories and big industrial concerns, and among port personnel and others.

Taking the group and sample surveys together, 16,000 adults were radiographed, and in 5% of these the findings suggested tuberculosis. But bacteriological confirmation was often impossible, for the collection of sputum was fraught with error and the setting up of laryngeal swab cultures unsatisfactory because incubator space was insufficient at the time. All these hazards were aggravated by a succession of technical mishaps, more numerous and harder to overcome than was expected. A further year or two, at least, and the help of international personnel, would have been required to make this survey successful.

The case-finding programme will go on. Advice was given before departure to continue the monthly survey of maternity cases at the maternal and child health centre and to refer to the chest clinic those with a pulmonary lesion.

Teaching and Training

From the beginning we realised that little would be gained by ex-cathedra teaching in English and throughout our two years we taught only individuals or small groups, in question-and-answer fashion. This kept tuition alive, allowed time for repetition and interpretation, encouraged thinking and free discussion, and eased tension and embarrassment. The teacher could soon tell whether he was understood and distinguish between the capable and those who took longer to comprehend. This vast project, with a life-time of a little more than two years, had in the first instance to make use of the ablest and train them to be teachers themselves. Standing rules of the team were to eschew speculations and unproven statements to refrain (above all) from talking down to the students, and yet to be firm and critical.

Of the medical subjects taught, two were given priority first, consideration for the patient's comfort, and, secondly, prevention and management of therapeutic catastrophes.

1 Wherever opportunity arose, attention to the very sick was impressed on medical and nursing staff. Many Thai doctors were as eager as those of other nations to give injections when the real need was comfortable recumbency and fluids. One could not emphasise too strongly the importance of combating pain by simple means, and the benefit of a local anæsthetic for minor interventions—using sharp needles. How to lift, how to feed, and how to give a drink to an immobilised patient were simple but indispensable demonstrations.

2 As tension pneumothorax, empyema, failed surgery, and other complications were at first encountered in considerable numbers, there were opportunities for analysing the causes of failures and the means whereby they could be put right. The importance of fluid and electrolyte replacement and of simple sedation was brought home to the medical staff time and again.

Diagnosis and differential diagnosis of chest conditions was taught in two sessions (to medical staff and visitors) on weekly selected radiological material with all the bacteriological, clinical, and social information. Stress was laid on the pathology of the lesion and on the planning of the stages of treatment. Each case was also considered in all its preventive aspects, the home visitor often being called to the conferences to supply information and receive instructions. Moreover, a two hour teaching ward round was held once a week in which for more than eight months the American thoracic surgeon always joined. Since one was adamant in requesting all the necessary examinations and tests, reports on precautionary measures in the homes, and accurate charts, these ward rounds elicited fruitful discussions, and with many other conferences they became a forum of happy team-

Notes and News

WORLD HEALTH ASSEMBLY

THE ninth World Health Assembly opened at Geneva on May 8, and it is expected that it will continue till May 26 The medical members of the United Kingdom delegation are Sir John Charles, Sir Eric Pridie, Dr H K Cowan, and Dr M T Morgan

In his inaugural speech Prof Jacques Parisot (France), the president, pointed out that national economics were based on human economy and that the productivity, welfare, and strength of a country were related to the "health capital of the population" To improve health on an international level governments and peoples must unite The world was growing smaller every day, inequalities in health were a danger to all and we needed a world wide offensive not only against diseases of the body, but also against diseases of the mind and against the social inequalities which breed conflict He was therefore especially glad to be able to welcome several new members to the World Health Organisation Morocco, Tunisia, and Sudan were admitted to full membership and the Gold Coast, Nigeria, and Sierra Leone to associate membership Professor Parisot regretted that the U S S R 's resumption of membership had been postponed

Mr Milton P Siegel, the assistant director general in charge of finance, was able to give an encouraging report of his department The financial position of W H O , he said, was the best since its start in 1948 During 1955 92% of the total contributions due had been paid and substantial arrears collected Dr M G Candau, the director general of W H O , reminded the assembly that the 1956 programme had had to be adapted to the budgetary level approved for 1955, though this did not meet even the minimum demands of member States He hoped that the assembly would make it possible to meet those needs in 1957

THE ROYAL SOCIETY

THE president and council of the Royal Society received guests at the annual conversazione on May 10 at Burlington House, where Science's latest was on exhibition For those anxious to catch up with what had been going on in scientific corners other than their own the evening was as attractive as usual And for those who felt that they were too far behind to catch up with anything, there were many encouraging exhibits which gave a nice straightforward picture of such delights, for example, as the ceiling temperature phenomenon in addition polymerisation reactions

Vitamin B_{12}, looking rather like an unknown political prisoner in some of the models, was the star of an effective demonstration arranged by Dr Dorothy Hodgkin, Dr E Lester Smith, Prof A W Johnson, and Sir Alexander Todd By a combination of chemical and crystallographic evidence, the structural formula of B_{12} has been deciphered The calculations established the presence in the molecule of a planar fragment with a structure clearly related to porphyrins, though in a quite unexpected way Nearby Prof W D M Paton was considering the chemical transmission of nerve effects in the isolated intestine No one had been certain which of the muscle stimulants in the wall of the small intestine transmitted activity from the nervous structures there to the smooth muscle By placing one electrode within the lumen and one outside the guineapig ileum, vigorous twitches were obtained with single shocks of 0 5 millisecond, and the preparation was found to be cholinergic in its properties Moreover when the tissue was treated with eserine, stimulation caused acetylcholine to appear in the bathing fluid in sufficient amounts to cause another unstimulated piece of intestine to contract

The kaolin model glaciers were a great success and several enthusiasts regretted that they had left their ice axes and crampons at home Mr W V Lewis and Mr M M Miller, of the department of geography at Cambridge, worked hard at their model ice falls down which they urged a mixture of one part kaolin to two parts water The kaolin glaciers crevassed and flowed realistically, and dust was scattered on the surface to illustrate the movement of the summer accumulation between the cleaner snows of winter The crowd watching the glaciers became so thick at times that they threatened to upset another formidable display of Nature's ingenuity—the model of the molecule (or rather a small part of the molecule) of deoxyribose nucleic acid, which had been constructed at the biophysics research unit of Ki College, London This strange substance seems to hold s of the secrets of the transmission of hereditary cha teristics, and it may be that the arrangement of the atom the molecule forms a sort of "code" for the transmissio information from one generation to the next

Those who feel that evolution is a dull business, which aggravatingly failed to attune itself to the pace of mod life, should see Dr H B D Kettlewell's splendid f *Evolution in Progress*, the story of natural selection "industrial melanism" About 70 species of moth in country are at the moment in the process of changing t complicated wing patterns, intended for concealment lichened tree trunks, boughs, or rocks, to all black, whic better suited to the dirty bark of industrial areas This first noted about 1840, and the rate at which the black fo are spreading is the most striking evolutionary change witnessed in any living organism Dr Kettlewell's study these moths and the birds that prey on them was viv illustrated in the film, which was taken by Dr Niko Tinberg It showed how the birds are responsible for the vir elimination of the white moths from polluted countryside how, in districts with purer airs, the black forms are the o that get plucked from the clean lichened tree trunks

THE DESERT AND THE ROSE

WITH increasing populations the world's need of fo continues to increase[1], and, because there is not mu unoccupied tillable land available for agriculture, mo attention has been given to the possibility of breeding cat and growing crops in the deserts

In 1952 the Institute of Biology organised a symposiu on the biology of deserts, and its proceedings have sin been published[2] Prof Frank Debenham points out th deserts are characterised by extreme heat by day and extrem cold by night, requiring special adaptation in their fau and flora Brigadier R A Bagnold, F R S , goes into t question of water supply and shows how man and the larg animals depend on nomadism for their existence in deser Prof F W Shotton discusses the use of the undergrou water which is usually too salt for irrigation Dr H Bo reminds us that, even if we find new sources of food in th natural vegetation of the deserts, the commercial productio of them would be a complex problem, and Prof Pa Vayssière shows that, as soon as introduced crops beg to grow, locusts immigrate to devour them Tackling deser from a different angle, Prof E P Stebbing explains how th arise and how to stop existing deserts from expandin Dr J S Weiner discusses man's adaptability to the dese and claims that "disorders occurring purely as a resul of the climate are to a large extent preventable and a matte of fairly simple hygiene", but Dr Edmond Sergent argue that it will not be feasible for either white or black colonist to *labour* in the desert Whites could do the administrati work but could not till the soil The only possible tillers of th soil of the deserts are the present inhabitants of those desert who will have to be helped to multiply so as to provid enough agriculturists Mr S M Manton, F R S , describe what he saw on a visit to Russia afforestation scheme hydro electric developments for irrigation of Asian deserts the tapping of underground water supplies, and improved methods of cultivating the deserts The new areas to be irrigated are said to equal in extent a third of the world's irrigated land, and the Russians hope that this transformation of the scene will produce for them a better climate, which in turn will enable more crops to be grown

These are grandiose schemes, but do they constitute the right way of tackling the question of increased food supplies Prof Hugh Nicol[3] holds that, in relation to the work it demands—making the underground water supply available and arranging to drain it away, mining and grinding and transporting the necessary gypsum for dressing the land and providing the fuel for all that—conversion of the deserts into agricultural land does not give an adequate return in food He points out, too, that industry, transport, and food production are in competition for a limited supply of fossil fuels phosphatic fertilisers *could*, with difficulty, be made other hospitals and medical schools, and consideration and care for the sick is propagated in pursuance of the W H O team's teaching

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[1] *Lancet*, 1950 i 406 , *Ibid* 1954, i 1023 , *Ibid* 1954, ii 713

[2] Cloudsley Thompson J L Biology of Deserts London Institute of Biology 1954 Pp 224 14s

[3] Nicol H Microbes and Us Pelican Books 1955 Pp 2 2s 6d

Hence the answer to my question ' Was it justified ? " is "Yes"—though with reservations The period of a little more than two years was much too short a time in which to complete and consolidate the work Though several doctors, nurses, and technicians were adequately trained, there was still a difference between those who had been trained and those who were ready to assume responsibility—and the latter were not numerous Every project needs a trial period during which criticism must be allowed though it may necessitate staff changes on either side Many Thai members had joined in the hope of eventually gaining a W H O fellowship abroad , and when this hope faded they had no special incentive left It was recognised too late—after all possible efforts had been made, and temporary improvement achieved—that we could not hope to secure the services of a sufficient number of qualified home-visiting nurses This state of affairs called for a change of policy A health-education programme should have assisted the campaign of prevention The first steps towards this end were taken by instructing students, and similar activities were in preparation , but time was too short for the scheme to be pursued Health education could have done much , for, from the public health point of view, the bodily cleanliness of the people—even of the poorest and their children—was an important asset On the other hand their canals were dirty, and their environmental sanitation deplorable

“IF I WERE ”

“If I Were Team leader” again of a tuberculosis control project, with the same facilities at my disposal, I would follow essentially the same pattern of planning for diagnosis and prevention and again aim at incorporating the tuberculous patient as a useful member of the family to which he belongs But I would ask my headquarters to consider the following points

1 Do not start a project until all the necessary equipment has arrived

2 Engage international staff in good time and arrange for language lessons pertaining to the country of assignment

3 Impress on the government the need to select able counterparts, because they will have to be the teachers of the future

4 Do not send a team without clerical help to a country where English is not the basic language

5 See that sufficient transport is available, assess the requirements for health visitors, and double the number of vehicles required by them Without satisfactory transport a domiciliary service in a hot climate cannot work and exhausts its members

6 See in time that the government is prepared to pay a good salary to drivers Bad drivers quickly ruin the cars

7 Allow doctors and nurses to drive vehicles, and insure them

8 Make sure that the government is willing to pay adequate salaries to technicians and nurses , for a project stands or falls by their skill, reliability and devotion

9 If after a certain period it emerges that nurses cannot be recruited for a tuberculosis project and salaries and amenities remain unsatisfactory, one had better prepare for a health-education programme in good time by employing lay personnel in large numbers on the model of a mass-B C G campaign

10 A tuberculosis project must have a social worker who will collect facts and figures, arrange for assistance and rehabilitation, and tap new resources

11 Impress on the government not to spend money on any major building programme until sufficient medical, nursing, and technical staff are trained One should expand in a cautious way, gain experience until the time when all requirements are clear, and then begin to make plans

12 Prepare convalescent homes with retraining facilities for the patients Such a scheme will also help to relieve pressure on hospital beds Convalescent homes can be administered by less qualified doctors and nurses

13 Where tuberculosis is widespread, arrange early for children's wards for the treatment of tuberculous meningitis, miliary infections, and infections of adult type

14 Never again embark on a tuberculosis control project of only two years' duration

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Conferences

ATLANTIC CITY MEETINGS

FROM A CORRESPONDENT

THREE important meetings are held annually in Atlantic City in the spring They are the gatherings of the American Federation for Clinical Research, the American Society for Clinical Investigation, and the Association of American Physicians This year the weather was kind and the boardwalk crowded between meetings Brief reports of a few of the papers follow , full reports will be published later in the journals of the respective societies

Studies on the L E cell phenomenon were reported by N B **KURNICK** He concluded that the abnormal factor present in the γ globulin of these patients alters the cell membrane so as to allow entrance of a serum proteolytic enzyme, which then destroys the inhibitor of desoxyribonuclease (DNase) This enzyme then attacks the chromosomes, yielding the depolimerised nuclear mass which characterises the L.E phenomenon He treated 16 patients with homologous whole blood (or leucocyte homogenates) intramuscularly, thus providing material which may either supply DNase inhibitor or adsorb circulating abnormal γ globulin (or both) Encouraging results were seen, and steroids could be withdrawn in almost all cases

J A **MOORHOUSE** and R M **KARK** reported their observations on the effect of tolbutamide (orinase) on blood-sugar levels during continuous feeding with first glucose and then fructose With glucose no effect was seen, whereas blood-sugar levels fell promptly with fructose They concluded that a primary effect of the drug on the liver had been demonstrated and that the data did not support a direct tissue action

G W **LIDDLE** J E **RICHARD**, and G M **TOMKINS** gave an account of the biological effects of a new series of corticosteroid analogues in which carbon 2 is methylated By this means the effects were greatly enhanced , the most potent member of the group (2 methyl-9 alpha fluorohydrocortisone) was three times as powerful as aldosterone, and the most effective mineralocorticoid yet described

C J **FISHER** and W W **FALOON** showed[1] that blood-ammonia levels in liver cirrhosis can be controlled by giving 12 g of neomycin orally daily This dose prevented mental effects, and allowed more protein to be given in the diet

A useful test for steatorrhœa was described by J **WENGER** and E C **TEXTER** They made a single determination of the blood carotene level, and showed its relationship to the 24 hour fæcal fat excretion It seems clear that, provided the carotene intake prior to the test is adequate, low levels imply some defect of fat absorption The simplicity of the procedure may make it a useful screening test for steatorrhœa, and an easy means of following the course of the disease

The first case of pyridoxine responsive anæmia in the adult was recorded by J W **HARRIS**, J M **PRICE**, R M **WHITTINGTON**, R **WEISMAN**, and D L **HORRIGAN** It appeared as an apparently unresponsive iron deficiency anæmia, without tongue or nerve involvement, and with no skin changes Hæmatologically the essential lesion was a reduced mean corpuscular hæmoglobin concentration with raised serum-iron level Pyridoxine hydrochloride (200 mg intramuscularly daily for five days) produced prompt remission, with a reticulocytosis of 50 8% on the seventh day After relapse had been allowed, it was shown that a similar but much less striking remission could be obtained with pyridoxine orally A specific defect in absorption of the vitamin was suggested as the cause

British Association for the Advancement of Science

The annual meeting of this association will be held in Sheffield from Aug 20 to Sept 5 Further particulars may be had from the association, Burlington House, Piccadilly, London, W 1

British Epilepsy Association

The annual meeting of the association will be held on Thursday, May 31 at 2 30 P M, at Manson House Portland Place, London, W 1, when Sir Henry Cohen will speak

The Doctor as Witness

On Monday, June 4, at 8 15 P M, at the Marlborough Day Hospital, 38, Marlborough Place, London, N W 8 Dr J C M Matheson principal medical officer of Brixton Prison, will speak on the Doctor as Expert Witness in Criminal Courts

London Amateur Boxing Association

A meeting of the medical officers of this association will be held at the Great Northern Hotel, King's Cross, London, on Thursday May 31, at 7 30 P M, when Mr Ian Robin will give a talk on ear, nose, and throat injuries

Convalescent Home for Diabetics

A convalescent home, which is open to male diabetics over 12 years of age from all parts of the country, has been opened by Sheffield Regional Hospital Board at Langwith Lodge Nether Langwith, Notts Application forms are obtainable from the matron

Growth and Development of Children

The annual meeting of the teams engaged on coördinated research on the growth and development of children will take place in London on July 9 and 10, at the Child Study Centre, Brunswick Square, W C 1, under the chairmanship of Prof Alan Moncrieff These annual meetings are sponsored by the Centre International de l Enfance, Paris It is hoped that representatives of teams from London, Paris, Zürich, Brussels Stockholm, Kampala, Dakar, and Louisville will be present

W H O Appointments

Dr Jessie Bierman, professor of maternal and child health at the University of California School of Public Health, has been appointed to the headquarters staff of the World Health Organisation as chief of the section of maternal and child health The appointment is also announced of Dr E E Krapf, associate professor of psychiatry in the University of Buenos Aires, as chief of the mental health section

North of England Otolaryngological Society

The prize which this society offers for original work in otolaryngology carried out in the North of England during the tenure of a senior registrar, registrar, house officer or clinical assistant post has been awarded this year to Mr R W Bailie for his paper on Lermoyez syndrome Entries for next year should be sent to the hon secretary, Mr R Thomas, 27 High Petergate, York, before Aug 1, 1957

Joint Cancer Consultation Clinics

The experiment in cancer treatment first organised by the Royal Marsden Hospital (then the Royal Cancer Hospital) in 1944 was described in our annotation of May 5 On May 11 and 12 the cooperating hospitals held their first general meeting, and there was a dinner to celebrate the 12th anniversary of the inception of the joint clinics Mr J M Wallace, a governor of the Royal Marsden Hospital, was in the chair, and Miss Patricia Hornsby Smith parliamentary secretary to the Ministry of Health was the chief guest Proposing The Cooperating Hospitals Scheme she said it was as much a matter of human relations as of science, and it had added a new dignity and meaning to the oft repeated precept that the patient came first Speaking of nuclear energy in medicine Miss Hornsby Smith emphasised the value of the work going on in many different hospitals and laboratories she often had to answer aggravating questions from people who assumed that research began and ended in the laboratory at Mill Hill Sir Max Page replied on behalf of the hospitals Prof D W Smithers welcoming the guests, wondered whether the joint clinics might not prove to be a pilot scheme for other regions and other specialties Sir Harry Platt responded for the guests

R A F Appointments

The following appointments in the Royal Air Force hav been announced Dr D Evan Bedford, civilian consulta in cardiology, Prof C V Harrison, honorary civilian co sultant in pathology, and Mr C Naunton Morgan, civil consultant in surgery

Appeal to Congress Organisers

One of the objects of the Council for International Orga sations of Medical Sciences (C I O M S) is to coördinat international congresses of medical and related science T avoid overlapping, congress organisers are asked to infor the C I O M S (Unesco House, 19, Avenue Kléber Paris 16 of their plans before fixing the dates of their meeting

Education of Subnormal Children

On May 9 Mr Dennis Vosper, parliamentary secretary to the Ministry of Education opened a school for educationally subnormal children in Brighton Provision for these children had been increased since the war but about 12,500 children were still waiting admission to special schools Though most of them were in ordinary schools Mr Vosper said that a further 75 special schools, providing nearly 9000 places were in course of construction or had been authorised Though the number of special school places had increased by 10,000 since 1949 the number of children awaiting places had remained almost constant "This clearly shows," Mr Vosper said "that we are all taking greater trouble in ascertaining the existence of this form of handicap Children who previously might have been left to cope alone with their disability are now seen more clearly to need assistance"

British Society for Research on Ageing

The annual meeting of this society will be held at the Ciba Foundation, 41, Portland Place, London, W 1, on Friday June 8, at 4 P M This will be followed by a scientific meeting open to non members when Prof K J Franklin and others will speak on reactions to standard stimuli at various ages and Miss Honor Fell, F R S, on the effect of vitamin A on embryonic epidermis of different ages

A joint meeting with Dutch Gerontologists in Amsterdam has been planned for July 27 and 28, before the International Physiological Congress in Brussels on July 30 Further particulars may be had from Mr G H Bourne, D SC, London Hospital Medical College, Turner Street, London, E 1

The Royal College of Surgeons of England have sent their congratulations to Mr Gerald S Hughes of York who has completed 50 years as a fellow of the college

Central Council for District Nursing in London —The council has published a supplement to their directory and streets list The supplement includes new blocks of flats and the roads which serve them Copies (1s 6d) may be had from the council, 25 Cockspur Street S W 1

A new edition of the Home Office pamphlet on *Duties of Doctors and Dentists under the Dangerous Drugs Act and Regulations* has been issued (H M Stationery Office Pp 16 9d)

Appointments

BLACK DAVID, M B Belf D O M S part time asst ophthalmologist Walton Hospital Liverpool
GRIMBLE A S M D Lond M R C P director of the department of venereal diseases Guy s Hospital London
YOUNG W B M B E B M Oxfd F R C S I D M R, D T M asst radiologist St Thomas s Hospital London

Colonial Appointments

ADAMS M D M B N U I special grade M O Kenya
BEDFORD P W, M B Leeds M O Sarawak
BRINGAN J W F R C S I D P H M O H, Gambia
CHEUNG K H M B Hong Kong D T M & H malariologist Hong Kong
CLARK A R L M B resident M O (intern), Uganda
HO YUEN M R C P specialist physician grade C Singapore
JUMEAUX C Y M B F R C S E specialist officer superscale grade A Federation of Malaya
MAGEE T P M B Glasg M R C O G M O grade A Trinidad
PARKER D J P M B Belf F R C S I senior specialist northern region Nigeria
PORTSMOUTH O H D M B Lond M O Kenya
QUARCOO F G K L R C P I M O Gold Coast
SHOUCAIR J S M D Edin M R C P medical specialist Jamaica
SMARTT C G F M R C S D T M & H specialist psychiatrist Tanganyika
YH-CHOY R T M B Lond M O grade C Trinidad

woman under forty was present, and the overpowering majority either wore spectacles or had some other more or less conspicuous physical defect One poor gentleman came in on crutches, another had the rolling eye of "inherited tendencies", and the little linen that was present was evidently on enforced leave from the wash tub

At first the "casual" thought the audience had collected itself as an outward and visible sign of the dire necessity for "improvement", and as a protest against the sins of their fathers who had taken no heed of the matter But as the meeting advanced and the view was delicately unfolded that marriages should be made with an eye more to the physical development of the race than to wealth, or beauty, or love, the "casual" found that he was grossly mistaken—the audience was there to protest against any interference with their individual freedom in matters of love and marriage One gentleman of ninety-odd emphatically and with many a senile tremor declared to his junior by a decade "we are not going to marry to please the State but to please ourselves" Another gentleman from the audience bounded on to the platform and with a tongue which sadly needed the agility of his toes, stammered that so long as there was 'L l l l love in the w-w w w world l l l-l love w w w w would l l l l laugh at l l-l l locksmiths"

The sides of the few complete men and women who were present now began to ache But that ache was nothing to the acute agony to which they were soon put at the hands of no less a person than the very celebrated professor, the man of science and world wide fame, who for more than half a century has been the brightest star in matters anthropological and whose paper on "Eugenics" it had been the object of the meeting to hear

The professor has a face of serene calmness and philosophical divinity, and his expression is one of angelic graciousness No more than a glance is needed to recognise that he is not as other men As the disembodied soul is to common clay, so is Professor Galton to the rest of humanity

That is what the casual enquirer thought After several male members of the audience had appeared upon the platform to criticise the "able and interesting" paper which the professor had read, a lady rose She was past the bloom of life and wore a large hat and spectacles

The professor bowed and courteously bent his head in the direction of the lady But a cold together with the changes which years are prone to work in the auditory canal, had impaired his hearing powers to such an extent that listening was palpably an effort, and he soon gave up the attempt and leaned back in his chair On the professor's left sat a young man already known to fame, and to him the great man turned—and then the audience occupying the few front rows of chairs were electrified, petrified, and almost electrolysed, by hearing his dulcet tones form the words "Fancy having a wife like that!"

The young man blushed The chairman turned a horror-struck countenance on the professor The lady paused The professor was the only unconcerned person on the platform He turned his divinely imperturbable face towards the chairman as though he would ask "Has she said anything very dreadful?" For one brief second the quivering silence lasted, and then (to her everlasting honour be it said) the lady resumed her remarks as though there had been no interruption

The paper of the learned professor had proved beyond the possibility of a doubt that men and women were perfectly ready to be influenced in their choice of each other by "Eugenics" But amongst the many arguments which were advanced against this theory there was none so overwhelming in its conclusiveness as those six little words which slipped so naturally from the professor's own lips "Fancy having a wife like that"

When the Man of Science judges by appearances what is the Man in the Street to do?

K Heanley
L.M.S S.A

Special Articles

IODINE AND FLUORINE

The nutrition panel of the food group of the Society of Chemical Industry held on April 11 the fourth and final meeting of a series concerned with Nutritional Requirements and Food Fortification [1]

Iodine

Prof Margaret Murray said that iodine had been recognised as a nutritionally essential element since Baumann in 1896 prepared "iodothyrin" from the thyroid gland and it was shown that its iodine content ran parallel with its physiological activity The iodine of the diet, which was mainly in the form of iodide, was taken up by the thyroid cells for the production of thyroxine and tri iodothyronine An inadequate intake of iodine led to thyroid dysfunction and goitre Because iodine was not abundant in foods generally, its level in drinking-water determined the adequacy of its supply Although inadequacy of iodine was the ultimate cause of most endemic goitre, other dietary factors, present in particular in the brassicæ, could act as goitrogenic or anti-thyroid agents In addition calcium could be goitrogenic The iodine requirement of man had not been accurately determined but was generally accepted as 100 µg per day The iodine of drinking-water was a critical factor in achieving this intake and 5 mg per litre was regarded as an adequate level

Mr J C M Holman discussed the use of iodised salt for goitre prophylaxis He emphasised that iodine must not be regarded as a cure for established goitre but largely as a prophylactic Many methods for goitre prevention had been tried including the use of iodised salt, the addition of iodine to water supplies, the administration of iodised tablets and sweets to school children and the application of iodine-rich fertilisers to vegetable crops Of these methods the iodisation of salt was the most satisfactory and had now been practised for over thirty years Remarkable decreases in goitre incidence had followed the introduction of iodised salt in many countries including the U S.A, Switzerland, New Zealand Colombia, and Poland No adverse effects had been observed In Britain iodised salt was available but not yet compulsory, although the Government had announced in 1950 its intention to implement the recommendation of the Medical Research Council that all free-running salt in domestic use should contain 1 part of potassium iodide in 40,000 parts of salt Iodide added to salt was stable for over two years if the salt was kept dry and free-running and contained a stabilising agent The desirable level of iodisation was determined by the average intake of salt and the average dose of iodine necessary to prevent goitre in a community There was accordingly wide variation, from 1 in 10,000 parts to 1 in 200 000 parts of salt, in different countries

In reply to a question on the possibility of iodisation leading to excessive intakes of iodine, Professor Murray pointed out that the levels used in fortification were far lower than those naturally in sea-foods, there was no evidence that iodisation constituted a danger

Fluorine

Professor Murray remarked that fluorine had not been shown to be essential for animal nutrition since no fluorine-free diet had yet been obtained Fluorine was found in varying amounts in the calcified tissue of the body, the amount increasing with age and fluorine intake Fluorine also accumulated in fossil bone and teeth, and the estimation of fluorine in fossils was an accepted method of dating them Fluorine was also present in the ash of kidney stones One of the chief sources of fluorine was drinking-water Most water-supplies in Britain contained less than 1 part of fluorine per 1,000,000, but there were several places with values of 2–3 parts per 1,000,000 In such areas the intake might amount to 3–4 mg daily from water The only foods rich in fluorine were sea-foods and tea The toxic level of intake of fluorine depended on its absorption and the efficacy

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[1] See *Lancet* 1955 ii 1184 *Ibid* Jan 7 1956 p 39

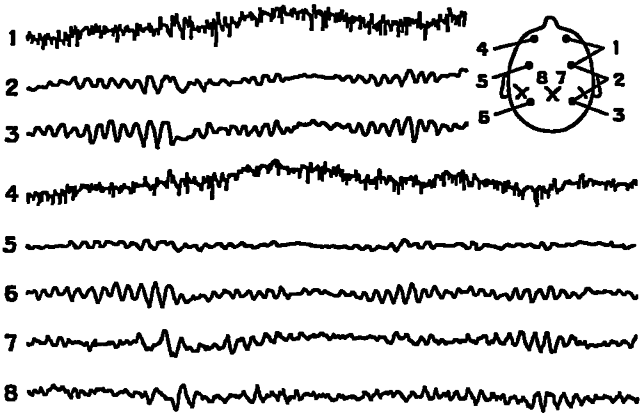

Fig 2—Electro-encephalograms from case 1, showing slow waves

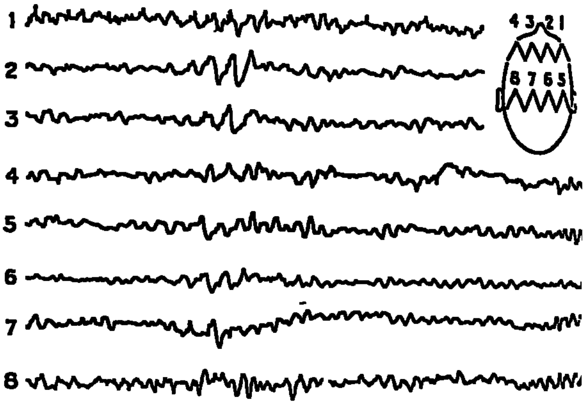

Fig 3—Electro-encephalograms from case 1, showing paroxysmal episode

Many were of long duration (up to 15 msec), polyphasic, and often of large amplitude (1–2 µV) In some instances where muscle weakness was severe all the residual motor units were abnormal and grouped, the volitional pattern being distinctive (fig 1)

These changes, described by Bauwens (1955) as typical of an early myelopathic lesion, are common to many diseases in which the lower motor neurone is involved at the cord level, but in our cases the absence of evidence of lower-motor-neurone degeneration, in the presence of prolonged paralysis, is striking, ruling out the possibility of poliomyelitis as the cause Cases of old post encephalitic parkinsonism were not found to show these electrical reactions

ELECTRO-ENCEPHALOGRAPHY

5 patients showing serious disorders of behaviour were electro encephalographed All were abnormal, and the abnormality was of a similar kind, with the presence of some bilateral activity in the 4–7 c/s range, in addition, 2 showed slower episodic activity Probably at the comparatively late stage at which the examinations were made the electro encephalographic changes observed were entirely non specific Similar abnormalities have been observed in patients with encephalitis lethargica

Two specimens of an electro encephalogram in the most severe case in the present series are shown in figs 2 and 3 The recording shows a fairly regular and partially responsive alpha rhythm at 10 cycles per sec in the postcentral leads at potentials up to 50 µV, sometimes spreading forward to the frontal leads It was associated with occasional slow waves at 3–5 cycles per sec , which were more prominent in transverse recordings, where occasional waves in short runs at about 6 cycles per sec occurred somewhat paroxysmally In all areas there were faster frequencies at about 20–24 cycles per sec at a low potential Being slight the abnormalities could be constitutional Repeat electro encephalography six months after the onset showed little change, as might be expected from the patient's clinical state Further examinations may determine whether the observed abnormalities are due solely to the present illness

This patient was also subjected to psychometric testing, which revealed organic impairment of the brain She showed some anxiety in the test situation, accompanied by an obvious desire to talk about her emotional problems

Case-reports

Case 1—A married female domestic worker, aged 44 developed an infection of the upper respiratory tract on April 14, 1955 On April 18 she complained of headache, lassitude shivering and cough and was admitted to the unit on April 20

On admission she was apyrexial, but her face was flushed She complained of severe headache and pain in her left leg, was mildly confused, and appeared to be uncoöperative probably because she could not maintain her attention when questioned She kept grimacing, making masticatory movements, and licking her lips Continuous clonic twitchings of the left side of her face and of her left sternomastoid muscle slight right ptosis, and bilateral weakness of her palate were present She had moderate neck rigidity with a positive Kernig sign The muscular tone in her legs was slightly increased, and her tendon reflexes were exaggerated Her abdominal reflexes were present but diminished , her plantar responses were flexor

Subsequent Course—Irregular pyrexia not exceeding 99 4°F persisted throughout her stay in hospital On the first day she had difficulty in swallowing fluids, but this did not recur The facial manifestations, including ptosis, gradually subsided after the first week Cramp like and distressing myoclonus affecting her entire left leg masked the paresis throughout her stay in hospital Her plantar responses became extensor, the right on April 22 and the left on April 25, and returned to normal only after two months Sensory disturbances were not observed, but her calf muscles and left quadriceps muscle were occasionally tender

Follow up—On Jan 10, 1956, clonus persisted in her left leg, and the electromyographic findings (fig 1) were unchanged She said she was liable to " cramp " in her left leg

Case 2—An unmarried female typist, aged 26, with five weeks' history of bilateral loin pain, radiating toward the groins, lasting for a few minutes at a time, of variable severity, and unrelated to exertion, and three weeks' history of frequency and dysuria had had her kidneys fully investigated at another hospital, where nothing abnormal was found and she was discharged with a diagnosis of " hysteria " Three days later on July 26 1955, she was admitted to this unit with severe headache, stiffness of her neck, backache occasional pains in her cervical and left dorsal regions, and weakness of her left hand and wrist In addition, she complained of a sense of pressure over her head, blurred vision severe vertigo, a feeling of heaviness in her legs, shoulders and upper arms, and what she described as a tremulous weakness most pronounced on her left side

On admission her temperature was 99°F She was thin and looked anxious, and a coarse intention tremor of slow rate and moderate amplitude affected her head and arms Slight generalised weakness was present in her left arm and leg her deep reflexes were normal abdominal reflexes present and plantar responses flexor Anteflexion of her head caused discomfort in the posterior cervical muscles, but true meningism was absent, Kernig's sign being negative No sensory loss was noted Both loins were tender, an enlarged gland was found in the left posterior cervical region and tonsillar glands were slightly enlarged

Subsequent Course—During the following week headache and general tremulousness increased accompanied by a lo of positional sense in the left foot The patient complained of severe pain in the lower lumbar region, radiating to the left buttock and thigh and aggravated by movement Complete loss of sensation to pain and light touch was noted from the mid calf level Joint sense and vibration sense were also impaired All tendon reflexes were depressed, the right

G M C ELECTION

SIR,—Because we think that younger men should take part in the leadership of the medical profession, my wife and I voted only for Dr Whiteside and Dr Dillon If others of like mind were to vote only for the younger, unsponsored, candidates and refrained from entering any votes for the official candidates, this might counter the heavy pressure of B M A canvassing and give the younger man a fairer chance

Port Talbot, Glamorganshire   R A ROBERTS

SIR,—I am in entire agreement with Dr Whiteside and Dr Dillon It is wrong that our money in the B M A should be used to canvass votes for men standing for the G M C I admire the pluck of these two who dared to stand against the "old brigade" May I wish them better luck next time on behalf of the 16,000 who voted for them

Wimborne Minster,
Dorset   E H MARKBY

BASAL HORIZONTAL LINES ON CHEST RADIOGRAPHS

SIR,—In mitral stenosis attention has been paid to the lungs as well as to the heart, and the horizontal lines seen in radiographs in the lower lung fields have attracted particular attention Dr Rossall and Mr Gunning (May 5) show that these lines are of clinical significance, indicating a disturbance of the pulmonary circulation of such a degree as to warrant valvotomy These lines, therefore, are sufficiently important that their anatomical counterpart should be clearly understood, and I write to correct a misunderstanding by Rossall and Gunning

They refer to papers of mine[1] and others[2] and speak of "accumulation of tissue-fluid in *interalveolar septa*" as the cause of the lines, but this is a misquotation I have shown, by comparison of radiographs and lung sections, that pathological changes in the *interlobular septa* are responsible for the lines Œdematous alveolar walls would be of such microscopic size that they would not show up as lines recognisable in radiographs The anatomy underlying the lines is that of the septa between lung lobules (which are also called "secondary lobules" by Miller[3]) and which are the smallest units of the lung separated from their fellows by fibrous septa These lobules are of various sizes but, on average, about 1 cm in diameter Kerley[4] thought that the interlobular septa were too short to account for the lines, but, in large sections prepared by the Gough and Wentworth technique, the septa can be readily traced from one lobule to the next deep into the lungs When the interlobular septa are sufficiently parallel to the X ray beam, and at the same time pathologically thickened, or laden with hæmosiderin or radio opaque dust, they will show up as lines In the septa is one of the systems of lung lymphatics, and Kerley is right in saying that these lymphatics are distended but the main bulk of excess fluid is in the connective tissue of the interlobular septa, which become widened

I agree with Rossall and Gunning that the rise of the left auricular and pulmonary venous pressure rather than the rise of the pulmonary arterial pressure is the cause of this interlobular septal œdema, and I think the following is the mechanical explanation In the interlobular septa are the pulmonary veins, and I have found these distended at the inner ends of œdematous interlobular septa The distended veins may have obstructed the lymphatic flow, and fluid which normally runs centrally is diverted towards the pleura This latter route is a normal one for the superficial part of the lung, but it may have to carry a larger volume of fluid when the pulmonary veins are overdistended When the volume is too great, the lymphatics become distended and the surrounding interlobular septal tissues become œdematous Such an explanation would account for œdema of the interlobular septa in the absence of œdema of the air spaces Bruwer et al[5] have also suggested, on theoretical grounds, that distension of pulmonary veins may cause lymphatic obstruction

Welsh National School of Medicine
Cardiff   J GOUGH

SIR,—The excellent paper by Dr Rossall and Mr Gunning provides yet further evidence to support the thesis previously presented[6] as to their pathological significance

Rossall and Gunning deal only with the production of this radiographic sign in cardiac disease (and particularly in mitral disease), and show that its presence is related to a dangerously high left auricular pressure In cardiac disease the lines indicate a state of pulmonary capillary, venous, and left auricular hypertension usually secondary to mitral disease or left-heart failure, and they provide a warning of impending alveolar œdema These lines, however, occur in many other states in the absence of cardiac disease or of pulmonary hypertension

There can be no doubt that they are caused by œdema (and later organised thickening) of the peripheral interlobular pulmonary septa[1 2 6 7] Œdema of these septa is produced by exactly comparable mechanisms to œdema elsewhere in the body—e g , the soft tissues of the legs

(*a*) Œdema may be produced by an increased capillary hydrostatic pressure This pulmonary capillary hypertension is usually secondary to the increased pulmonary venous and left auricular pressures due to mitral stenosis In mitral disease, therefore, the occurrence of this radiological sign indicates pulmonary capillary hypertension and provides a valuable indication for intensive treatment including valvotomy[6] In pulmonary arterial hypertension secondary to congenital systemic pulmonary vascular shunts, the capillaries are usually protected from the hypertension by the rapid fall of blood pressure in the narrowed pulmonary arterioles As Rossall and Gunning show, it is well known that in these cases of pulmonary hypertension secondary to congenital heart-disease, the pulmonary capillary and left auricular pressure rarely exceeds the plasma colloid osmotic pressure of 25 mm Hg, and therefore pulmonary interstitial œdema and its corresponding radiographic sign do not occur In left heart failure, however caused, the lines may be seen when the pulmonary venous and capillary pressure is sufficiently raised[6 8]

(*b*) Œdema may be caused by lymphatic blockage, as in mediastinal reticuloses, sarcoidosis, pneumoconiosis, lymphangitis carcinomatosa and possibly bronchiectasis When the impairment of lymph drainage is sufficient to cause œdema of the pulmonary interstitial tissues, the identical horizontal lines are seen on the radiographs

(*c*) Œdema may be caused by increased permeability of the capillary membranes This change occurs in pulmonary[9] as well as in systemic capillaries and explains the occasional occurrence of these lines in chest radiographs in acute nephritis (even in the absence of left heart failure), allergic lung conditions, and exposure to toxic gases

(*d*) Œdema may be caused by reduced plasma colloid osmotic pressure, as in hypoproteinæmia, and although I personally have not seen these transverse lines in this condition they should theoretically occur

In (*d*) and particularly in (*c*) the illness may be acute, and it is likely that the interstitial pulmonary œdema may be obscured by the accompanying alveolar œdema

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Follow-up —On Nov 23 and Dec 22 she still had muscle weakness, walked with a limp, and was easily fatigued, sensory loss was still present On Jan 13 her right leg was still stiff and weak, and her knee jerks were still much exaggerated, but her general condition had improved

Case 8 —A girl, aged 9, complained of headache and nausea on Oct 15, 1955, and had a temperature of 100 8°F She had tenderness of her calf muscles but no neck rigidity, and all her reflexes were present Next day she vomited once, her legs ached and could not bear her weight, and she was admitted to the unit

On admission she was apyrexial, and she remained so throughout her stay in hospital Both legs were weak, the right more than the left Her leg reflexes were within normal limits Much muscle tenderness in both calves was noted

Subsequent Course —Both ankle and knee jerks became exaggerated, and weakness, particularly of dorsiflexion, increased on the left side Seven days after the onset the legs became more painful and there appeared to be spasm in the calf muscles After a further week paresis abated, and three weeks from the onset the patient was walking well and was free from pain

Comment

In all the recorded outbreaks of cases like the foregoing the investigations have been hampered by the fact that there have been no deaths and no infective or toxic agent has been found Unlike the cases previously recorded, however, the present cases were sporadic and, so far as could be ascertained, did not give rise to any outbreaks Inquiry at other fever hospitals did not reveal any similar experience, but, in view of the difficulty of diagnosis, some cases may easily have been overlooked

The lack of spread of infection to the nurses was probably related to the relatively low infectivity at the stage of the disease at which the patients were admitted, and to strict measures for control of spread in the unit, including isolation in separate rooms during the period of presumed infectivity and the use of masks by nurses and ancillary personnel If, as is assumed, this disease follows infection of the respiratory tract, probably infectivity is limited to the first ten to fourteen days, as in most virus diseases, including poliomyelitis

Summary

From April 1 to Oct 31, 1955, 51 cases of confirmed poliomyelitis, of which 29 were non-paralytic, came under treatment During the same period 8 cases were observed in which the diagnosis was acute encephalomyelitis

The motor weakness, rigidity, exaggerated reflexes without muscular wasting, sensory disturbances, and normal cerebrospinal fluid suggested a disease other than poliomyelitis This was confirmed by serological tests for all three types of poliomyelitis virus

Electromyography showed absence of the denervation characteristic of poliomyelitis and the presence of long polyphasic units with reduced interference pattern characteristic of a myelopathic lesion In 1 case a repeat examination after five months showed no change

Persistent proneness to fatigue was a troublesome sequel in 6 cases

5 cases presenting behaviour changes were examined by electro encephalography Although abnormalities were detected in all the cases they were non specific and may be constitutional

5 of the 8 cases showed residual disabilities

Since this paper was completed, 3 additional mild cases have been admitted under our care

Our thanks are due to our colleague, Dr W St J Buckler, for the electrodiagnostic investigations and comment, Dr W A Cobb, of the electro encephalography department, National Hospital for Nervous Diseases, Queen Square, for recordings and comments and the director and staff of the Virus Reference Laboratory, Colindale for laboratory examinations and much helpful advice

References at foot of next column

FURTHER OUTBREAK OF A DISEASE RESEMBLING POLIOMYELITIS

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FROM time to time since 1948, outbreaks have been reported of an illness which in many respects resembles poliomyelitis, but which differs from poliomyelitis in its epidemiology, in the mildness of the illness itself, in the high proportion of normal cerebrospinal fluid (C S F) found, in the absence of any detectable virus and in the frequent psychological changes (Sigurdsson et al 1950, Pellew 1951, Acheson 1954, Macrae and Galpine 1954, White and Burtch 1954) I report here another such outbreak—a very small one—because it may help to establish the existence of a disease which has been graphically, if somewhat negatively named "not poliomyelitis" (*Lancet* 1954)

The patients in the present series were previously fit young soldiers, of whom all but 1 lived in the same barrack block in Berlin The 1 exception was an orderly who, having nursed the other patients, was himself a close contact Although the numbers involved were small—7 cases only—the disease was clear cut and the outbreak explosive, the last case being taken ill only eight days after the first

Clinical Features

The illness ran a fairly uniform course, starting with headache which was followed in most cases some three days later by pains in the limbs and back and commonly by photophobia The principal clinical features and laboratory findings are shown in the accompanying table, and the following case, representative of the series is described in some detail

Case 2 —The patient, aged 19, had been well until three days before admission when mild frontal headache developed while he was playing football This persisted, becoming very much worse and waking him from his sleep on the day of admission For two days he had noticed that bright lights hurt his eyes and for a day had had some aching in his shoulders By the time he was admitted, on Nov 15, 1954, his shoulder pain was quite severe and he had some pain in the right leg

On examination he was flushed and ill, with a temperature of 100 2°F No abnormality was to be found outside the central nervous system He was fully conscious with slight neck stiffness, but Kernig's sign was negative Photophobia was severe, and there was moderate conjunctival injection No nystagmus was detected, although upward gaze was painful No muscle weakness or wasting was to be found, but there was considerable tenderness of the trapezii, left lower intercostal muscles, right quadriceps, and left calf muscles There were no sensory changes, deep reflexes were brisk and equal, and plantar responses were flexor

Investigations —Lumbar puncture on the day of admission produced clear colourless C S F at a pressure of 180 mm of water, containing less than 2 cells per c mm and 40 mg of protein per 100 ml with no excess of globulin, the values for sugar and chloride were normal White blood cells in peripheral blood numbered 11,700 per c mm with a normal differential count No albumin was to be found in the urine

Progress —On the fourth day of his illness some slight weakness of the right trapezius and deltoid, and of the

DR RAMSAY, DR O'SULLIVAN REFERENCES

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/8 in in diameter, were situated both on the mesenteric and on the antemesenteric borders of the affected gut beneath the peritoneum Partial gastrectomy was undertaken, and the postoperative convalescence was uneventful Pathological examination revealed pyloric hypertrophy with a small pyloric ulcer

Hackney Hospital
London E 9

R F READ

GIANT HYPERTROPHIC GASTRITIS

SIR,—Giant hypertrophic gastritis is so rare that few have the opportunity to treat many cases As stated by Dr Williams (April 7), gastrectomy is usually considered necessary when this condition gives rise to severe blood loss I have devised a less mutilating operation, and report here two cases in which it was undertaken

CASE 1—A woman aged 67, gave a history of many years' indigestion, worse for the past twelve months Her appetite had for this time been extremely poor, and she had lost a little weight On examination she was a frail old lady There was tenderness and a rather doubtful mass in the epigastrium Barium meal showed a filling defect in the mid zone, thought to be a carcinoma

Laparotomy was performed on Dec 11, 1952 The stomach, though it felt curiously thickened, was clearly not the site of a typical carcinoma The anterior wall was incised and immediately the gastric mucosa protruded, at first resembling a papilloma However, it was soon clear that it was a case of giant hypertrophic gastritis The mucosa could be lifted out of the opening without dimpling the muscle and serosal layers I was then faced with the question whether to perform a total gastrectomy The ease with which the mucosa could be lifted out of the stomach suggested that it might be possible to remove some of the redundant mucosa only To my delight, after incising the mucosa I was able to separate about 3 square inches from the muscularis Bleeding was slight and easily controlled without clamps Suture of the mucosa restored the continuity of the lining Recovery was uneventful and she remained well until the middle of 1955 She has at present symptoms similar to those of a gastric ulcer, but X ray examination shows only the enlarged mucosal folds Her appetite is not very good but she remains reasonably well on the medical regime used in peptic ulcer cases Re examination of the preoperative radiographs shows appearances typical of giant mucosal folds

CASE 2—A man, aged 30, had had severe, almost continuous epigastric pain for about twelve days, slightly better for the last two days He had vomited several times He had a past history of indigestion, with pain about an hour after food This had been investigated elsewhere, without a definite diagnosis being made On examination he was a sallow, anxious man There was no mass but some tenderness in the epigastrium Barium meal showed a filling defect on the greater curve but it was not typical of a carcinoma Gastroscopy showed no tumour but large folds, it was not realised, however, how large they were

Laparotomy was undertaken on March 3, 1953 The stomach was palpably thickened and felt somewhat like a bag of worms It was incised, and again the mucosa protruded like a papilloma I decided to follow the same course as in the previous case, and I removed 4–5 square inches of mucosa Bleeding was not severe and suture restored the lining satisfactorily He was followed up for over eighteen months and remained quite well although for some months he occasionally had indigestion He had had a great fear of cancer which had to be overcome Barium meal in May, 1953, showed hypertrophic folds but considerably less pronounced than before operation

On reflection I am sure I should have removed more mucosa in the first case I also think it would be quite easy to remove more mucosa than in case 2 This could perhaps be better done through two incisions Diagnosis should be easy before operation, as the radiographic appearances are so typical, but operation may still be undertaken to rule out a carcinoma Fortunately, if the diagnosis has not been made it will become obvious on laparotomy, especially if the stomach is opened Should the operation of mucosal resection fail, it could be repeated, or a total gastrectomy performed

Shenfield Essex

W D PARK

RESIN-REINFORCED PLASTER-CASTS

SIR,—I feel obliged to attempt to dampen the enthusiasm expressed by Mr Morrison (April 21) for the resin-reinforced bandages ('Gypsona-Extra')

Through the kindness of Messrs Smith & Nephew I had an opportunity to try these bandages when they were in the experimental stage, and my first reaction was one of enthusiasm Since the gypsona extra have come on the market for ordinary use I have used them exclusively in the sizes in which they are available My enthusiasm has by now considerably diminished

I agree that there is very little wasting of the plaster content I am not so convinced of the other advantages claimed for these plasters I have been particularly impressed by the fact that they take a long time to become quite rigid, compared with the ordinary gypsona bandages, in spite of the catalyst

I did not form this impression when I was using the experimental bandages on clinical trial, but I have observed this slowness particularly in the gypsona extra bandages now on the market This difficulty is overcome to some extent by squeezing the water out of the bandage very strongly, but it is not eliminated by this Between the moment of initial drying of the plaster and the development of complete rigidity there is a rather long phase in which the plaster appears hard but can be easily indented with moderate pressure of the hand Unless one is aware of the long duration of this phase there is a danger that the shape of the plaster may become distorted from the pressure of the surface on which it rests if it is not protected by suitable padding This long phase of plasticity has a further disadvantage if one is applying a plaster which has to be moulded on a limb It makes it difficult to mould the plaster accurately around bony points *When it is moulded in at one place it tends to bulge* out nearby like a rubber ball partly distended with air

Because of the slow drying of these plasters I have found it necessary to use for a cast a quantity of plaster not very much less than that used with ordinary gypsona The only alternative to this is to keep the patient a long time in the plaster room, because if the patient is transported back to the ward while the plaster is still in the plastic" stage there is a strong likelihood that the plaster will be spoilt

Though it is not a point of great importance, the finish of these plasters does not compare with the finish of the *ordinary gypsona plaster*

I would like once again to make a plea for the more universal use of the casts made out of a combination of 'Glassona' and ordinary gypsona By using a light base of gypsona on which the glassona can subsequently set slowly it is possible to make a very light cast for any region These casts are possessed of excellent rigidity so that, for instance, a spinal jacket can be split on one side and slipped off and put on again without losing its shape, and the forearm cast applied, say, for tenosynovitis can be split on one side and slipped off and reapplied and used in much the same way as a block leather support

I think it would be a great pity if either gypsona or glassona were taken off the market and replaced by the new gypsona-extra bandages

County Hospital Lincoln

DAVID F THOMAS

ADDICTION TO METHYLATED SPIRIT

SIR,—Many features described by Dr MacDougall and Mr MacAulay (April 21) were also present in methylated-spirit drinkers among alcoholics admitted to Warlingham Park Hospital in recent years—for instance, "emotional blunting, a tendency to vagrancy, pessimism, and depression" As Dr MacDougall says, quite a few methylated spirit drinkers can be rehabilitated The proportion of-methylated spirit drinkers was somewhat higher among our alcoholic patients (varying over the years from 10 to 20%) and there were several women among them, including one with optic atrophy The average age at which these people began to take methylated-spirit was 35 6 years (i e, in the "chronic phase" of alcohol addiction), after having consumed excessive an epidemic of Bornholm disease in Oxford, Warin et al (1953) found only 8% of cases with neither abdominal nor chest pain and only 8% with limb pains In addition, the inability to isolate the Coxsackie virus did not support such diagnosis

Leptospirosis was excluded on epidemiological grounds, by the negative agglutination tests, and by the absence of jaundice or albuminuria Moreover, in this series vomiting was slight, but it must be admitted that the conjunctival injection and limb tenderness were reminiscent of leptospiral infection

That the outbreak was of a single disease entity must, I think, be accepted because of its restricted nature and the consistent clinical picture with regard to both symptoms and physical signs That it was the disorder described as "Iceland fever" by White and Burtch (1954) and as "not poliomyelitis" by *The Lancet* (1954) is suggested by the following features

(1) The limited nature of the outbreak In this respect the present series is very similar to those described by Macrae and Galpine (1954) and by Acheson (1954) in nurses' homes

(2) The extreme muscle tenderness with neither paralysis nor reflex changes

(3) The high proportion of cases with normal C S F

(4) The mild, but persistent, mental changes, and the persistent headache, were particularly striking features The mental changes seen in other outbreaks were stressed by Macrae and Galpine (1954) and by Pellew (1951)

Two features of the outbreak described by Pellew (1951) were seen here one was hyperacusis, of which 2 patients complained, the other was recrudescence of the symptoms after several days, which was most noticeable in case 4 who had extreme muscle pain and tenderness The conjunctival injection in 5 of the 7 cases has not been described in any outbreaks While no reflex changes or persistent weakness occurred, objective evidence of neurological involvement was afforded by the presence of nystagmus in 5 cases—a common finding in the outbreak described by Acheson (1954) The transitory erythematous rash seen in 2 patients has not been described elsewhere

Future work may show that the group of outbreaks reviewed in *The Lancet* (1954) are not a homogeneous group, and indeed, cases described by Acheson (1954) with prominent neurological signs may differ from the milder cases described by Sigurdsson et al (1950) and White and Burtch (1954), which the present series more nearly resembles For the purpose of prognosis, it is well to recognise this group of infections with their explosive epidemiology, since the outlook is so much better than in true poliomyelitis

Summary

In November, 1954, there was an explosive, but limited, outbreak of a disease resembling poliomyelitis, affecting 7 soldiers in Berlin

The syndrome was marked by headache, limb pains, and muscle tenderness, photophobia and hyperacusis were common, and in some cases headache and depression persisted in convalescence

The C S F was normal in every case but 1 No virus was detected, and agglutination tests were negative

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CLINICAL FINDINGS SIX YEARS AFTER OUTBREAK OF AKUREYRI DISEASE

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In 1948–49 there was an extensive epidemic of 465 cases simulating poliomyelitis in the town of Akureyri in northern Iceland (Sigurdsson et al 1950) The population of Akureyri being 6900 the attack rate was 6 7% Paresis was observed in 129 cases There were no deaths The attack-rate was highest in the age group 15–19 but was also high among young adults generally There were very few cases in children aged less than 5 years

The disease was accompanied by low pyrexia, which sometimes persisted for weeks, and by pains in one or more limbs and in the nape and back Muscle tenderness, often restricted to small areas, was also a prominent symptom The aches often persisted long after the disappearance of all objective signs Disturbances of sensation were not infrequently observed, and complaints of nervous instability, sleeplessness, and loss of memory persisted in many cases for a long time afterwards

Fæces were tested for poliomyelitis virus and for Coxsackie virus, but no virus was found

Since 1950 several outbreaks have been described which very much resemble Akureyri disease (Pellew 1951, Acheson 1954, Macrae and Galpine 1954, White and Burtch 1954, Gear 1955) The symptoms and epidemiological behaviour of these infections are hardly sufficiently characteristic to enable all these various outbreaks to be classified together before information on their specific cause is obtained However, it seems very likely that these epidemics constitute a nosological entity, but the relationship, if any, to poliomyelitis remains obscure Several workers besides ourselves have attempted to isolate an infective agent from this type of case, but nobody seems to have succeeded so far

The protracted and even relapsing nature of the infection was one of the features which distinguished it rather clearly from poliomyelitis In numerous instances vague but annoying symptoms persisted a long time after the infection was presumably over

This prompted a renewed study of some of the patients examined in 1949

Material and Method

One of us (K R G) went to Akureyri in June, 1955, and subjected 39 previous patients to a complete neurological examination Only patients who had been examined shortly after the outbreak six years ago were examined this time All the former patients except 1 with gastric ulcer were back at their usual work There were 33 females and 6 males The attack rate during the epidemic was higher in females (8 3%) than in males (5 1%)

Results

Table I summarises the results of the clinical examination It will be seen that only 12 of the 39 patients (31%) were free from objective clinical signs, and only 5 patients (13%) considered themselves completely recovered

Table II shows how frequently the various signs and symptoms were found six years after the patients fell ill In 1949 several of the patients were neurotic and showed functional symptoms This was still the case in June, 1955, but only those symptoms which seemed to be organic have been included in the tables as he fell many times on this short journey There has been no change in his electro encephalograph, which shows a typical spike and wave pattern

CASE 2 —An imbecile girl, aged 12 years, had had very frequent petit-mal attacks since admission The attacks were not so severe as in case 1 and it was impossible to record their frequency accurately Her walking was very unsteady although she did not often fall No drugs had proved very beneficial and the best regimen seemed to be primidone 0 25 g thrice daily and dexamphetamine 2 5 mg twice daily To this was added mepacrine and since then the frequency of her attacks has been reduced and she walks much more steadily

Arellano and Alejandro stated that a period of excitation occurred a few days after the course of mepacrine, but neither of these patients showed this I hope that others will try this apparently safe therapy

Botleys Park Hospital
Chertsey Surrey

GORDON DUTTON

RADCLIFFE RESPIRATION PUMPS

SIR,—We are much interested in the description of the Radcliffe respiration pumps by Dr Ritchie Russell and his colleagues in your issue of April 28

They state that the use of a free dropping weight is the best method known to them of producing a positive pressure wave, because it removes the need for a safety-valve and gives a "square" (and therefore maximally shortened) pressure-wave Avoidance of the need to fit a pressure limiting device does not, in our view, make much difference, since a weight-operated safety-valve, for example, is simple and reliable The square form of positive-pressure wave is not limited to weight-operated pumps but can be obtained with lever operation and a cam-operated valve timed to allow a build-up of pressure before opening

There are obvious limits to what can be done by shortening the positive-pressure wave to keep mean intrathoracic pressure at a low level, and Maloney et al[1] found that respirators of the intermittent positive-pressure type did not compare favourably in their circulatory effects with those having a negative-pressure phase We can see, however, that a square curve with an abrupt flow of tidal air is useful in ensuring early opening of a pressure operated valve such as the Stott or the Smith-Clarke,[2] although this advantage disappears if a mechanical valve is used

It may turn out that negative pressure in expiration is of crucial value only in an occasional case and that its effect does not bulk large in a series, especially as the Oxford workers have had good results without it We are interested to see that the latest modification of the Radcliffe pump recognises a potential value in negative pressure by following the Smith-Clarke positive-negative respirator[3] in providing for its employment as well as by fitting a cam operated mechanical inspiratory/expiratory valve—which we believe appreciably increases the safety of intratracheal pressure respiration

Whitley Hospital, Coventry

J F GALPINE
COLM BRADY

REVISION OF THE CURRICULUM

SIR,—In answer to Dr Walker (April 28) it may not be generally known that a tutorial system similar to that envisaged by him is in existence in the clinical school at Oxford

An individual attachment to a tutor has long been an integral and valued part of the preclinical course here When the clinical school was opened it was decided to extend this system of personal tuition into the years the student spends in hospital The practice is to attach each student to a member of the staff the period of attachment varies, but during the course of his training he receives individual tuition in turn from a physician, a surgeon, and an obstetrician The form which this tuition takes is left to the tutor concerned It may be discussion of current research, essays on selected subjects, or more systematic instruction in a field of medicine in which the student is known to be weak

We believe that these tutorials form a valuable part of the curriculum in that they are one of the surest ways of stimulating discussion between pupil and teacher, and of fostering the student's interest in the advancement of medicine

University of Oxford

JOHN BADENOCH
Director of Clinical Studies

HOME CONFINEMENT

SIR,—I feel that I must reply to some of the things that Professor Russell says in his paper last week He quotes me as saying that the home is the right place for a confinement What I have consistently said is, that producing a family is the essence of making a home, and it is reasonable to expect a normal and physiological process to occur there, provided that the home is fit for a confinement to take place there and of course that the case is a normal one

My real point in writing this letter is, however, to agree with Professor Russell that it is high time for the maternity services to be rationalised and coordinated—our difficulty may be in agreeing how the coordination should occur From my experience we may find that some at least of the difficulties lie at the door of the teaching hospitals Allowing for their special position, it is not unreasonable to expect them to take their quota of social cases, and to become real partners in a coördinated midwifery scheme, we must not forget that the general practitioner has an important part to play

I think, however, that it is an excellent thing that we should have an exchange of ideas, and a desire to improve upon a standard of midwifery that has probably never been better While welcoming the setting up of the committee to consider the midwifery service, it is perhaps unfortunate that there appears to be little representation from the local-authority side which has been responsible in the past for the over-all supervision of the midwifery in its area

Public Health Department,
Sheffield

LLYWELYN ROBERTS

ADMINISTRATION OF IRON IN ANTENATAL CLINICS

SIR,—Dr Edgar and Dr Rice state (May 5) that they were compelled to use tabellæ ferri sulphatis as there was no suitable alternative and at the time of planning the trial ferrous gluconate was not available This would appear to date their work back by some four or five years

A more recent development in oral iron therapy has been provided by ferrous succinate ('Ferromyn'), which I have shown[1] to evoke a satisfactory clinical response in the treatment of iron-deficiency anæmia due to pregnancy. With administration of one tablet three times a day 105 mg of bivalent iron is made available for hæmopoiesis, and this small dose rarely causes any intolerance 52 patients with severe hypochromic anæmia due to excessive demands for iron in pregnancy were given this daily dose and all responded, the average mean daily hæmoglobin rise being 1% (0 148 g per 100 ml)

These results compare favourably with those of Dr Edgar and Dr Rice using the ferrous sulphate salt, 5 4% of their patients being excluded from the investiga-

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TABLE I—ADMISSIONS AND DEATHS FROM INFECTIONS OF LOWER RESPIRATORY TRACT IN CHILDREN AGED LESS THAN 2 YEARS IN 1953 AND 1954

Diagnosis	Admissions		Deaths	
Staphylococcal pneumonia				
Certain	21 (*4%*)	35 (*6 5%*)	4 (*16 5%*)	8 (*33%*)
Probable	8 (*1 5%*)		0	
Complicated	6 (*1%*)		4 (*16 5%*)	
Other pneumonias	53 (*10%*)		8 (*33%*)	
Other infections of respiratory tract				
Bronchitis Bronchiolitis	442 (*83 5%*)		8 (*33%*)	
Total	530		24	

We review here the cases in which *Staph aureus* was isolated and contrast them with the others admitted in the same period

Reasons for Lung Puncture

Staphylococcal pneumonia used to be diagnosed mainly at necropsy (Macgregor 1936), it was diagnosed in life only on aspiration of an empyema

Kanof et al (1939, 1953), Campbell et al (1954), and Wallman et al (1955) have built up a picture of the clinical and radiographic features of staphylococcal pneumonia, but their cases were, for the most part, either complicated by empyema or not proved bacteriologically if the infants recovered before an empyema was formed

Cultures from the upper respiratory tract are uninformative because of the high carriage rate in healthy persons, and blood culture is rarely positive in primary staphylococcal pneumonia (Kanof et al 1939)

In view of the histological findings of Reimann (1933) and Gibson and Belcher (1951) that large numbers of staphylococci are present in the early stages of staphylococcal pneumonia it was reasonable to hope that lung puncture might yield information about the infecting organism, and thus allow earlier diagnosis and treatment Moreover the propensity of the staphylococcus to develop resistance to antibiotics might make the isolation of the organism and the determination of its sensitivity important to the treatment

Material

530 infants, aged less than 2 years, were admitted in 1953 and 1954 with infections of the lower respiratory tract and were diagnosed variously as having bronchitis, bronchiolitis, bronchopneumonia, and pneumonia (including virus and neonatal) Of these 530 infants 88 had radiographic signs of pneumonia, and 35 we diagno as having staphylococcal pneumonia (table I)

Although staphylococcal pneumonia accounted for only a small percentage of the admissions in the age group with infections of the lower respiratory tract it accounted for nearly half of those with radiographic evidence of pneumonia and for a third of the deaths from infection of the lower respiratory tract

In view of the difficulty of being certain of the diagnosis in each case of staphylococcal pneumonia and to facilitate description the cases have been divided into three groups as follows

(1) *Certain staphylococcal pneumonia* —These 21 cases are considered proved for the following reasons 17 had both clinical and radiographic signs of either pneumonia or fluid together with the isolation of *Staph aureus* from either pleural pus or lung juice, and in 4 fatal cases *Staph aureus* was cultured from the lung at necropsy

(2) *Probable staphylococcal pneumonia* —These 8 cases did not present the fully developed clinical picture of 5 infants in whom *Staph aureus* was obtained by lung puncture and culture, 4 presented atypical clinical appearances, and the remaining 1 cleared unusually rapidly, 1 infant in whom lung puncture proved negative on admission had a typical clinical course and responded typically to treatment, and in the remaining 2 cases no lung puncture was done, the diagnosis depending in 1 of them on typical pneumatocele formation seen on radiography, and in the other on a staphylococcal osteitis of the maxilla draining pus into the mouth When pneumonia of the right lower lobe developed in this infant two days later it was considered to be due to inhalation of staphylococcal pus from the mouth We therefore believe that all those 8 cases were probably staphylococcal pneumonia, most of them being earlier and milder than usual

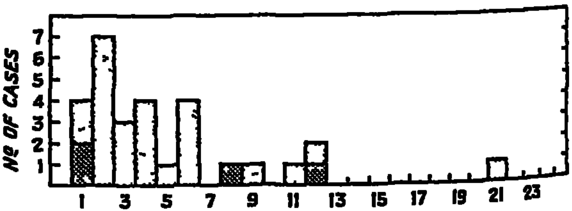

Fig 1—Age-distribution of staphylococcal pneumonia of infants Fatal cases are shown by hatching

(3) *Complicated staphylococcal pneumonia* —These 6 cases were secondary to serious underlying disease, and are not considered further here, because they did not present the usual picture 3 had fibrocystic disease of the pancreas, 1 congenital heart disease, 1 renal insufficiency, and 1 a muscular dystrophy These 6 had the highest mortality (4 deaths)

Clinical Features of Staphylococcal Pneumonia

To obtain an over all picture of staphylococcal pneumonia in infants we have studied the certain cases and the probable cases as representing a fair sample They are considered together in table II Although the inclusion of the probable cases is subject to criticism their omission would be even more misleading because the early stages of staphylococcal pneumonia would not then be fairly represented

Fig 1 shows the age distribution and confirms the high mortality in the first few weeks of life

The usual picture was of a toxic infant, with grey cyanosis and respiratory distress The hallmark of established staphylococcal pneumonia on clinical examination was obvious signs of either consolidation or fluid in the chest, this was present in 24 of 29 cases, whereas in the other 53 radiographically diagnosed pneumonias it was noted only in 7 In most cases there was an antecedent infection of the upper respiratory tract This, considered with our findings of an increased incidence during the winter months (fig 2) in step with the more numerous admissions of infants with infections of the lower respiratory tract, bears out the view that

TABLE II—CLINICAL PICTURE OF STAPHYLOCOCCAL PNEUMONIA IN INFANTS

—	Certain	Probable	Total
No of cases	21	8	29
Age	2 wk –21 mos	5 wk –6 mos	2 wk –21 mos
Onset			
Preceded by infection of upper respiratory tract	16	4	20
Acute or fulminating	4	1	5
Pyrexia > 100°F on admission	13	4	17
Signs of pneumonia	19	5	24
Leucocytosis > 18,000 per c mm	9/16	1/5	10/21
Radiography on admission			
Opaque lung field (empyema)	4	0	4
Pneumatocele without empyema	6	3	9
Pleuritis	5	1	6
Non specific infiltration	3	4	7
Not radiographed	3	0	3
Free empyema	7	0	7
Deaths	4	0	4

Only about 10% of the households presented special difficulties of the problem-family type and the opportunity was taken to attempt some improvements in their way of life The remaining 90% were helped to the mutual advantage of both the family and the county council. This valuable service seems likely to expand

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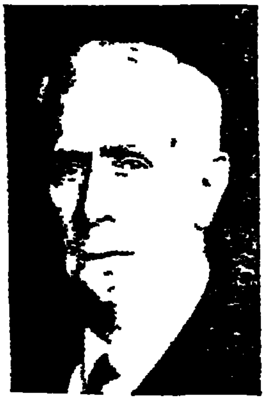
Obituary

SHELDON FRANCIS DUDLEY

K.C.B O.B.E., M.D Lond LL.D Edin F.R.C.P F.R.S

Sheldon Dudley was born in the Royal Naval sick-quarters at Lisbon in 1884 the son of Deputy Inspector-General John Dudley He grew up in an age when sons, especially Service sons followed in their father's footsteps, and he passed directly into the Royal Navy from St Thomas's on qualifying in 1906 His life reflects the opportunities and limitations of the Naval Medical Service He spent, as he once said twelve years at sea as a general practitioner and practised as a part-time specialist in six subjects, winning distinction in all and for his research on immunology election to the fellowship of the Royal Society.



[illegible]

When the 1914–18 war broke out, with service in Mediterranean and China stations already behind him, he was acting as pathologist and venereologist at the R.N. hospital at Chatham. During the war he also served as P.M.O of the R.N. Air Service in Dunkirk and of H.M.H.S. *Agadir* After the war he became pathologist at Haslar and at the R.N. Medical School Greenwich Here his research on the immunology of diphtheria was begun Of these years H J P writes:

"I was greatly privileged to know Sheldon Dudley during the most fruitful period of his research career when he was grappling with the control of diphtheria at the Royal Hospital School, Greenwich, and developing a practical and philosophic interest in epidemiology With a changing population of 1000 boys there had been no fewer than 385 cases of diphtheria between 1919 and 1927 mostly concentrated into two major epidemics At that time artificial immunisation had not been started and Dudley was able to use the material for initiating his well known studies of herd immunity

"An immunisation scheme for the school was authorised somewhat tardily in 1928, and resulted in the almost complete disappearance of clinically recognisable diphtheria Dudley's success at Greenwich and the observations made concurrently in fever hospitals and elsewhere that diphtheria could be virtually abolished even when exposure might be constant and intense undoubtedly influenced the authorities in their decision to introduce the national immunisation campaign in 1940

"Bacteriologist statistician immunologist and epidemiologist Dudley was of outstanding intelligence and originality of mind A keen and persistent investigator he used to good purpose the basic immunological knowledge derived from the laboratory experimentation of A. T Glenny I found it very stimulating to listen to his penetrating and practical survey of current problems Pertinent questions were always being asked, and he had plenty of new ideas, none of which proved to be a bad one in retrospect—an exceptional achievement Opportunities for further research were seldom wasted and his notes were always kept so carefully and accurately that analysis of his data was relatively easy His capacity for putting his finger on essential details undoubtedly served him well when he later shouldered heavy administrative responsibilities"

In 1930 after a further spell of service at sea, he was promoted surgeon captain and returned to Greenwich as director of medical studies and naval hygiene at the medical school In 1935 he was appointed M.D.G and three years later medical officer in charge of the R.N. Hospitals at Chatham. After 1941 his appointment as medical director-general in years of strenuous warfare filled his days with administration to the exclusion of research and clinical medicine Of this inevitable but frustrating separation and of its effect on Surgeon Vice-Admiral Dudley's last years a colleague writes:

"As a research-worker Dudley possessed outstanding gifts—vision scrupulous honesty, a capacity for taking infinite pains, and a comprehensive grasp of a problem These qualities were happily revealed while he was medical officer in charge of the Royal Naval Medical School at Greenwich in 1930–32 when his work on immunisation against diphtheria was carried out For this research he used the boys at the Royal Hospital School then occupying the buildings which now house the National Maritime Museum and it was from his study of the results of the Schick test that he developed his theory of herd immunity His approach was impersonal: the boys were a perfectly controlled sample of the human herd and a sick-berth staff dormitory in a naval hospital or a room at a Royal Naval barracks were ideal media in which to test his views on the spread of droplet infection It was natural for him to enjoy working among statistics and in their interpretation he showed the full power of his mind This was never more brilliantly expressed than in his Milroy lectures of 1931 on the distribution of infectious diseases in the Royal Navy, in the preparation of which he analysed and reinterpreted all the returns made in the *Health of the Navy* since the inception of this blue-book. This work led to a close association with the late Major Greenwood and to Dudley's election to the fellowships of the Royal College of Physicians and the Royal Society

"As a Gilbert Blane medallist Dudley was singled out for promotion which inevitably but unfortunately removed him from research to administration When he was appointed medical director general in 1941 he had to assume a heavy burden at a critical period It was lightened for him only by the interest he felt in the many research problems created by the need for protection from new weapons or in new conditions But he could not give this interest free rein and while his representatives on the Medical Research Council's committees occupied his chosen province he himself was bound to administrative work.

"When 1944 came and he was due to retire the end of the war was in sight and it was felt unwise to change horses in midstream and so he continued in office to the end. Perhaps the strain had been greater than he or anyone else had realised and when he was free at last to return to research he appeared unable to summon the energy Instead he became medical officer in charge of the Royal Naval Hospital at Bermuda thus coming to serve as a surgeon captain in the island where the former director-general of the Army Medical Services was to become governor He held the office for nearly two years and then entered on a final retirement from which he emerged only with the publication of two books—*The Four Pillars of Wisdom* and *Our National Ill-Health Service*"

R C M adds

"I had known Sir Sheldon very many years, but did not fully appreciate his great attributes and virtues until I had the pleasure and privilege of serving with him in the Medical Department, Admiralty during the turbulent years of World War II He was rather reserved and it was difficult for strangers to break the ice, but once that was done there was revealed a kindly humble honest, and very human being

"His main interest in life was highly scientific epidemiology, embracing bacteriology and allied science I could not help but feel that he placed medical administration on a much lower level than his epidemiology! His outlook was philosophical in its widest sense

"However in spite of his essentially professional make up he was always very helpful in administrative matters He remained calm when chaos reigned and always gave a sound lucid and logical decision under trying circumstances. His sense of humour never left him, and it was very profitable indeed to listen to him expounding some immunological or other theory during a convivial evening in a medical mess.

"During his active career he reinstated the Naval Medical Service in the medical world, and those of us who knew him will always remember his friendly smile His advice was always encouraging and of great value His wisdom was prodigious"

Results

24 infants recovered completely, 1 is left with bronchiectasis, and 4 died

Recoveries (24)

In nearly half the infants who recovered, the pneumonia i in a relapsing course It was here that the duration of treatment came into question It seemed that a comparison of the duration of the initial treatment of those who relapsed with that of those who made an uneventful recovery might help to decide the optimal length of treatment It was possible to assess 19 infants 11 recovered uneventfully after eighteen days' treatment, whereas the 8 who relapsed had an average of only eleven days' initial treatment The following case provides the most salutary warning, there being two relapses

A baby boy, aged 3 months, was admitted with three days' history of anorexia, snuffly nose, and cough

On examination he had a temperature of 99 2°F, nasal discharge, and signs of pneumonia at the right base Radiography showed consolidation and pneumatocele formation On thoracic puncture a small blob of pus appeared, and this grew penicillin resistant *Staph aureus*

Treatment —The baby was treated with erythromycin for twelve days at the end of which his chest seemed clearer both clinically and radiologically Eleven days after the end of this course of treatment his cough returned, he lost weight, his temperature rose to 99 6°F, and the signs at the right base became more obvious Lung puncture was repeated, and this time no pus was obtained, but the juice again grew penicillin resistant *Staph aureus* After eighteen days' further treatment with erythromycin the baby still had signs at one base, so, after three days' interruption, treatment was continued for another fortnight, by which time the clinical signs had almost disappeared, the white cell count had fallen from 15,600 to 9300 per c mm, and the chest on radiography was nearly clear

The reasons which led us to relatively short treatment were, inter alia, the rapid clinical response, the apparent well-being of the infants, and the consciousness of using wide spectrum antibiotics with their particular dangers to infants The necessity for prolonged treatment to prevent relapse in deep seated staphylococcal infection has long been recognised and is emphasised by Kirby et al (1953) and Neligan (1955) Both the relapsed cases and the uncomplicated recoveries seem to show that at least from twenty one to twenty-eight days' treatment with appropriate antibiotics, whether singly or in pairs, is indicated The radiographic change persisted so long (average three months) that the advice of Kanof et al (1953) to continue treatment until the chest is radiographically clear could not have been followed in many cases When a relapse took place, the warning signs were anorexia and lack of weight-gain, followed later by leucocytosis and pyrexia

Bronchiectasis (1)

This infant did not present the usual clinical picture of staphylococcal pneumonia on admission, having wide spread crepitations without signs of consolidation It was only after a lack of response to ten days' treatment with penicillin followed by eleven days' treatment with chlortetracycline that a lung puncture was done in an area where clinical and radiographic consolidation had appeared The strain of *Staph aureus* recovered from his lung was sensitive to erythromycin only He responded initially to this antibiotic, but we stopped treatment after eight days, not realising then the necessity for prolonged antibiotic cover He relapsed and did not clear completely on a second and longer course of erythromycin

Deaths (4)

The 4 deaths (mortality 14%) took place at the ages of 1 month 7 weeks 8 months, and 1 year 3 infants died within a few hours of admission and before any antibiotic could have taken effect They could have been saved only by earlier diagnosis and treatment The f infant was aged 1 month and had an overwhelmi infection but survived five days despite profoun polymorph leucopenia

TABLE IV—DIFFERENTIAL DIAGNOSIS

Disease	No of cases	No with physical signs of consolidation or of fluid	No in which radiography showed empyema or pneumatocele	Initial thora puncture*		
				Staph aureus	Other organisms	[illegible]
Staphylococcal pneumonia	29	24	13	22	0	3
Other pneumonia	53	7	0	1	[illegible]	[illegible]
Other infections of lower respiratory tract	442	0	0	0	2	[illegible]

* Thoracic puncture was mainly restricted to infants suspected having bacterial pneumonia

As Wallman et al (1955) point out, the mortality i still about 50% in the first month of life

Antecedent Staphylococcal Infection

In view of the high staphylococcal carriage rate in th noses, eyes, and umbilical stumps of neonates, and th concern over the treatment of minor infections in ver young infants (Forfar et al 1955), we tried to discov any such incidents in our series The results were follows

Of 18 infants born in hospital 15 were not known to hav had any infection, 1 had had ophthalmia neonatorum at th age of 5 or 6 days and was admitted with staphylococca pneumonia at the age of 16 days, 1 had had a stye at the age 7–10 days and was admitted with staphylococcal pneumo at the age of 4 weeks, and the mother of 1 admitted wi staphylococcal pneumonia at the age of 14 weeks had had breast abscess on the seventh day after delivery There w no history of neonatal infection in 5 infants born at home, a in 6 infants the facts are not known

The numbers are small, but, since 23 of the 29 infant were aged 6 months or less, and 14 were aged 3 month or less, the small number with a positive history of overt infection suggests that other factors, such as nasal carriage, are more important (Court et al 1955), at lea so far as staphylococcal pneumonia is concerned

The main problem, as Barber and Burston (1955 suggest, is to discover what makes the staphylococcu become invasive In the present series it looks as if a antecedent virus infection is the most likely factor in view of the seasonal incidence and the history (table II)

Discussion

The deaths and the history of antecedent infection o the upper respiratory tract in many cases show that we have much to learn about when the picture change from a respiratory infection of presumed virus origin to the usually more severe staphylococcal invasion, which demands more urgent and specific treatment In our series the history did not seem to differ much from that of dozens of children admitted with other respiratory disease The main differences were found on clinical examination, radiography, and lung puncture The results are summarised in table IV

If our findings are representative and the probable cases are accepted as true cases, any infant aged le than 2 years with clinical signs of pneumonia or of fluid ha more than three chances to one of being infected with *Staph aureus*

The radiographic findings of empyema or of pneumatocele appear to be pathognomonic

The radiographic evidence of pleuritis or of localised pleural exudate in 6 infants on admission confirms the general belief of early involvement of the pleura This pleural involvement without free empyema wa case was carried steadily and purposefully to its proper conclusion He seldom spoke about his surgical work, the more's the pity that we shall not hear his Bradshaw lecture which was to be given this year Though shy and somewhat ill at ease on the platform, he was a most effective speaker in committee, where he never said an unnecessary word when he spoke he did so with wisdom and to the purpose, sometimes even trenchantly, for his character displayed a nice blend of firmness with quiet and somewhat reserved friendliness As a chairman he had no superior, hardly a peer Business was conducted with expedition and yet every member was heard, younger members of the staff of his hospital were thankful to find a chairman prepared to give attention and consideration to their views His actions and judgments were tempered by a strong sense of fairness and justice he was thus able to contribute in no small measure to the happy relation existing between his hospital and the university At the Royal College of Surgeons, as in his hospital, his gifts as a counsellor soon became evident But it will be as a private counsellor (his advice was often sought on personal matters) that he will be remembered by many, as a raconteur who would enliven his colleagues with stories culled from his experience and told with his especial brand of humour and charm and as a friend"

Mr Scott Mason leaves a widow, Dr Helen Fox, the anæsthetist and two sons and a daughter

HYACINTH BERNARD WENCESLAUS MORGAN

M D Glasg

Dr H B Morgan, who died at his home in London on May 7 was for the last fifteen years one of the small band of medical members of Parliament He was also medical adviser and consultant specialist on industrial disease to the Trades Union Congress, and many of his contributions to parliamentary debates reflected his interest in industrial medicine and his wide experience of its problems

[Daily Herald

He was born in Grenada in the West Indies and obtained much of his education through his own efforts He won a scholarship at the Grenada grammar school and after working as a civil servant there he saved a little money and came to this country to study medicine At Glasgow University with the help of scholarships and bursaries, he managed to complete his course and in 1909 he graduated M B The same year he won the Scottish inter-university McCunn research scholarship Soon afterwards, he came to London and held house-appointments at several hospitals, including Great Ormond Street In 1914 he obtained his M.D with commendation and also took the D P H

During the 1914–18 war he served as a surgical specialist at Horton War Hospital After he was demobilised he settled in practice at Greenwich and also for some years held a part-time appointment under the Ministry of Pensions As a student in Glasgow he had become interested in politics He now turned to them again and stood as a Labour candidate for the London County Council in Greenwich in 1922 and again in 1925 Later, after he moved his practice to Camberwell, he stood unsuccessfully for North-West Camberwell in several parliamentary elections He was finally elected in 1929, only to be unseated in 1931 He did not return to the House of Commons until 1940 but after that he sat continuously until he retired last year He represented in turn Rochdale and Warrington

His last years in private practice, before he retired in 1931, were spent in Paddington He also held several consulting posts with trade unions, including the Union of Post Office Workers, and these led to his appointment as medical adviser to the T U C He was a consulting physician to the Manor House Hospital and he held the Louis Starling lectureship on industrial diseases

Dr Barnett Stross, M P, writes

"For many years before I was elected to serve in Parliament I knew Dr Morgan I had heard him lecture on industrial disease and on many occasions corresponded with him He was the most approachable of men and always delighted to help a colleague with advice and give assistance from his own varied and wide knowledge On the subject of the injured or diseased worker he was a zealot and an enthusiast Every case he advised on was to him a living issue He saw the social background and suffering of those who were deprived of their means of livelihood almost as a personal problem He struggled against injustice as if it were always directed against his own person When he showed suspicion and intolerance of authority it was because he was ever watchful on behalf of those whom authority might oppress

"I never knew him speak slightingly in private conversation of any one in the House He combined a most redoubtable capacity for public controversy with personal charm Every one liked him and those who knew him longest miss him most"

In 1930 Dr Morgan married Miss Mary Powell who survives him with two daughters

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Diary of the Week

MAY 20 TO 26

Tuesday, 22nd

WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY
5 P.M (St. Mary's Hospital Medical School, W 2) Prof F W Rogers Brambell D SC F R S Transmission of Passive Immunity
INSTITUTE OF NEUROLOGY Queen Square W C 1
5 P M Dr O Magnus (Holland) Functional Localisation in the Amygdaloid Nuclear Complex
INSTITUTE OF DERMATOLOGY Lisle Street W C 2
5 30 P.M Dr L Forman Cutaneous Manifestations of Visceral Malignancy

Wednesday, 23rd

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
5 P.M *Endocrinology* Prof A C Frazer Dwarfism and some Nutritional Factors
POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road W 12
2 P M Dr E S Anderson Enteric Phage typing
INSTITUTE OF DISEASES OF THE CHEST Brompton S W 3
5 P.M Dr Kenneth Robson Diagnosis of Bronchial Carcinoma
INSTITUTE OF DERMATOLOGY
5 30 P.M Dr Arthur Tickner Fats and the Skin
BRITISH ASSOCIATION OF SPORT AND MEDICINE
5 30 P M (Westminster Hospital Medical School Horseferry Road S W 1) Prof A E Kennedy The Psychological Approach to Sport

Thursday, 24th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr Edwin Clarke Hypertensive Encephalopathy
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P M (Hammersmith Hospital Ducane Road W 12) Prof James Young Pelvic Osteoarthropathy
INSTITUTE OF DERMATOLOGY
5 30 P M *Dr J O Oliver* Animal Parasites in Skin Diseases
BRITISH INSTITUTE OF RADIOLOGY
8 30 P M (32 Welbeck Street W 1) Prof F W Spiers D SC Radioactivity in Man and his Environment (Presidential address)
NUFFIELD ORTHOPÆDIC CENTRE Oxford
8 30 P.M Mr J C Scott Influence of Stress on Structure
UNIVERSITY OF ST ANDREWS
5 P.M. (Queen's College Small's Wynd Dundee) Dr D J M Mackenzie Health Problems in an African Territory
UNIVERSITY OF DUBLIN
4 30 P M (Trinity College) Prof A St G Huggett Environment of the Fœtus and Postnatal Health (John Mallet Purser lecture)

Friday, 25th

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS 58 Queen Anne Street W 1
5 P M Dr Louis M Hellman (New York) Tubal Plastic Operations (Green Armytage Anglo American Sterility lectureship)
ROYAL SOCIETY OF MEDICINE
5 P M *Pædiatrics* Dr F J W Miller Mr Denis Browne Tuberculous Cervical Adenitis
POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A M Sir Gordon Gordon Taylor Malignant Disease in the Vicinity of the Hip joint
FACULTY OF RADIOLOGISTS
5 P.M (Royal College of Surgeons Lincoln's Inn Fields W C 2) Prof Robert McWhirter Prognosis in Breast Cancer
ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington W 2
5 P M Prof Gordon Lennon Carcinoma of the Ovary
GUY'S HOSPITAL MEDICAL SCHOOL London Bridge S E 1
5 P M Prof P M S Blackett F R S Elementary Particles of Nature (Fison lecture)
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road W C 1
3 30 P.M Mr Wallace Black Differential Diagnosis of Ulcers in the Mouth and Pharynx.

Q fever, and lymphocytic choriomeningitis, as well as titrations of streptococcus M.G. agglutinins and heterophil antibodies.

There was clinical or radiographic evidence of pulmonary consolidation in 42 cases and evidence of inflammation of the lower respiratory tract without consolidation in 28. Serological studies revealed that 17 patients had influenza A, and the virus was isolated from the lungs of 2 other patients. There were significantly raised titres in the complement-fixation test for influenza B in 3 cases, psittacosis L.G.I. group in 3, and Q fever in 2. The streptococcus M.G. and cold agglutinins were raised in 4. Not less than an eightfold rise in titre was considered significant in these serological tests.

Sputum obtained on admission of the patients to hospital gave rich growth of *Streptococcus pneumoniæ* in 8, *Strep. pyogenes* in 6, *Escherichia coli* in 8, *Hæmophilus influenzæ* in 3, *Klebsiella pneumoniæ* in 1, *Mycobacterium tuberculosis* in 2, and coagulase-positive *Staph. aureus* in 4.

The 4 cases with coagulase-positive *Staph. aureus* in the sputum were admitted in the middle of an influenza A epidemic in the first quarter of 1953. The organism was present in very large numbers, and in 3 cases it was grown in pure culture. All 4 patients were extremely ill, and 2 of them died. A brief description of these cases follows.

INFLUENZA COMPLICATED BY SECONDARY STAPHYLOCOCCAL INFECTION

Case 1.—A housewife, aged 53, was admitted to hospital with the diagnosis of bilateral bronchopneumonia after four days' increasing chest pain and dyspnœa. Despite oxygen, penicillin, and aureomycin her condition deteriorated rapidly, and she died within twelve hours of admission. *Staph. aureus* was isolated in pure rich culture from her sputum. The organisms were sensitive to penicillin, chloramphenicol, aureomycin, and streptomycin. Influenza-A virus was isolated from the lungs post mortem.

Case 2.—A draughtsman, aged 63, who had had chronic bronchitis for six years was admitted to hospital with three weeks' history of increased breathlessness and cough. Clinical examination suggested diffuse bronchopneumonia, which was confirmed by chest radiographs showing patchy consolidation of the upper lobes and a cystic pattern over the rest of the lung fields. The patient improved rapidly on general therapy. *Staph. aureus* was isolated in rich culture from the sputum along with a scanty growth of hæmolytic streptococci. Complement-fixation tests for influenza A showed on admission a titre of 1/64, which remained constant for two weeks. Seven months later the titre for influenza A was less than 1/8.

Case 3.—A man, aged 72, who had had chronic bronchitis for many years, was admitted gravely ill with extreme dyspnœa and cyanosis. Clinically there were signs of bronchopneumonia throughout his lungs. Despite treatment with oxygen, penicillin, and digoxin he died within eighteen hours of admission. *Staph. aureus* was grown in pure rich culture from his sputum. His white-cell count was 86,000 per c.mm. (neutrophil polymorphs 42.5%, neutrophil metamyelocytes 21.5%, neutrophil myelocytes 17.5%). A complement-fixation test for influenza A showed a titre of 1/512. Attempts to isolate influenza virus from lung tissue post mortem failed.

Case 4.—A woman, aged 80, was admitted to hospital with a week's history of acute respiratory infection. Examination showed diffuse bronchopneumonia, particularly in the lung bases. Extreme weakness, cyanosis, and dyspnœa persisted for four days, after which improvement was steady. *Staph. aureus* was isolated in profuse growth from her sputum. Complement-fixation tests for influenza A on the first, sixth, nineteenth, and thirty-seventh hospital days and seven months later showed titres of 1/16, 1/128, 1/128, 1/64, and less than 1/8 respectively.

OTHER CASES WITH STAPHYLOCOCCI IN SPUTUM

During the year under review 9 other patients were found to have a coagulase-positive *Staph. aureus* in one or more specimens of sputum but not on admission. None of these patients had influenza, and none was in hospital during the epidemic period.

In 6 of these patients the growth of staphylococci was scanty and took place in solitary specimens when the patients were recovering satisfactorily from a lung infection or had recovered completely. For these reasons little meaning can be attached to the presence of the staphylococci. From the sputum of the remaining 3 patients *Staph. aureus* was isolated more than once. 2 of these patients had lung tumours, and the 3rd was a chronic bronchitic aged 64.

The clinical and bacteriological evidence therefore favoured the view that the staphylococci found in the cases of influenza were producing a severe disease, whereas those found in other cases were not. Special serological tests described below produced further evidence in favour of this conclusion.

Antibody Studies

During the 1951 influenza A epidemic our attention was directed to post-mortem findings on 2 patients who had died with fulminating pneumonia after a very brief illness. The stained films of pus from the trachea and lungs of both these patients were so rich in staphylococci that they resembled the smear of an actual colony. *Staph. aureus* was isolated in pure culture from both patients. Unfortunately no attempt was made to determine the presence of influenza virus.

This rapidly fatal illness in previously healthy persons and the ubiquity and profusion of the cocci in the lungs suggested that the local tissue and humoral antibody defences had been overwhelmed. We thought it would be profitable to investigate the circulating antibodies to *Staph. aureus* during such an infection. This was done on the sera from the patients in our series with acute infection of the lower respiratory tract, from healthy persons, from patients with minor staphylococcal lesions, and from 6 patients with severe non-pulmonary staphylococcal infections.

The antibody to the α-lysin of the staphylococcus was chosen as the most convenient index of the humoral antibody level. Not only do virulent strains of *Staph. aureus* produce α-lysin but also the titration of this lysin and its antibody is technically precise and relatively simple.

TABLE I—LEVELS OF STAPHYLOCOCCAL α-ANTITOXIN IN HEALTHY PERSONS, PATIENTS WITH INFECTION OF LOWER RESPIRATORY TRACT, AND PATIENTS WITH NON-PULMONARY STAPHYLOCOCCAL LESIONS

Serum antitoxin levels (I.U. per ml.)	Influenzal pneumonia				Non-influenzal infection of lower respiratory tract				Healthy persons	Patients with minor skin lesions	Severe non-pulmonary staphylococcal lesions
	Acute phase	After 1 week	After 2 weeks	After 3 weeks	Acute phase	After 1 week	After 2 weeks	After 3 weeks			
0.05	4	0	0	0	0	0	0	0	0	0	0
0.2	3	1	3	2	1	0	0	0	5	1	1
0.4	7	8	7	6	13	12	11	9	32	6	2
0.8	4	7	4	4	21	22	20	14	40	9	2
1.6	1	1	1	0	15	13	13	10	23	8	1
3.2	0	0	0	0	1	1	1	0	0	2	0
Total	19	17	15	12	51	48	45	33	100	26	6

without sulphur or elemental sulphur could be obtained from gypsum , but in either case, he says, it would be necessary to consume an extra amount of coal about equal to the weight of sulphur produced or replaced The fixation of atmospheric nitrogen by the bacteria of leguminous plants is possible only if there is also an ample supply of phosphorus, calcium, magnesium, and sulphur, and the artificial fixation of atmospheric nitrogen by man depends on the use of coal both as a source of energy (though there it can presumably be replaced by nuclear fission) and for chemical reasons So far, " the consumption of wasting assets has merely been shifted from nitrate to coal" about 5 tons of coal being needed to fix 1 ton of atmospheric nitrogen Further, the more nitrogenous fertiliser is used the greater is the demand for alkaline earths Therefore the more factories we build for making such fertiliser, the more lime and other earthy base we must supply not merely to neutralise the resultant acidification of the soil, but also for incorporation in the additional crops—the target of all this effort Nicol tells us that 18½ million tons of fertilisers will have to be provided to every 1 million tons of nitrogen produced synthetically from the air Any extension of food production will therefore depend on further chemical, engineering, and industrial effort leading to additional consumption of fuels and other wasting assets Fuel, he remarks, "is as essential to food production on a present day scale as it is to the continued existence of air lines"

At the end of all this endéavour, we must also take account of the tendency of the soil towards homœostasis In Nicol's words "Whatever man does towards raising the level of organic matter and available nitrogen in the soil, his efforts at striking a higher balance will be resisted and opposed by the soil microbes and other natural agencies These agencies will coöperate to destroy and remove any unnatural excess of organic matter and to restore the proportion of organic matter to what is natural to the soil" Even when, in the ordinary course of affairs, the nitrifying bacteria of the soil convert ammonia or ammonium salts into nitric acid, a demand for alkalis is set up to neutralise the acidity, which is inimical to both the bacteria and the plants Apart from supplying such alkalis there is no point in "feeding" the soil bacteria, which constitute a very finely balanced system Increase in the supply of any one material merely throws the system out of equilibrium The same principle applies to artificially irrigated land (including deserts) the natural equilibrium has been upset, and the price must be paid either in fuel or by going without the crops Though, by sufficient effort, the desert can be made to blossom as a rose, we cannot expect much return from its cultivation unless we have the fuel to make fertilisers for it, to irrigate and drain it, and to distribute the food it grows

A DAY HOSPITAL

A DAY hospital and treatment centre for 30 patients has been opened at Whitchurch Hospital, Glam The former bakery and tailor and bootmaker's shops of the hospital have been converted by the maintenance staff into a two storeyed building On the ground floor there is a waiting-room and records room, accommodation for the visiting E N T surgeon, dentist, and chiropodist and a group therapy room with seating for 50 patients On the first floor there are three consulting rooms, a medical library, and a room for the clinical clerks Patients will attend the hospital from 9 A M to 5 P M and will return to their own homes each evening They will be selected from those attending psychiatric outpatient clinics and from among the convalescent hospital inpatients who are ready to return home but who still need to continue their treatment Dr T J Hennelly, the superintendent, describes the new venture as providing treatment at the hospital rather than in the hospital

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University of Oxford

Dr R M Bannerman has been elected to a Radcliffe travelling fellowship

University of London

On March 21 the degree of M S was conferred on C Naunton Morgan and R J H Smith

University of Glasgow

On April 30 the degree of PH D in medicine was conferred in absentia on Ian Macadam, B SC

Royal College of Surgeons of England

At a meeting of the council on May 10, with Sir Harry Platt, the president, in the chair, Mr A Lawrence Abel was elected vice president in place of the late Mr Scott Mason Dr Bernard Johnson (Middlesex Hospital) and Prof M Lucas Keene (Royal Free) were admitted to the fellowship, having been elected as medical practitioners of twenty years' standing Mr David Trevor (Charing Cross) was admitted to the court of examiners Mr Lawrence Abel was appointed Bradshaw lecturer for 1956

The Cartwright prize for 1951–55 was presented to Mr B E D Cooke and a certificate of honourable mention to Mr N L Rowe The Robert Jones travelling fellowship was awarded to Mr Michael Alms The Gilbert Blane medal for 1956 was awarded to Surgeon Commander J M Holford, the Mitchiner medal to Lieut Colonel R E Waterston, and the Lady Cade medal to Air Commodore C A Rumball The Begley prize was awarded to C R N Ashbee (St Bartholomew's Hospital Medical School)

Postgraduate diplomas and diplomas of membership were conferred on the candidates named in the report of the comitia of the Royal College of Physicians (*Lancet*, May 5, 1956, p 644)

Royal College of Surgeons of Edinburgh

At a meeting of the college held on May 9, with Sir Walter Mercer, the president, in the chair, the following were admitted to the fellowship

P L Berger, John Bingham A C Bowring M E J Brightman, Ivan Coll, Harold Collinson, G I B da Costa G A Dalton Prakash Chandra Dubey, D B Eaton, A W Eklund C A Ezike C L Greaves, M B Johnson, E P J King R P Leake J I de Boer Leembruggen D O Maisels, N K G Mendis J H Miller A H Mizrachy, Hari Mohan James Morgan Nuggihalli Ranganath Aiyengar Narayan K G Orr J R Page Hyman Perkin Kamalesh Pandurang Prabhu Mohammad Abdul Qayyum, L A Sarembock, F W Shea C A Shearer D M Sinclair, Dhurandhar Prasad Singh R D Smith B D Stringer J N Tennant, I C K Tough, Robert Yule

University College of the West Indies

The University of London has taken this university into a special relation by which students of the college work for degrees of the university, the examinations for the degrees being held in Jamaica under the supervision of examiners appointed by the university Students who pass obtain a full degree of the University of London as external students Holders of the M B , B S degrees obtained in this way are entitled, on application, to registration by the General Medical Council The following have been successful

Dorrit V M Box, L M Burke C J Charles D E Christian, R I Forbes H R Francis B A Q Hamilton Smith K A W McKenzie O D O Minott D B Mitchell Pamela E B Rodgers, A R Walwyn M O Woo Ming (October 1954) Betty Millbourne Clark (April 1955) L B Bannister T E Been R K Berry, F N Boland G B P Cummins Barbara E Johnson S S Lutchman, Myrtle E Mitchell, D I M Picou Premchand Narpat Ratan N L Read R O Saunders K L Standard K M W Tang Norma C M Theobalds (October 1955)

London College of Osteopathy

The Leverhulme Trust Fund is providing scholarships to enable qualified medical men and women to study osteopathy at this college They will cover the cost of fees and maintenance The course begins next October, and application should be made before June 30 Particulars may be had from the secretary of the college, 24, Dorset Square, London, N W 1

Royal Northern Hospital, London

This hospital is celebrating its centenary from June 25 to 30 this year The programme includes medical and surgical demonstrations at the hospital and a dinner at the Royal College of Surgeons on June 26, which the Duke of Gloucester will attend

Royal Medical Benevolent Fund

The annual general meeting of this Fund will be held on Tuesday, June 5, at 5 P M , at 11, Chandos Street, London, W 1, with Lord Webb Johnson, the president, in the chair

Hunterian Society

The subject for the gold medal essay of 1956 is the Care of the Growing Child in General Practice The competition is open to all doctors in general practice Further details may be had from the hon secretary of the society, Mr R S Murley, 95, Harley Street, London, W 1

COMBINED SURGICAL AND PHYSICAL TREATMENT OF SUPERFICIAL SEPSIS

Philippe Bauwens
M R C P
PHYSICIAN IN CHARGE, DEPARTMENT OF PHYSICAL MEDICINE

M G Cox
M A, M B Camb, F R C S
SURGICAL REGISTRAR

Anthony B Coyer
M B Durh, D Phys Med
SENIOR REGISTRAR, DEPARTMENT OF PHYSICAL MEDICINE

ST THOMAS'S HOSPITAL, LONDON

The casualty department at St Thomas's Hospital has a close liaison with the department of physical medicine, which provides treatment by physical methods in minor sepsis This has shortened the patient's period of incapacity, compared with routine surgical treatment alone The time saving is of great economic importance since the majority of such patients are wage earners

Stimulated by the high incidence of superficial sepsis and septic wounds, particularly of the hands, during the war years in London, one of us started using a section of the physical medicine department for the treatment of these conditions (Bauwens 1940) He worked in conjunction with the resident assistant surgeon and his staff, who performed the necessary surgery

A similar organisation exists at present, staffed by trained physiotherapists who apply all dressings and use various physical treatments These include local heating by means of short-wave diathermy, infrared radiation, or micro waves, which result in increased circulation and the activation of defensive processes in the affected area, and ultraviolet radiation, again usually applied locally with the aid of the Kromayer lamp, the therapeutic effect of which results from destructive action on bacteria and increased rate of proliferation of tissue cells (Bauwens 1950) Occasionally ultrasonics are found to be of value in early cicatrisation, especially in the case of ulcers, where thickening and scarring of adjacent skin delay full healing (Curwen 1953)

In the lower limbs, sepsis, laceration, and ulceration are commonly complicated by œdema which retards healing Such conditions are greatly improved by the application of strong elastic bandaging, first advocated by Bisgaard (1948) and later developed by Curwen and Scott (1952)

The effects of treatment are of course greatly enhanced by complete rest of the parts directly or indirectly involved Thus many cases of sepsis of the upper limb digits, hand, or forearm are helped by temporary splinting with Kramer wire and the use of a sling, in the initial stages At the same time, in order to prevent stiffness, the immobilised joints are put through a full range of active movements at each attendance

The routine treatment of carbuncles includes shaving and cleansing the surrounding skin with surgical spirit and applying a counter-irritant dose of ultraviolet light After this, it is swabbed with a 1 in 1000 solution of biniodide of mercury in acetone The skin is then immobilised with elastic adhesive bandage, leaving a window over the pointing area of the carbuncle This allows purulent matter to discharge freely and prevents its contact with the neighbouring skin and infection of surrounding hair follicles Short-wave treatment is applied twice daily followed by occasional E 4 doses of ultraviolet rays when the slough separates Dry dressings are applied regularly over the exposed part of the carbuncle

As an indication of the value of this combined surgical and physical treatment compared with surgical treatment alone, one type of lesion—paronychia of the hand digits—was singled out for investigation The condition was sufficiently prevalent to provide significant numbers for both experiment and control, and allowed of easy objective assessment

Method

One of us (M G C) for a period of six months saw all the cases of acute paronychia of hand digits in the hand clinic of the casualty department Patients who were suspected of having pus under the base of the nail were treated by wedge incisions of the nail-bed angles combined with total nail removal under digital block anæsthesia (Rodney Smith 1954)

Immediately postoperatively the nail-bed was dressed with tulle gras and covered with gauze and wool, and the arm was placed in a sling Each patient was inspected the following day by M G C and referred for treatment to the department of physical medicine Here, treatment consisting of short wave diathermy heating was applied twice daily for periods of about ten minutes, starting about twenty-four hours after the initial operation Local applications of ultraviolet radiation in E 3 and E 4 doses were given by means of the Kromayer lamp every other day Where infection was severe, the open area was dusted with 2% aureomycin in K 28 starch powder Sterile tulle gras dressings were reapplied daily The patients were discharged by one of us (M G C) when the surface was dry and the patient considered fit for work without a dressing 118 patients over 14 years of age, and 23 children aged 13 years or less, were treated by this combined routine

As a control series, 33 consecutive patients aged 14 years or more were submitted to the surgical routine already described without receiving any physical treatment They were re dressed the following day with 1 in 1000 solution of proflavine hemisulphate and thereafter seen at intervals of two to three days when similar dressings were applied until the wound had healed and the patient was fit for work

Cases of acute paronychia complicated by adenitis or lymphangitis were not included in this investigation since they were given, concurrently, systemic antibiotic therapy

Results

30 patients over 14 years of age (group A) treated by combined surgery and physical methods alone were discharged after an average time of 4·3 days

88 patients over 14 years of age (group B) with more severe sepsis, necessitating the local application of starch powder containing 2% aureomycin, treated by combined surgery and physical methods were discharged after an average time of 5·3 days

23 children aged 13 or less (group C) treated by combined surgery, physical methods, and local application of starch powder containing 2% aureomycin were discharged after an average of 4·1 days

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DR DUNCAN EVANS, DR MYRDDIN EVANS
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ENCEPHALOMYELITIS SIMULATING POLIOMYELITIS

A MELVIN RAMSAY
M A, M D Aberd
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IN the summer of 1955 cases of encephalomyelitis simulating poliomyelitis appeared in North-West London The general picture and the results of investigation, however, have shown that a diagnosis of poliomyelitis is untenable, pareses unaccompanied by wasting, tendon reflexes generally unaffected or exaggerated, sensory disturbances, normal cerebrospinal fluid, and electromyographic studies which fail to reveal any evidence of neuronal degeneration indicate a different ætiology and pathology Similar outbreaks have been reported from Adelaide (Pellew 1951), Coventry (Macrae and Galpine 1954), New York (White and Burtch 1954), London (Acheson 1954), and Durban (Cheetham, personal communication) The obscure infection responsible for an epidemic among the nurses of the Royal Free Hospital, Gray's Inn Road (see *Lancet* 1955), was probably of a similar nature It is probable that the outbreak in Iceland in 1948 (Sigurdsson et al 1950) was an aberrant form of poliomyelitis, as the spinal fluid proved abnormal in every instance in which it was examined

We describe here 8 cases, variously notified as meningitis, poliomyelitis, and pyrexia of unknown origin, which occurred between April 1 and Oct 31, 1955 During that period 51 patients with confirmed poliomyelitis (22 paralytic, 29 non-paralytic), slightly more than the yearly average since 1947, were admitted to the Infectious Diseases Unit at this hospital They were aged 9–45 years and were all female except 1, aged 27 1 belonged to the non resident staff of a London teaching hospital, where one or two similar cases occurred among the nurses, and another had been an inpatient at a neighbouring hospital None of the patients had been in contact with each other or, so far as could be ascertained, with cases of the current infection among the nurses at Gray's Inn Road These cases were notified to the medical officers of health of the various boroughs in which they resided as acute infective encephalitis, in accordance with the regulations in force from Jan 1, 1950

Clinical and Other Features

CLINICAL PICTURE

The onset was generally insidious, with various initial symptoms Headache, pains in the limbs, and giddiness were prominent in most cases Lassitude and inertia (drowsiness in 3 cases), nuchal pain, symptoms of infection of the upper respiratory tract with sore throat, vomiting, paræsthesiæ, anorexia, and nausea, were present in over half the cases Muscular cramps, twitchings, pain referred to the ears, and transient or persistent tinnitus were also noted On admission lymphadenopathy affecting chiefly the posterior cervical lymph nodes was found in 7 cases various grades of neck stiffness, paresis, and exaggerated reflexes in 6, objective sensory impairment and muscle tenderness in 5, cranial-nerve involvement in 4, extensor plantar responses in 3, nystagmus in 2, and diplopia in 1 The left side of the body, especially the left lower limb, was mainly affected In 1 patient mild hepatitis developed and was confirmed by liver function tests, it was impossible to say whether this was part of the disease, the result of giving chlorpromazine, or an independent infective or serum hepatitis Pyrexia did not usually exceed 100°F and tended to recur transiently with relapse of symptoms The stay in hospital lasted from nineteen to ninety-four days Recovery was slow, and convalescence protracted, with mental and physical fatigue and emotional instability in half the cases 3 cases show persistent weakness and sensory impairment four to six months after the onset

BLOOD PICTURE

In all the cases the blood picture was characteristic of a virus infection—i e, neutropenia with inconstant abnormal lymphocytes The term "abnormal lymphocyte" is somewhat loose but means here the next stage to the abnormal mononuclear cells characteristic of "glandular fever," no instance of which was encountered in this series Blood smears taken from cases of poliomyelitis, febrile catarrh, and the present infection were submitted to several experienced hæmatologists, who were unable to detect any distinguishing feature which could assist the differential diagnosis

CEREBROSPINAL FLUID

The cerebrospinal fluid was normal in every case except 1 in which the protein level was 50 mg per 100 ml, a repeat examination after thirteen days in 1 case was still normal The Wassermann and Kahn reactions were negative

VIRUS INVESTIGATIONS

Despite intensive investigations, in collaboration with the Virus Reference Laboratory, Colindale, an ætiological agent has not been isolated Throat washings and/or fæces were examined in tissue culture of monkey kidney for poliomyelitis and Coxsackie and other viruses Screening by serological testing of paired sera for lymphocytic choriomeningitis, mumps, leptospirosis, and all three immunological types of poliomyelitis was negative in each case

ELECTROMYOGRAPHY

All 8 cases exhibited muscle weakness and were submitted to electrodiagnostic examinations Usually the weak muscles showed abnormalities of motor unit activity revealed by the electromyographic pattern, but in no instance was evidence of lower motor neurone degeneration detected Thus nerve conduction was retained, muscle responses were brisk to direct long duration stimuli (100 msec), and intensity duration curves showed rheobases within normal limits and threshold intensities for 1 msec stimuli less than twice the rheobase Electromyographic exploration of the muscles showed no spontaneous activity, in particular no fibrillation potentials, but on volition the number of motor unit potentials was reduced (reduced interference pattern) with a tendency to occur in groups of up to 6 potentials,

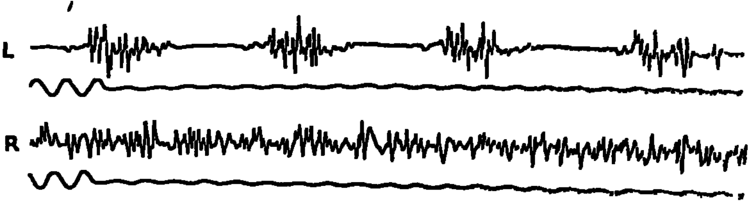

Fig 1—Electromyographs from case 1: *upper register, from left tibialis anterior muscle on maximal volition, showing grouping of large polyphasic motor unit potentials; lower register, from right tibialis anterior muscle on maximal volition, showing complete interference pattern of normal motor unit potentials.* (Calibration 500 and 100 µV at 50 cycles per sec)

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acute episodes. Ultimately there was no response to bigger doses, and she died after 3 years' treatment. The diagnosis was confirmed at necropsy.

Chronic Bronchitis

CASE B.—A housewife, aged 41, with increasingly severe bronchitis for 18 years, each intercurrent infection causing many weeks of great incapacity, showed an excellent response to oxytetracycline, with greatly reduced cough and dyspnœa. Her sputum, which had amounted to 4 oz. daily, was reduced to $^{1}/_{4}$–1 oz.; she felt much better generally and gained 8 lb. in weight. Upper respiratory infections rarely necessitated bed rest or caused much incapacity. She remains greatly improved, having continued the treatment for $2^{1}/_{2}$ years with doses varying from 1 to 3 g. daily. *Hæmophilus influenzæ* was last recovered from her sputum after $1^{1}/_{2}$ years' treatment when it remained sensitive to oxytetracycline. The sputum now persistently contains *Proteus vulgaris*, which seems to have no adverse effect on the patient's condition.

CASE C.—A policeman, aged 51, with increasingly severe bronchitis for 5 years was admitted to hospital extremely ill and in heart failure. He made a dramatic recovery on oxytetracycline and was able to return to duty for 2 years and thus to qualify for his pension. He has been less breathless, and his sputum has been reduced from 2 oz. to less than 1 oz. daily. His general condition has remained much improved, and his weight is 2 stone greater than before treatment. He has had one period of 3 weeks in bed following an upper respiratory infection, but his general improvement has been maintained for $2^{3}/_{4}$ years to the present time on continued oxytetracycline, the dose varying from 1 to 3 g. daily. *H. influenzæ* has been obtained intermittently from his sputum, and on the last occasion, after $2^{1}/_{4}$ years' treatment, it remained sensitive to the antibiotic.

Seven other patients were still receiving oxytetracycline at the time of the last report (Helm et al. 1954). Treatment was discontinued in four of these for the reasons set out in the accompanying table. In two of the other three patients improvement has been maintained up to the present time.

One, who was originally admitted to hospital acutely ill with heart failure, has had two further but less severe episodes of failure while administration of the antibiotic has been continued for $2^{1}/_{2}$ years. Although his improvement has been least distinct of all in this group he has been able to lead a normal quiet retired life, and his condition has deteriorated when attempts have been made to stop treatment. His sputum has remained reduced from 2 oz. to 1 oz. daily, and *H. influenzæ* was last isolated from it after a year's treatment, when the organism remained sensitive to oxytetracycline.

RESULTS OF TREATMENT OF THIRTY-EIGHT PATIENTS WITH OXYTETRACYCLINE

Diagnosis	No.	No. remaining on treatment at time of last report (1954)	No. remaining on treatment with benefit to present time	Reason for abandoning treatment in others
Chronic staphylococcal bronchopneumonia	1	1 (30 mos.)	0	Died after 3 years' treatment
Bronchitis	17	9 (7–20 mos.)	5 ($1^{1}/_{2}$–$2^{3}/_{4}$ yr.)	2 patients responded well but treatment was stopped in order to obtain an autogenous vaccine. 1 patient responded well but had recurrent diarrhœa and treatment ultimately had to be stopped. 1 patient had relatively slight benefit and treatment was therefore stopped
Infective asthma	13	0		
Bronchiectasis	7	4 (6–8 mos.)	3 ($1^{1}/_{2}$ yr.)	1 patient had relatively slight benefit and treatment was stopped
Total	38	14	8	

Another patient, also admitted in heart failure, has continued to take 0·5 g. of oxytetracycline twice daily for 20 months. His sputum volume was reduced early from 4 oz. to 2 oz. daily, and it has remained consistently at this level. It has been mucoid since the first week of treatment and *H. influenzæ* has not been found since then. This patient feels very well generally, but he is compelled to lead a sedentary life owing to the breathlessness resulting from his severe emphysema.

The third patient still receiving oxytetracycline responded well initially to 1 g. three times a day. His sputum, previously mucopurulent for years, became mucoid within a week, and its volume was reduced from 3 oz. to 1 oz. daily. He continued satisfactorily for 9 months on a maintenance dose of 0·5 g. twice daily, but unfortunately the treatment was inadvertently stopped at this time. Within a fortnight pus had returned to the sputum, the daily volume of which rose to 2–3 oz. Oxytetracycline therapy was restarted, but, although he has improved again to some extent, he has never regained the condition he had reached before the treatment was stopped. His sputum is still mucopurulent and amounts to about 3 oz. daily after a further 10 months' treatment. It contains many *H. influenzæ*, which are resistant to oxytetracycline.

Bronchiectasis

Four patients with bronchiectasis were continuing treatment at the time of the last report (Helm et al. 1954). In one the benefit was relatively slight, and oxytetracycline was stopped with the object of substituting treatment with an autogenous vaccine. The other three have maintained their improvement in a remarkable way to the present time. All had up to 4 oz. daily of mucopurulent sputum, which has been reduced to 1 oz. or less and is mucoid in each case. All patients have gained weight.

One, a schoolmistress, is especially glad to have greatly reduced cough and sputum. She had an attack of asthma—the first for years—soon after starting oxytetracycline but this responded to routine treatment and there has been no recurrence. *H. influenzæ* was isolated once during treatment (after 10 months) from this patient's sputum, but sensitivity tests were not carried out.

No pus or *H. influenzæ* have been found in the sputum of either of the other two patients at any time since treatment began. One persistently harbours *Pseudomonas pyocyanea*, which apparently has no adverse effect on the patient. Both have less breathlessness, and one maintains that she has "not felt so well for 20 years."

TOXIC EFFECTS

Diarrhœa has been the only side-effect encountered, but in only one patient was it so severe that oxytetracycline had to be discontinued. Liver-function tests have been carried out on five patients, but in each they have remained normal. These findings have been confirmed in other patients treated in the same way but not included in the present series. One of these died in heart failure after a year's treatment with oxytetracycline. At necropsy there were changes in the liver typical of congestive cardiac failure but no evidence of any toxic effect of the antibiotic.

Discussion

At the beginning of this investigation (Helm et al. 1954) thirty-eight patients were started on oxytetracycline therapy (one with chronic staphylococcal bronchopneumonia, seventeen with chronic bronchitis, thirteen with infective asthma, seven with bronchiectasis). Of these eleven of the asthmatics were considered not to have a true infection, so twenty-seven infected patients remained. A good early response to oxytetracycline was obtained in twenty-four patients, but for various reasons plantar response was flexor, and a left plantar response could not be elicited. A week later the patient complained of pain in the left side of her face and neck, next day lower right facial palsy was noted and paresis of the left foot increased. After a further week pain of pleural type developed in her left chest but clinical and radiographic examination was negative. By the end of August her general condition had improved and complaints of pain were infrequent, but the signs in the central nervous system were virtually unchanged. On getting up, although her sense of balance was normal and Romberg sign negative, she walked on a wide base with a tabetic type of stamping gait. Graduated exercises effected slow but steady improvement.

Follow up.—On Nov. 22 she had returned to work, but she complained of undue fatigue toward the end of the day. Weakness affecting her right lower face, left arm, and left leg and sensory loss in her left leg were still present. On Dec. 14 there was general improvement but still much weakness and sensory loss in her left leg, with right lower facial weakness.

Case 3.—An unmarried female domestic worker, aged 20, developed malaise and giddiness on Aug. 11, followed by headache, faintness and lassitude, on Aug. 15. She was admitted to the unit next day.

On admission her temperature was 99.4°F, and she appeared to be mentally dull but well oriented. Slight neck rigidity was present, but Kernig's sign was negative. There was slight impairment of muscle power in the flexors and extensors of her right knee. Her deep reflexes were within normal limits, abdominal reflexes present, and plantar responses flexor. She had a coarse tremor of her head and arms, especially on sitting up. A few small glands were palpable in the posterior cervical region.

Subsequent Course.—Her temperature settled within twenty-four hours of admission and, except for a rise to 99.4°F on Aug. 30, the patient remained apyrexial. Neck rigidity increased considerably and persisted for four days. Bilateral palsy of her external recti muscles was noted on Aug. 22, and her knee-jerks became exaggerated. Tremulous movements of her head and arms persisted and were aggravated by movement or by sitting or standing. The patient became emotionally unsettled and discharged herself on Sept. 4. During a period spent subsequently at a convalescent home she complained of further attacks of giddiness and was readily fatigued and notably lacking in energy.

Case 4.—A married housewife, aged 40, developed occipital headache, severe giddiness, vomiting and pains in her nape and limbs on Aug. 18, 1955, all symptoms were aggravated by movement and usually relieved by recumbency.

On admission to the unit on Aug. 20 her temperature was 99°F, and she was anxious sweating, moderately flushed and exhibiting much tremor of her arms. Some neck rigidity was present, but Kernig's sign was negative. She had slight generalised muscle weakness, her deep reflexes were within normal limits, abdominal reflexes absent, and plantar responses flexor. No sensory impairment was detected.

Subsequent Course.—The illness was characterised by intermittent bouts of low grade pyrexia. Shortly after admission the patient complained of pains and paræsthesiæ in her legs of sufficient severity to interfere with sleep. On Aug. 21 weakness appeared in her left leg with increase of subjective phenomena without demonstrable sensory loss. This was followed two days later by tremulousness of the right lower part of her face and by left lower facial weakness with left hemiparesis and hemianalgesia, the latter was maximal distally. The deep reflexes were diminished in her left arm, but her knee and ankle jerks became exaggerated. Her right plantar response was extensor, her left could not be elicited. Bouts of vomiting inertia giddiness, and tinnitus came on irregularly, usually coinciding with low grade pyrexia. When the patient got up, her gait was uncoördinated and her giddiness increased. On Oct. 4 mild hepatitis developed, and thereafter the patient became emotionally unstable and discharged herself on Oct. 18.

Follow up.—On Dec. 9 her general condition showed definite improvement, she was steady on her feet, and her gait had obviously improved, but she still complained of nausea, flatulence, and persistent tinnitus in her left ear. She had slight weakness of dorsiflexion of her left foot, but otherwise her muscle power was normal, and all evidence of sensory loss had disappeared, although considerable tremor of her hands persisted.

Case 5.—A male instrument maker, aged 27, had coryza during the first week of August and complained of sore throat from Aug. 12 to 15. On Aug. 17 he developed numbness of the right side of his face, loss of taste over the right side of his tongue, and repeated attacks of vomiting and giddiness. He could not retain fluids during the next ten days and was admitted to the unit on Aug. 27.

On admission his temperature was 99.8°F and he looked extremely ill, toxic, and dehydrated. A sparse maculopapular rash was present on the front and back of his thorax. Nystagmus was present on lateral deviation to either side but coarser to the left. Sensation to fine touch was completely absent over the distribution of the right 5th cranial nerve, there was hyperæsthesia to pinprick over the same area, temperature sensation was normal. He had mild paresis of the right side of his face, and his tongue on protrusion deviated to the right. Taste sensation was absent over the whole of the right side of his tongue. His deep reflexes were exaggerated, abdominal reflexes present, and plantar responses flexor.

Subsequent Course.—Occasional peaks of pyrexia not exceeding 100°F occurred throughout his illness. Vomiting continued for two days after admission. Dehydration and electrolyte balances were corrected with intravenous fluid therapy. Sensation began to return to normal after ten days, at the same time his facial paresis steadily abated. On Sept. 16 his plantar responses had become extensor, and he had a fine tremor of his arms and legs, slightly more exaggerated tendon reflexes on the right side, and slight facial paresis on the left. Impairment of his sense of balance and occasional attacks of giddiness were noted when the patient was allowed to get up, but otherwise his convalescence was uninterrupted and progressive. The sense of taste is still absent from the right side of his tongue, but in other respects his recovery is now complete.

Case 6.—A female professional dancer aged 28, had coryza from Sept. 14. Two weeks later she developed sore throat and acute vertigo lasting two or three hours. On Sept. 30 she had abnormal sensations, including numbness in both legs, especially the left.

On admission she was apyrexial, with no meningism although full neck flexion caused discomfort in her neck muscles. Power, tone, and deep reflexes were normal in her arms. Her abdominal reflexes were present. She had diminished power in both legs especially the left, her deep reflexes were within normal limits, and both plantar responses were flexor. There was an area of impaired tactile sensation around her left knee joint. A few shotty glands were palpable in the left posterior cervical triangle.

Subsequent Course.—The patient remained apyrexial throughout her stay in hospital. The hypo-algesia and hypo-æsthesia of her left leg increased for a few days after admission and involved the limb up to the mid thigh. Joint sense and vibration sense were also impaired over her left leg. On Oct. 5 rotatory nystagmus was noted, and the patient complained of diplopia on looking directly upwards, there was no evidence of ophthalmoplegia. When she got up, her rigid gait resembled that found in poliomyelitis with spasm, but her deep reflexes were exaggerated.

Follow-up.—Proneness to fatigue persisted, but otherwise the patient appeared well.

Case 7.—A girl, aged 15, had coryza intermittent headache, and weakness in her right leg on Oct. 1 1955. A week later her leg felt numb and afterwards became painful on movement.

On admission to the unit on Oct. 10 she was apyrexial, and she remained so throughout her stay in hospital. Slight neck rigidity was present. No abnormality was noted in either her cranial nerves or her arms. Her abdominal reflexes were absent on the left side, and she had weakness of the extensors and flexors of her right knee joint and the plantar flexors of her right foot. An area of sensory loss was present over the medial aspect of her right calf. Her leg reflexes were equal but exaggerated, her plantar responses were flexor. Apart from slight faucial injection and a few small glands in the left posterior cervical triangle there were no other abnormal findings.

Subsequent Course.—All the muscles in her right leg became weaker, and her right gluteus maximus muscle was found to be affected. Paresis was greatest in the plantar and dorsiflexors of the ankle. Sensory loss and motor weakness were present throughout the patient's stay in hospital. She was discharged on Nov. 1.

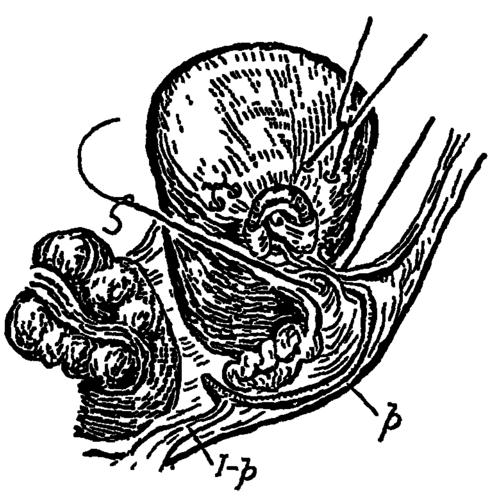

Fig 3—Polyethylene cord passed into uterus through peritoneal lined opening. p, polyethylene cord; I p, infundibulo pelvic ligament.

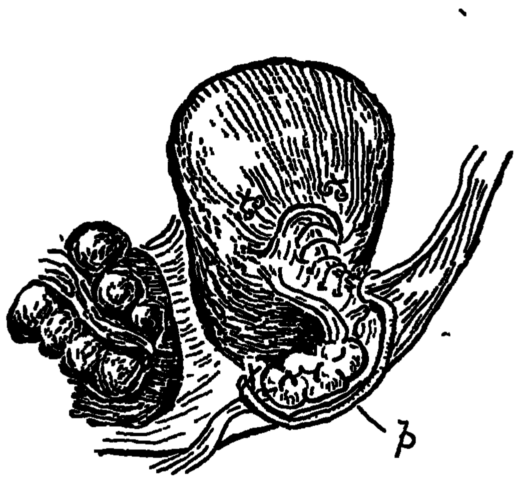

Fig 4—Polyethylene cord enclosed in peritoneal channel by continuous suture over round ligament. p, polyethylene cord.

the uterine wall (fig. 2). The cornu of the other side is reamed and peritonised in the same way. Polyethylene cord 2 mm. in diameter is passed into the uterine cavity through the artificial aperture (fig. 3). The free ends of the polyethylene cord are sutured to the infundibulo pelvic ligament near the ovaries. A peritoneal channel is made around the polyethylene cord on each side, where it emerges from the uterine aperture, for 3–4 cm. by a suture of continuous 00 chromic catgut; in this way the round ligament is oversewn by a fold of broad ligament to enclose the polyethylene cord (fig. 4).

Where an ovary has previously been removed the operation is done on one side only, and the uterine end of the polyethylene cord is brought through the cervix. The polyethylene cord is left in situ for 90 days. The patient is given vitamin C 200 mg. t.d.s. for 6 weeks before the operation and antibiotics cover for 90 days afterwards.

Discussion

Surgical methods for treating occlusion of the uterine tube have been reviewed and discussed by Siegler and Hellman (1956) and Greenhill (1956). The methods used have been mainly either partial reconstructive plastic techniques (Szendi 1953, Jarvinen 1954) or tubo uterine implantation (Green Armytage 1952). More recently transplantation methods have been tried, with either amniotic membrane (Ten Berge and Tik Lok 1954) or, experimentally in dogs, segments of vein or artery (Davids and Bellwin 1954). Foreign material—e.g., polyethylene tubing and membrane—have also been used (Mulligan et al. 1953).

There are some objections to the use of transplantation methods mainly because of tissue reactions; to some extent the same objection might be raised in the case of foreign substances such as polyethylene. There exist also the uncertain effects of such synthetic materials in the special circumstances of fertilisation and cleavage in the uterine tube.

The present operation, which has been devised to circumvent these difficulties, is based on the fact that the ovarian germinal epithelium and the peritoneum both have their origin in the cœlomic epithelium of the young embryo (the uterine tube also is closely related developmentally to the cœlomic epithelium since it arises by infolding of this membrane). Therefore there is a rational basis for reconstructing a uterine tube from peritoneal epithelium.

Oversewing the round ligament into the wall of the reconstructed tube is designed to assist the transport of the ovum which is mainly effected by the activity of the uterus. Together with the uterine tube, the uterus and round ligaments undergo contraction at ovulation, and it is presumed that, at this time and at subsequent fertilisation, muscular contractions of these structures continue whether or not the uterine tube is present. The lack of cilia in the reconstructed tube is of lesser importance since the uterine tube is normally incompletely ciliated; transportation of the ovum is almost certainly effected normally by muscular activity of the tube and uterus.

Where less extensive reconstruction is required, the same principle could be applied by a simple modification of technique. So far partial reconstruction according to this principle has not been described.

Summary

A total plastic reconstruction of the uterine tube from local peritoneal tissue is described, and the theoretical basis for the operation is outlined.

The operation consists of oversewing the round ligament with broad ligament peritoneum over a former of polyethylene cord; a new interstitial section and uterine ostium are reamed and lined by uterine peritoneum.

Four operations have been done using this technique.

Where complete replacement of the tube is not required a simple modification using the same principle may be tried.

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CARCINOMA OF THE BRONCHUS

HISTOLOGICAL CLASSIFICATION

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NUMEROUS histological classifications of bronchial carcinoma have been suggested. These have often been based upon absurdly few cases, but Barnard (1938) and Bryson and Spencer (1951) classified a large amount of necropsy material.

At this laboratory we have for the past four years classified lung cancer in the manner described by Walter and Pryce (1955) and find this to be satisfactory from the point of view of the histologist, but during an investigation into the possible relationships between blood groups and cancer it became obvious that a more precise technique of classification was needed.

Most workers recognise three types of lung cancer—the oat cell, the squamous cell, and the *adenocarcinoma*—although not always by these names. There remains in all series a residue of "mixed," "large cell," "*polygonal*,

CLINICAL AND LABORATORY FINDINGS

—	Case no						
	1	2	3	4	5	6	7
Date of onset (Nov 1954)	5	6	8	8	10	11	13
Headache	+	−	−	−	−	−	−
Limb pains	−+	+	+	−−	−	+	−
Vomiting	−	−	−	−	−	+	−
Photophobia	+	+−	−	−	+	+	−
Hyperacusis	−	+	−	−	−	−	−
Pyrexia	+	+	−	+	+	+	+
Neck stiffness	+	+	+	+	+	+	−
Kernig's sign	−	+	−	+	−	+	−
Muscle tenderness	−	++	+	−−+	+	+	−
Muscle weakness	−	+	−	+	−	+	−
Conjunctival injection	+	+	−	+	+	+	−
Nystagmus	−	−	+	−	+	+	−
Painful eye movements	−	+	−	−	+	−	−
Rash	−	+	−	−	−	−	−
Persistent headache	+	+	+	−	−	−	−
Mental changes	+	+	−	−	−	−	−
C.S.F.	Abn *	N	N	N	N	N	N
White blood cells (per c mm)†	9700	11 700	12,600	15 300	13,100	14,200	13 200

* 6 cells per c mm Protein 85 mg per 100 ml
† Differential count normal in all cases

extensors of the left wrist became manifest This weakness had disappeared by the morning of the seventh day Reflexes were undisturbed On the evening of the seventh day his condition became generally worse with increased photophobia, occipital headache, and pronounced increase in limb pain Further examination of the C.S.F. again revealed no abnormality After this exacerbation, which lasted for thirty six hours, the patient's condition steadily improved, and fourteen days after the onset he had no symptoms beyond a varying degree of headache At this stage a diffuse erythematous rash on the trunk developed and persisted for forty-eight hours On discharge a week later he was well, apart from continuing headache, which was indeed still present three months later There was no muscle tenderness or weakness, nor any change in the tendon reflexes During the latter part of his illness he had become depressed and morbidly introspective about his symptoms

Laboratory Investigations

In all cases the C.S.F. was examined, total and differential white blood cell counts were done, and the urine was tested

The C.S.F. was normal except in 1 case, where the fluid contained 6 lymphocytes per c mm and 86 mg of protein per 100 ml, with a moderate increase in globulin, the Lange curve was normal, as were the values for glucose and chloride

In all cases a slight leucocytosis was found, with normal differential pattern (see table)

No abnormality was found in the urine

Agglutination tests against influenza A and B, brucellosis, and leptospirosis were performed on serial specimens from all patients, all were negative and no rising titres were observed No cold agglutinins were detected in the blood of any of the patients at any stage

Fæces from the 4 most severe cases, including the 1 patient with an abnormal C.S.F. were inoculated into mice and tissue cultures were set up for Coxsackie and poliomyelitis viruses at the Institute for Research into Poliomyelitis, Hamburg, in no case was any virus isolated

Discussion

Epidemiology

All the patients had been in Berlin for at least four weeks before the outbreak, and none of those who before this time had come from England had come from an area where poliomyelitis was epidemic or endemic Four weeks before the outbreak there had occurred in the army population of the city a single case of poliomyelitis, but there was no possible direct contact between this case and those described here In the preceding month there had been 21 cases of poliomyelitis notified in the civilian population of the Western sectors, but none of these had occurred in the British sector, where the troops were stationed Figures for the Russian sector were unobtainable

As I have said, all the 6 "primary" cases came from the same barrack block, and the 7th case was in an orderly who had been nursing the initial 6 The men slept in small barrack rooms, and, while no two cases came from the same room, case 1, in his capacity of night orderly sergeant, had had close range conversations with all the other patients within a few days before admission His "date of onset" preceded all others by at least a day While the explosiveness of the outbreak gave the initial impression that this might be a food- or water-borne infection, it is improbable that this was so That it was more likely to have been airborne was suggested by two facts Firstly, the entire battalion was fed from a communal kitchen and shared communal canteen facilities, yet the cases occurred among the occupants of one block only Secondly, 1 case occurred in a nursing orderly, when hand-washing and disposal of excreta were being stringently observed

The time relation of the initial outbreak to the infection of an orderly within four days of coming into contact with the affected men suggests a short incubation period —certainly not more than four days

While there were clinical differences between this syndrome and poliomyelitis, it was the epidemiological pattern which first indicated that this was not poliomyelitis In outbreaks of poliomyelitis more than one case in a single household is not uncommon, but an outbreak of poliomyelitis proper can rarely, as in the present series, start explosively, affect only a few close contacts, and end as rapidly as it has begun

Diagnosis

When the 1st case was seen, with headache, limb pains, photophobia, neck stiffness, and an abnormal C.S.F., non-paralytic poliomyelitis was diagnosed with a fair degree of confidence, and the illness was notified as such, and the 2nd case a day later, with normal C.S.F., was again regarded as poliomyelitis When, however, all the cases appeared, none with persistent paralysis and only 1 with abnormal C.S.F., it was clear that this diagnosis could no longer be entertained

In poliomyelitis the C.S.F. may be normal apart from an increase in the protein content with no corresponding pleocytosis, or even completely normal, but such a state is usually found in no more than 5% of cases McAlpine et al (1947) and Toomey (1941) go so far as to say that in such cases poliomyelitis should not be diagnosed, but certainly, more than one abnormal C.S.F. would be expected in an outbreak McAlpine et al., in a review of 104 cases, found, too, that less than a quarter were non paralytic It was therefore, by viewing the outbreak as a whole in its epidemiology and clinical features that it was differentiated from poliomyelitis This is the experience also of others (Sigurdsson et al 1950, Acheson 1954, Macrae and Galpine 1954)

Virus meningitis and the various forms of encephalitis were excluded by the normal C.S.F. The clinical picture resembled that of true influenza, to exclude this with certainty is difficult, but the limited outbreak, the absence of the disease in the neighbourhood, and the negative agglutination reactions were thought to put it out of court Bornholm disease was considered, but in this series the clinical picture differed from that usually described, in no case was there any abdominal or chest pain, the pyrexia in all cases was mild, and the limb pains were not spasmodic In their study of

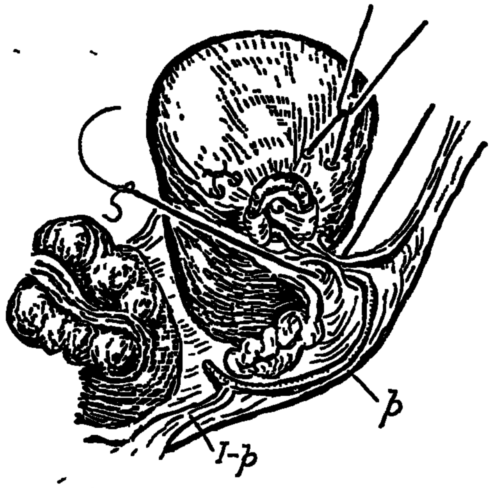

Fig 3—Polyethylene cord passed into uterus through peritoneal lined opening p, polyethylene cord, I p infundibulo pelvic ligament

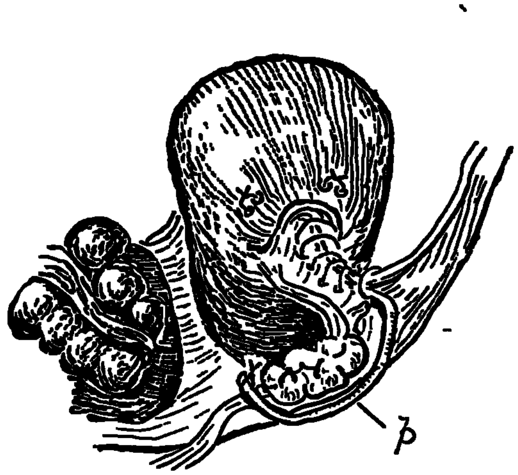

Fig 4—Polyethylene cord enclosed in peritoneal channel by continuous suture over round ligament p, polyethylene cord

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CARCINOMA OF THE BRONCHUS
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Most workers recognise three types of lung cancer—the oat cell the squamous cell, and the adenocarcinoma—although not always by these names There remains in all series a residue of " mixed," " large cell," " polygonal

TABLE I—CLINICAL FINDINGS IN 39 PATIENTS SIX YEARS AFTER HAVING AKUREYRI DISEASE

—	No	Completely recovered		Nervous and neurological complaints	Muscle tenderness	Neurological signs
		Subjectively	Objectively			
Severe cases in 1949	23	2	5	19	12	15
Slight cases in 1949	16	3	7	13	8	3
Total	39	5	12	32	20	18

Disturbances of cutaneous sensibility were slight, but in all the cases their distribution either followed the nerves or corresponded to spinal segments

Discussion

There is increasing evidence that a previously unrecognised infection has presented in various parts of the world during the past seven years A complete description of the clinical features of the infection will not be attempted here, but the workers cited above are in relatively good agreement about the clinical picture

The main features of the disease may be said to be as follows

The incubation period is probably about a week, the onset of symptoms may be sudden in some cases but more often it is insidious, the initial symptoms are usually low pyrexia with headache, especially in the back of the head and nape, and pains in the back and shoulders are very common and often radiate into one or more limbs

The painful muscles are usually tender to the touch—sometimes extremely so The patient complains of tiredness particularly after even slight exertion These symptoms usually either improve or disappear within a few days to a few weeks but may persist for months or even for years Many patients complain of sleeplessness, nervousness, and loss of memory

In some cases paresis develops from two days to four weeks after the onset of the disease In some patients there is a relapse, paresis attacking a new limb after paresis earlier elsewhere in the body A relapse of paresis has been observed as late as eight weeks after the first paresis

Paresis is usually limited to either one muscle or a group of muscles but may affect either a whole limb or more than one limb The tendon reflexes are usually present, although decreased, except in the most severe cases Even if true paresis seems only slight, the affected limbs tire very easily

Paresis tends to improve, but improvement may be very slow

Disturbances of skin sensibility are common Many patients complain of numbness or of paræsthesiæ in the affected limbs Hypoæsthesia or hypoalgesia are sometimes observed in the affected limbs

TABLE II—RESIDUAL SIGNS AND SYMPTOMS FOUND SIX YEARS AFTER ATTACK OF AKUREYRI DISEASE

Signs and symptoms	No of cases which were severe in 1949 and now show symptoms	No of cases which were slight in 1949 and now show symptoms
Nervousness and general tiredness	18	10
One group of muscles or one limb tires easily	7	
Muscle pains	16	8
Paræsthesiæ	4	
Sleeplessness	4	2
Loss of memory	5	3
Paresis	8	1
Atrophy of muscles	4	2
Reflex anomalies	4	1
Tenderness of muscles	10	
Tenderness of nerves	2	
Hypoalgesia hypoæsthesia or dysæsthesia	8	
Slight decrease of sensation to vibrations	3	
Slight ataxia of one limb (?)	2	
Slight decrease of deep sensibility (?)		1

True stiffness of the neck is seldom observed, but the patients often feel pain in the neck and down the back when the head is bent forward Lasegue's sign is occasionally positive

Nervousness, loss of memory, sleeplessness, and general tiredness are very often complained of and may persist for a long time

The number of cells in the cerebrospinal fluid is apparently within the normal range in most cases

No deaths have been reported, there has therefore been no opportunity of studying the distribution and nature of possible anatomical lesions

The findings reported here indicate that, in some cases, many of the signs and symptoms may persist at least for several years

We suggest that this condition be called (as in Iceland) Akureyri disease rather than (as some call it) Iceland disease until a more appropriate name can be suggested when we know more about its cause and the anatomical basis for the signs and symptoms which characterise it

Summary

The clinical findings in 39 patients six years after an attack of Akureyri disease are described

Many of the patients still complained of nervousness, tender muscles, pains, and tiredness

Signs of paresis, hypoalgesia, and hypoæsthesia were not uncommon, and other complaints are listed

A short description of the clinical features of Akureyri disease is given on the assumption that at least several of the outbreaks resembling it and described during the past six years form with it a nosological entity

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STAPHYLOCOCCAL PNEUMONIA IN INFANTS

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EACH winter many infants aged less than 2 years are admitted to Dudley Road Hospital with acute infections of the lower respiratory tract Since cultures made from the upper respiratory tract are so uninformative, we decided to culture lung juice obtained by thoracic puncture (Eyre 1910, Abdel Khalik et al 1938, Alexander et al 1941) in selected cases

Like Alexander et al (1941) we found no ill effects from this procedure, and we tentatively extended it but never used it as a routine Our early results suggested that, in infants with either bronchiolitis or bronchopneumonia without clinical evidence of consolidation, thoracic puncture yielded lung juice that was usually sterile In infants with definite local signs of consolidation thoracic puncture often yielded lung juice from which bacteria were grown, most commonly a coagulase positive *Staphylococcus aureus*—which is what is meant in this paper by *Staph aureus* In 1953 and 1954 thoracic puncture was therefore confined mainly to infants with localised signs of pneumonia will stand up to much wear if they are squeezed and not wrung out The work of the nurses is also decreased because the washing of many packs is avoided

Disadvantages of these sponges are that they are somewhat bulky, blunt dissection is not so easy as with gauze, and they may get covered with a layer of fibrin during operations unless frequently washed Nevertheless I believe that the virtues of these sponges make them worthy of a more extended trial in surgery

I am indebted to the manufacturers, Messrs Sponcel Ltd, 40, Chancery Lane, London, W C 2, for their help with this trial They are willing to supply any size required

REFERENCE

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PREVENTION OF STREPTOMYCIN DERMATITIS IN NURSES

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CONTACT dermatitis in persons handling streptomycin was reported by the Council on Pharmacy and Chemistry (1947), and by Rauchweiger et al (1948) who described 6 cases in nurses Crofton and Foreman (1948) reported 4 cases of dermatitis in about 80 nurses handling streptomycin in the early trials made by the Medical Research Council

The Ministry of Health (1953c) estimated the prevalence of sensitisation in handling antibiotics to be as high as 3 5% By far the largest number of the nurses were sensitive to streptomycin, and most of the remainder to penicillin, 188 cases of streptomycin sensitivity were reported from 146 centres

Anyone concerned in the manufacture, preparation, or other handling of streptomycin may develop sensitivity, but by far the highest incidence is in nurses The greatest risk seems to be to those preparing and injecting the solution

The main use of streptomycin being in the treatment of pulmonary tuberculosis, the largest number of injections is given in chest hospitals and sanatoria Since the modern tendency is to give streptomycin for increasingly long periods, any sanatorium or district nurse may be called on to give a very large number of injections

So far as nurses are concerned, the problem falls into two parts the avoidance of sensitisation and the protection of the sensitised

The Ministry of Health (1953a) lists thirteen possible precautions or variants of precautions in giving the drug At the same time the Ministry of Health (1953b) issued advice by an expert committee on the prevention of skin reactions These precautions can be summed up by saying that a strict and rigorous drill is essential to those administering antibiotics, from the preparation of the dose through the injection to the final disposal of the utensils It was, however, reported that despite adherence to the most careful technique and the wearing of gown cap, and mask nurses had still become sensitised The *British Medical Journal* (1953) described these precautions as inadequate and suggested additional measures including the exclusion of anyone with a history of allergy or dermatitis the preparation of injection solutions in a central department, and the delegation of the task of preparing and administering streptomycin to one or two nurses in each ward The last named recommendation, though it would reduce the general risk would increase that of nurses selected for the duty

The sensitised are at an unfortunate disadvantage professionally and possibly clinically The nurse, particularly in a sanatorium, who cannot give streptomycin is handicapped in her profession and provides an administrative problem in hospitals already short of staff In addition her health may be endangered if she later needs streptomycin for herself as a patient A further danger is that sensitisation to one antibiotic is often associated with sensitisation to another Some of those whose reactions have been mild have been able to return to giving injections, but many have been permanently unable to do so Crofton (1953) succeeded in desensitising 2 nurses but says that to do this may take several months and produce minor reactions According to the Ministry of Health (1953c) other workers have had less success Apart from removing the patient from the contaminating substance no other treatment is curative

Method

I have found that sensitisation can be avoided if streptomycin is injected from cartridges by what may be described as a "no touch" technique because there is little risk of the handlers coming into contact with the streptomycin, which is contained in a glass cylinder sealed at each end with rubber The rubber at one end acts as the plunger, and the other end is pierced by the dummy needle on the inside of a 'Mitrex' syringe, an all metal syringe similar in principle to a dental syringe and separable into its component parts and easily sterilisable The only parts of the apparatus that come into contact with the streptomycin solution are the dummy needle and the needle through which the injection is given The nurse who prepares and measures the dose is exposed only to the risk of disposing of the needle and one small part of the metal syringe

Case-reports

Case 1—A male nurse, aged 40, had a previous history of unspecified dermatitis in childhood but no skin complaints or allergy since He had first given streptomycin in 1946 and had had symptoms of sensitivity three days after his first contact, by which time he had given only five or six injections He developed severe circumorbital œdema and an irritating erythematous rash which affected his hands severely and his forearms slightly His fingers became œdematous, and the rash progressed to vesiculation and desquamation He was ill for about three weeks Over the next few years he made repeated efforts to give streptomycin but always had a return of symptoms despite the most stringent care His condition became such that he "dared not go into a room while an injection was being prepared or given" He was not sensitive to other antibiotics

Since August, 1955, using cartridges, he has been able to give twenty injections of streptomycin daily without *incurring* any reactions During this time he once attempted to give streptomycin by the usual method but underwent his usual reaction to it

Case 2—A female nurse, aged 35, first started giving streptomycin in mid 1948 She had no previous history of either skin disease or allergic complaint In various hospitals and centres she gave large amounts of streptomycin but had no reactions until July, 1953 She said she had become over confident in handling streptomycin and, in particular, was careless in expelling the excess of any dose into the air and in handling syringes when putting them into the steriliser after use Her reaction was striking, with severe circumorbital œdema and catarrhal conjunctivitis, a generalised erythematous rash (on the first occasion it was suspected of being measles), malaise and pyrexia up to 103·1° lasting a week The rash on her forearms and hands vesiculated finally became eczematous, and remained for three months although the rash elsewhere on her body cleared within two weeks She was off duty for four months

In the latter part of her convalescence she was given an intradermal test involving the injection of a small amount of streptomycin ' This produced not only a large weal and flare but also a mild recrudescence of the rash

After recovery an attempt was begun by a dermatologist to desensitise her, but she refused to continue with this because the first and second injections produced itching of the skin and she was afraid of a relapse She made two subsequent attempts to give streptomycin but on each occasion after five or six injections, had a reaction

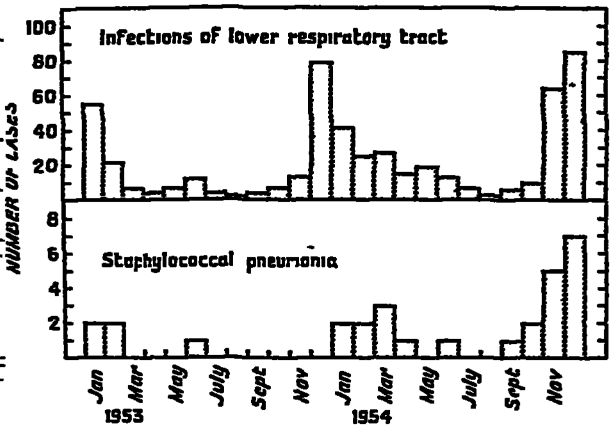

Fig 2—Seasonal distribution of infections of lower respiratory tract and of staphylococcal pneumonia.

even this so-called primary staphylococcal pneumonia is probably secondary to an antecedent virus infection (Chickering and Park 1919, Scadding 1937, Wallman et al 1955)

Radiography

The radiographic appearances varied considerably and, as Campbell et al (1954) found, changed very rapidly A small opacity would become generalised pleuritis or an empyema, or blebs would appear with alarming speed. Of 26 infants radiographed, 4 had an opaque lung field and presented little difficulty in diagnosis after examination of the pleural fluid Of the remaining 22 infants radiographed only 9 had signs which differentiated them from other cases of pneumonia these findings being those of pneumatocele or bleb formation, which were considered by Blumenthal and Neuhof (1946) to be typical of suppurative pneumonia but are often confused with congenital cysts of the lungs (Conway 1951) In 6 other cases there was localised pleuritis at an early stage, shown by a thickened pleural edge or by a diffuse "ground glass" opacity over one zone but these were not sufficiently clear cut to be diagnostically helpful

Bacteriology

Swabs

Laryngeal, postnasal, or throat swabs taken from 19 infants revealed *Staph aureus* in 5 of them, this is lower than the expected staphylococcal carriage-rate in the upper respiratory tract, probably because dry swabs were used Blood was not cultured except in 1 infant (in whom it proved sterile)

Thoracic Puncture

This consisted in inserting a dry sterile 16 gauge or 18 gauge needle attached to a 5-ml syringe into the affected area after preparing the skin with either iodine or spirit If no exudate was obtained from the pleural cavity, the needle was advanced a further centimetre or two, suction on the syringe being maintained during both insertion and withdrawal If visible exudate was seen in the syringe it was inoculated directly on to either blood-agar or chocolate agar plates If no exudate was seen, the needle was inserted into a bottle containing 5 ml of glucose broth, which was sucked up into the barrel of the syringe and discharged back into the bottle After incubation over night the broth was subcultured on to the solid media

25 infants were subjected to thoracic puncture Although 8 presented clinical evidence of pleural effusion, only 4 had frank empyemata on admission In the remaining 4 a small drop of pus appeared in the syringe and was cultured direct All 8 specimens yielded *Staph aureus* in pure culture In 17 cases no visible exudate was seen in the syringe, and on these the value of lung puncture as a diagnostic aid can be assessed In 14 of them *Staph aureus* was cultured at the first attempt so culture of lung juice in these infants enabled staphylococcal pneumonia to be diagnosed early and contributed to their recovery from the acute stage, in none of them did an empyema develop On the other hand, in 3 infants the initial lung puncture was sterile and misled us

The question of false positives must also be considered In more than 100 lung punctures done before during, and after the present series *Staph aureus* was isolated in 3: 2 of these children were aged more than 2 years, and 1 infant with a positive lung puncture had no other evidence of pneumonia It is presumed that this was due to the accidental introduction of *Staph aureus* from skin or air into the broth, as occasionally happens in blood-culture

Sensitivities

Each strain of *Staph aureus* isolated from the cases admitted in 1954 was tested against six antibiotics (penicillin, streptomycin, chloramphenicol, chlortetracycline, oxytetracycline, and erythromycin) by the following method

A single colony of *Staph aureus* was spread evenly over an agar plate in three directions to ensure a smooth confluent growth Six 'Sentest' tablets (Evans Medical Supplies Ltd) were placed at equal intervals round the plate Each tablet contained a given amount of the various antibiotics penicillin 0 5 I U, streptomycin 20 µg chloramphenicol 40 µg, chlortetracycline 10 µg oxytetracycline 10 µg, and erythromycin 1 µg After incubation over night the results were read according to the zones of inhibition of growth around the tablets varying from very sensitive to resistant

For our present purpose the strains are classified only as either sensitive or resistant, the method not being sufficiently accurate for more detailed division (table III) The correlation between chlortetracycline and oxytetracycline was absolute, except for 1 case where complete resistance was shown to chlortetracycline and slight sensitivity to tetracycline

TABLE III—ANTIBIOTIC SENSITIVITY OF STRAINS ISOLATED FROM TWENTY INFANTS

No of infants	Penicillin	Streptomycin	Chloramphenicol	Chlortetracycline	Oxytetracycline	Erythromycin
4	S	S	S	S	S	S
11	R	S	S	S	S	S
1	S	P	S	S	S	S
1	S	S	S	P	S	S
2	P	R	S	S	S	S
1	R	P	P	R	P	S

R resistant　S sensitive

All the strains were sensitive to erythromycin, all but 1 sensitive to chloramphenicol, and all but 2 to both chlortetracycline and oxytetracycline

Treatment

This followed the current lines of alleviating anoxæmia with oxygen and bringing the infection under control with an appropriate antibiotic as soon as possible At the beginning of the study penicillin was usually given at the start of treatment, later on we learned to suspect staphylococcal infection on clinical grounds and tended to use erythromycin pending the results of bacteriological examination Erythromycin was used in 17 cases altogether, but our results do not show it to be, either alone or in combination, superior to other antibiotics It is now our practice to keep erythromycin in reserve for cases showing bacterial resistance to all the other antibiotics Where an empyema had developed, either penicillin or streptomycin was injected locally In 1 case a pneumothorax developed, necessitating intercostal drainage with water-seal

Result

The humidifier was first tested by mouth-breathing with a healthy person. With a room temperature of 18°C the temperature of the inspired air was 26–27°C. The water content was equivalent to a humidity of 70–80% saturation at body-temperature. Since this is equivalent to 130% saturation at 26°C it is likely that some of the water was in droplet form.

The apparatus was then used in ventilating a very heavy man (about 120 kg.) who needed a tidal air of about 600 c.cm. With a room-temperature of 14°C the temperature of the inspired air was 24–25°C. The temperature of the expired air after passing out through the humidifier fell to 15°C. The water content of the inspired air was equivalent to a humidity of 70–80% saturation at body-temperature. The amount of water collecting in the expiratory tube after passing through the humidifier was very small. On one occasion it was collected for three hours and found to be 10 ml.

The respiratory gas pressure at the endotracheal junction was recorded in this case with the humidifier in place complete and then with the gauze removed. There was no appreciable difference in the two curves. The relatively high pressure needed for the ventilation was normal for this patient and a consequence of his massive chest.

This patient was successfully ventilated for nine weeks with the humidifier. Throughout this period his bronchial secretions were thin and easily aspirated. The humidifier was also used for 5 other patients, in 1 for nine weeks. In all cases the bronchial secretions remained thin.

Discussion

The water content of inspired air produced by this apparatus, equivalent to 70–80% saturation at body temperature, was considerable though short of the physiological figure. While this apparatus was being used, the bronchial secretions remained thin and were easily aspirated. The Danish originators of this technique of positive pressure ventilation seem to have used methods of humidification which probably produced a much lower humidity without harmful results in their very large series of cases. Probably a lower content than physiological is satisfactory. If this is so, the small size and simplicity of this apparatus are great advantages. Anchored firmly in the infraclavicular fossa it takes the weight of the inflating tubes and prevents them from pulling on the endotracheal tube. The small volume of air this apparatus encloses adds little to the work of the inflating pump. It is true that the volume must be included in the patient's respiratory dead air space, but it is considerably less than the decrease in dead space due to a tracheotomy (Radford et al. 1954). The resistance of the gauze to the air flow is surprisingly little.

Summary

A simple humidifier for positive pressure ventilation through a tracheotomy is described.

It has been used with satisfactory results in 5 cases.

It produces a water content equivalent to 70–80% saturation at body temperature.

Its advantages and disadvantages are discussed.

I wish to thank Dr. Ruth Grose for her assistance, and Dr. J. Macrae for his help and encouragement with this paper. This apparatus can be obtained from Willcocks (Clevedon) Ltd., Clevedon, Somerset.

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ACUTE MYELOID LEUKÆMIA AFTER RADIOACTIVE-IODINE THERAPY

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IN view of the association between ionising radiations and leukæmia we report here the case of a patient who was treated with radioactive iodine for thyrotoxicosis and later died of acute leukæmia.

Case-report

A married woman, aged 67, was first seen by Dr. H. F. S. Pearson at the Whittington Hospital in May, 1953. She had congestive heart failure apparently induced by bronchitis, but it seemed to Dr. Pearson that she was also thyrotoxic, and after her recovery she was referred to the department of endocrinology at New End Hospital. Here she complained of a recent increase in irritability and anxiety. For the previous two years she had been intolerant of heat and had perspired more freely than usual. Her weight had decreased from 11 st. 4 lb. in 1945 to 8 st. 4 lb. in 1951 and 7 st. 4 lb. in 1952 and was then 6 st. 9 lb.

On examination she was thin and tremulous, with pulse-rate 120, blood-pressure 230/130 mm. Hg, and frequent extrasystoles. No signs of congestion were present. A bilateral nodular and partially retrosternal goitre was present. In view of the patient's condition and the possible technical difficulty of thyroidectomy, treatment with radioactive iodine was proposed.

Treatment.—Carbimazole 10 mg. t.d.s. with thyroid gr. 1 was given daily from July 8 to Aug. 11, 1953, when the dose of thyroid was reduced to gr. $^1/_2$ daily. The patient was admitted to New End Hospital in September, 1953, when thyrotoxicosis was still present and signs of cardiac failure had reappeared. After all treatment had been stopped on Sept. 16, 1953, radio-iodine tests (table I) and a blood-count (table II) were made. A therapeutic dose of 17 mc of ^{131}I was given orally on Sept. 23, 1953. Effective half-lives of 7·0 and 7·6 days in the body and neck were observed as a result of this dose. The energy absorption * in the neck during the first fortnight after treatment was 22,000 rad. More than 90% of the total integral dose was received during the first twenty-four hours, 0·16 megagramrad being absorbed during the first day and about 0·001 megagramrad daily thereafter.

Course.—After the radio-iodine treatment in September, 1953, the patient improved and became euthyroid. Although the congestive cardiac failure did not disappear it greatly improved, and the patient's main complaints were of a troublesome cough and slight dyspnœa on exertion in the winters of 1953–54 and 1954–55. In January, 1954, her condition was considered clinically to be euthyroid, a finding which was confirmed by a radio-iodine excretion test (table I). On April 3, 1955, she was readmitted for assessment when she was considered to be relatively well and euthyroid, with a minor degree of congestive cardiac failure. When due for discharge, however, on April 6, 1955, she had painless hæmaturia for three days. The only clinical abnormality noted was several enlarged cervical glands. Severe progressive anæmia developed, but no other gross hæmatological abnormality was rticularly noticeable in 2 infants who died within a w hours of admission, a little fibrino-purulent exudate as present between the otherwise adherent thickened yers of pleura

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* The energy absorbed by the blood is calculated by assuming that the β radiation due to an activity in the blood itself of 1 μc per ml. is 0·418 rad per hr. and that the γ radiation is contributed from the activity dispersed through the body as a whole. Bush's (1949) tables give, for a patient weighing 45 kg. and 156 cm. tall, a value of 0·255 rad per hr. per μc per kg. of body weight. The dose to the marrow is assumed to be of the same order as that to the blood. The presence of bone surrounding the marrow would only affect the γ contribution and would only be significant during the first twenty-four hours, when it might increase the total from 2·87 rad to 4·00 rad at the most. It would be an increase of less than 10% over the first fourteen days, or even of the total received, and the other errors are far greater than this.

Pus in the aspirating needle or syringe depends on its lance passage through a purulent area rather than herent pleura Washing out the syringe and needle ith broth therefore seems to afford the best chance of covering the organism, although it carries with it the creased risk of accidental bacterial contamination

Despite the warning given by Lelong and Alison (1953) at "La ponction exploratrice peut être dangereuse dans s cas" we had no direct sequelæ of thoracic puncture this series, but 1 infant had a pyopneumothorax ght days later The fact that this complication is very ommon in staphylococcal pneumonia seems to exonerate he lung puncture from blame We repeated thoracic uncture in several relapsed cases without producing ny untoward result Before, during, and since the eriod covered by this report more than a hundred lung unctures have been done in various infections of the ower respiratory tract on 4 occasions a partial pneumothorax developed but caused no detectable symptoms nd the air was reabsorbed in a few days

It therefore seems that the first definite sign of localised neumonia in infants aged less than 2 years demands mmediate treatment as a potential staphylococcal nfection We do not suggest the use of lung puncture as a routine diagnostic measure at this stage, but its use has made us more familiar with the early signs of staphylococcal pneumonia in infants, and this recognition has in some instances perhaps led to more effective initial treatment reflected by somewhat lower empyema and mortality rates than those usually reported

If present trends continue (Barber and Burston 1955), the list of antibiotics likely to be effective will grow shorter, and in this unhappy event lung puncture may have to be done routinely to determine the sensitivity of the "unconquered staphylococcus"

Summary

In 1953 and 1954 35 cases of staphylococcal pneumonia were diagnosed in 530 infants, aged less than 2 years, admitted with infections of the lower respiratory tract Of the 35 cases 29 were "primary"

In 14 out of 25 cases lung puncture contributed to early diagnosis of staphylococcal pneumonia

Results of treatment confirm the necessity for long-continued administration of antibiotics

We wish to thank Prof J M Smellie for advice and criticism in the preparation of this study, and our ward sisters and house physicians for their skill and cooperation

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STAPHYLOCOCCAL INFECTION OF THE LOWER RESPIRATORY TRACT IN ADULTS WITH INFLUENZA

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Until 1932 influenza could be diagnosed only on clinical grounds, but nowadays the relationship of influenza virus to epidemic influenza and to the "influenzal" pneumonias can often be established by demonstration of either the virus or specific antibodies in the serum

Staphylococcal pneumonia is rare but seems to occur most commonly as a complication of influenza The number of patients with staphylococcal pneumonia and satisfactory evidence (demonstration of either virus or antibodies) of recent or current influenza is unfortunately small

3 rapidly fatal cases of staphylococcal pneumonia which also yielded influenza virus were reported by Scadding (1937) and Stuart-Harris et al (1938) Single cases were recorded by Stokes and Wolman (1940), Himmelweit (1943), and Burnet et al (1946), and 2 by Parker et al (1946)

Evidence of coincident or recent infection with influenza virus has been provided by hæmagglutination and complement-fixation tests in a greater number of patients 45 of 54 cases of staphylococcal pneumonia were studied in Sheffield and other areas in 1949–51, and cultural or serological evidence of influenza either coincident with or shortly before the lung involvement was obtained in 24 (Williams 1953)

Staphylococcal pneumonia in the absence of influenza is very rare, but there are several instances of staphylococcal pneumonia in which search for the influenza virus was unsuccessful (Andrewes et al 1935, Pearson et al 1941, Stuart Harris et al 1949)

There is no evidence that the influenza virus isolated from cases of staphylococcal pneumonia has unusual properties, but Stuart-Harris (1953) comments that a large quantity of the virus can be detected in the lungs Until recently there had been no extensive study of the staphylococci found in sputum or lungs of patients with pneumonia during influenza epidemics, but it is agreed and emphasised by all workers that the staphylococci are present in prodigious numbers Bacteriophage typing of strains of *Staphylococcus aureus* from cases of influenzal pneumonia was done by Williams et al (1953), who found that the proportion of group I strains from non-fulminating types of pneumonia did not differ significantly from that in the nose of healthy carriers (about 25%), whereas 56% of strains from fulminating cases were of this group Since the excess of group-I staphylococci was observed in strains from a variety of sources and in two different epidemics, Williams et al believed it to be significant Not all the strains associated with the fulminating disease were resistant to penicillin

Clinical and Bacteriological Studies

During 1953 clinical and laboratory investigations were made on all adult patients with acute infection of the lower respiratory tract in the wards of the medical unit in the Cardiff Royal Infirmary Routine studies of 70 patients included frequent bacteriological examination of sputum and complement-fixation tests for evidence of infection with the viruses of influenza A and B, psittacosis, lymphogranuloma inguinale (L G I)

Secretions, which up to now had only been slight, gathered in large amounts in the nasopharynx, and cyanosis appeared for the first time. Tracheal and mandibular tug with twitching of the facial muscles was prominent. The patient's general condition degenerated rapidly. Since we had no previous experience with intermittent positive pressure respiration (I.P.P.R.) in infants we were reluctant to perform a tracheotomy, and so we tried a cuirass respirator. This was a failure and the patient's condition became desperate.

Tracheotomy and Artificial Respiration

A tracheotomy was done under local anæsthesia, and a flexometallic tube no. 1 inserted and stitched in. The V-shaped metal end was of the wide-bore type.

Ventilation was performed by means of "finger respiration." A continuous flow of oxygen was led into one limb of the V-tube; closing the end of the other limb produced inflation of the chest, while passive expiration occurred when the finger was removed. Various rates of flow were tried and it was found that a flow of 4 litres per minute was the most satisfactory.

Attempts were made during the next hour or so to provide mechanical respiration by means of the Radcliffe respiration pump, using air which was forced down one limb of the V piece. A water manometer, which could be set to allow the escape of air if the pressure rose above a set figure, replaced the Borden pressure gauge. Tubes of various lengths and diameters were placed over the free limb of the V piece, as in some anæsthetic techniques. The minute volume delivered down the other limb was increased; but ventilation remained inadequate, the heart rate slowed, and cyanosis followed, and finally this method was abandoned.

The original arrangement was restored with a Stott valve (Smith et al. 1954). A gasmeter-type spirometer at the outlet of the Stott valve showed the degree of ventilation, which was kept at 2.6 litres per minute as recommended by Spalding (1955). The water manometer was set to blow off at 8 cm. of water; the actual pressure used was about 6 cm.

Difficulties now arose with regard to the CO_2 tension. It was felt that it would be almost impossible to obtain arterial samples for gas analysis from such a small subject, and the CO_2 content of the expired air was measured as described by Harries and Lawes (1955), but little information of value was obtained by this method. The stroke rate of the machine was increased to its maximum of 45 per minute by altering the cogs. The depression of the water-level in the manometer suggested that possibly the inspiratory pressure was being maintained for too long a period, but this we were unable to alter.

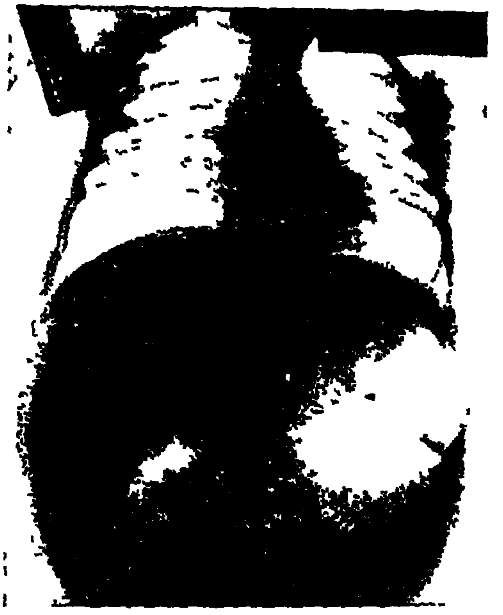
Hypercapnia

During the next two hours there was intermittent twitching of the facial muscles, the nose, the fingers, and the frontalis muscle with pronounced tracheal and mandibular tug. Repeated measurements of volume of the expired air showed that a minute volume of 2.6 litres was being maintained. Increasing the oxygen concentration did not appear to affect the twitching. The CO_2 content of the expired air at the outlet port of the Stott valve had risen from 1 to 2%. Muscular twitching has been reported to be a common sign of hypercapnia (Leake and Waters 1929, Waters 1937), and a return to finger respiration was made for short intervals to remove the assumed excess of CO_2. On each occasion this caused the twitching and tug to disappear within a short period.

After five hours on the machine the patient's condition became much worse. Twitching with tracheal and mandibular tug became pronounced, and the pulse was hardly perceptible. Aminophylline was administered, without effect. Mechanical ventilation was abandoned and a return made to finger ventilation with immediate improvement. An electrically controlled humidifier (Russell and Schuster 1953) was incorporated into the system but caused some difficulty because of condensation of water vapour, and eventually the humidifier was switched off.

Progress

Volunteers, including housemen and hospital assistants, were organised into six-hourly shifts, each shift consisting of two people who worked alternately for fifteen-minute periods. As the personnel were untrained in finger respiration the machine was used as a metronome; it was so altered that if the operator followed the machine by eye or by ear the inspiratory period was just under 0.5 sec. and the expiratory period approximately 0.7 sec. with the respiratory rate about 45 per minute.



Radiograph showing dilatation of stomach without surgical emphysema of mediastinum.

This system worked well for thirty hours. The infant was turned regularly at intervals, though air entry was good in all areas and there were no adventitious sounds except when the tube was allowed to slip too far in. Suction of the pharynx was only occasionally needed and suction down the tube was rarely necessary.

Twenty-four hours after the tracheotomy the infant opened her eyes and appeared to be conscious. Attempts at spontaneous respirations were made by the patient, but these became feeble if allowed to continue unaided for more than forty-five seconds.

Gastric Dilatation

Thirty-six hours after I.P.P.R. had been instituted the clinical picture changed rapidly for the worse. The abdomen became distended, and so ventilation was impeded. Some partially digested milk was vomited. Insertion of a rectal tube produced a large amount of fæces, and shortly afterwards the distension subsided and ventilation was more easily performed. An hour and a half later the distension returned to such a degree that it was only with the greatest difficulty that any ventilation could be achieved.

There was no air entry at either base and very little elsewhere; suction through the stomach tube produced nothing. By gentle pressure on the distended abdomen, however, large amounts of air and some fluid were squeezed out of the stomach and the distension became considerably less. Ventilation was now satisfactory. Radiographic examination at this stage showed "distended stomach; no sign of surgical emphysema in the mediastinum or free air in the peritoneal cavity" (see figure).

In the next six hours there were three further attacks of acute dilatation of the stomach, each of which prevented any visible movement of the chest wall or abdomen and led to cyanosis and cardiovascular changes. Each attack was relieved with difficulty by gently squeezing the abdomen, suction through the stomach tube having little effect. During these attacks care was taken that the inspiratory pressure did not become excessive, and such ventilation as could be achieved was by intermittent insufflation, the excess air escaping from the partly closed end of the free limb of the V piece during inspiration.

Deterioration and Death

On the third day after admission the abdomen was distended to a far greater extent than previously; the chest wall appeared to be fixed in the maximum inspiratory position and no air entry could be heard in any area of the lungs. Each attempt at inflation appeared to make the distension worse. A similar state of affairs, where the chest was fixed in the maximum inspiratory position but without abdominal distension, had been seen by us in an adult where the cuff had herniated round the end of the endotracheal tube, forming

TABLE II—STAPHYLOCOCCAL α-ANTITOXIN LEVELS (I U PER ML) OF 4 PATIENTS WITH COMBINED STAPHYLOCOCCAL AND INFLUENZAL INFECTIONS

Case no	On admission	After 1 week	After 3 weeks	After 8 weeks
1	Not detectable	Died		
2	Not detectable	0 3	0 8	Not assessed
3	Not detectable	Died		
4	Not detectable	0 2	0 8	1 6

Materials and Technique

Serial dilutions of inactivated patient's serum made up to a unit volume of 0 4 ml with saline solution were mixed with 0 4 ml of toxin diluted with a mixture of 3 parts of saline solution and 1 part of broth to contain Lh/10 or in some cases Lh/50 The serum-toxin mixture was incubated for 30 minutes in a water-bath at 37°C 1 drop (0 025 ml) of 20% thrice washed rabbit red blood cells was then added to each tube, and the tubes were placed in the 37°C water-bath for one hour The end-point was taken as the last tube showing lysis of any degree

Standard antitoxin, diluted to contain 0 5 international units (I U), was used as a control and a method of calibration in each batch of tests

Results

240 sera from 70 patients with infection of the lower respiratory tract, including 19 with proved influenza A, 100 sera from apparently healthy people, 26 sera from persons with superficial staphylococcal skin lesions, and 6 sera from patients with severe non-respiratory staphylococcal lesions were examined by this method Tables I and II show that in the 70 patients with infection of the lower respiratory tract, except 4 in whom there was no detectable antibody, the levels of circulating antitoxin ranged from 0 2 to 3 2 I U per ml, and that the distribution was similar to that in the group of 100 healthy people and 32 persons with non-pulmonary staphylococcal lesions

The 4 patients in whose serum there was no detectable antibody were those who had severe combined influenzal and staphylococcal infections 2 of the patients died but in the 2 survivors circulating antibodies developed within a week of admission to hospital (table II) At no time was free toxin found in the circulation of these patients No change in titre of the circulating antibodies to α-lysin was detected in the weekly serum specimens in any of the other 66 patients with infection of the lower respiratory tract

In healthy persons circulating antibodies to the staphylococcal α hæmolysin range from 0 2 to 2 0 units (mean about 0 7 unit) (Seeley et al 1944, Widholm 1951, Marks 1953) In cases of staphylococcal infection of the skin the antibody often remains at the normal level, but when the lesions become chronic it may rise to 8 or more units per ml We have not been able to discover any published instance, or any other instance in our own observations apart from the 4 cases recorded here, in which the antibody titre was below a detectable level at any time

Discussion

It is clear from our own experience and that of others that staphylococcal invasion of the lower respiratory tract in adults, producing severe and often fatal illness, is practically limited to the time of influenza epidemics On occasions it has assumed epidemic proportions with a very high fatality-rate Several workers have recently drawn attention to the different ways in which staphylococcal pneumonia can occur in association with influenza, and these reports have to some extent corrected the over-emphasis on the case fatality In most patients definite evidence of the association of staphylococcal and influenzal infection is wanting, and much work is needed before the degree of association of virus and staphylococcal infection can be assessed

Further investigation is also needed to determine whether the strains of *Staph aureus* or of the influenza virus causing this illness, particularly in its fulminating form, have any special virulence or toxigenicity The work done by Williams et al (1953) suggests that staphylococci of a particular bacteriophage type are significantly associated with the fulminating infection, but this awaits confirmation, and nothing has been recorded of any other special characteristic

The exact role of virus and staphylococcus in producing the lung lesions is far from clear Most workers agree that the staphylococcus grows and flourishes in the bronchial tree where the epithelium has been damaged by a preceding or co existing infection with influenza virus This presumably applies also to the relation between *Strep pyogenes* or *H influenzæ* and the influenza virus, because it is clear from published accounts that pneumonia attributed to these organisms at the time of influenza epidemics is in many cases indistinguishable clinically or pathologically from that caused by *Staph aureus* (Dwinnell 1919, Tytler et al 1919, Winternitz et al 1920, Wollenman and Finland 1943) It is not clear whether these bacteria are present fortuitously or transmitted in association with the virus

It is striking that the 4 patients in whom there was no detectable antibody to staphylococcal α hæmolysin during the acute phase of the illness had severe pneumonia in which influenza A and *Staph aureus* coexisted This suggests that the circulating antibody had been neutralised by the toxin produced as a result of the massive infection of the lower respiratory tract with staphylococci

Finally, in view of the low levels of staphylococcal antitoxin in the serum of these 4 patients, we suggest that, in addition to antibiotics, staphylococcal antitoxin may be of use in treatment if given at an early stage and in adequate dosage

Summary

Of 70 patients with infection of the lower respiratory tract 4 had combined infection by *Staph aureus* and by influenza-A virus, 2 of them died

In these 4 patients the normal circulating staphylococcal antibody to α hæmolysin appeared to have been completely neutralised by toxin produced in the lungs

372 specimens of serum, including 32 from patients with other staphylococcal conditions, were examined for antibody to staphylococcal α-hæmolysin In none of these was the antibody titre below the normal range

The association of *Staph aureus* and influenza virus in the causation of severe and often fatal pneumonia is reviewed

We wish to thank Prof Harold Scarborough and Prof Scott Thomson for advice and criticism

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Lymphosarcomatosis

The disease was arrested in 3 of 5 cases, but no sign of improvement was noted in the 2 others One of the patients, whose course of treatment ended six months ago, is back at work and needs no further treatment

Hodgkin's Disease

In 6 of 14 cases of lymphogranulomatosis we obtained excellent results the lymph-glands became smaller and the pyrexia disappeared In 4 other cases the results were favourable, but the remaining 4 patients died before the course of treatment was completed

Carcinoma

We tried B C M on 40 patients with cancer of the lung, in 20 of them the pain became less and the general condition easier, and a few put on weight We also tried B C M on 28 patients with non-pulmonary cancer In 1 of these inoperable cancer of the pancreas was found at laparotomy, after a course of B C M his vomiting, abdominal pain, and diarrhœa ceased and he went back to work A woman with ovarian cancer lost some of her metastases and is now being treated as an outpatient

CONCLUSIONS

B C M is apparently active against many malignant disorders, but especially against tumours of the lymphoid system Its special advantages are low toxicity and the fact that it may be administered to outpatients

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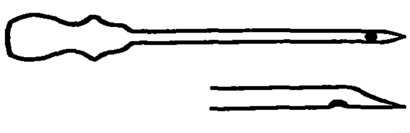
New Inventions

MODIFIED INTRAVENOUS-DRIP NEEDLE

Anyone who has had to set up an intravenous-saline infusion or blood-transfusion at all frequently must have had the annoying and worrying experience of seeing the drip stop, owing to the bevel of the needle coming up against the vein wall and thus becoming obstructed Commonly this can be corrected by arranging a small wad of cotton-wool under the junction of the needle hub and rubber tubing but the obstruction is liable to recur and give trouble, particularly in operation cases where the site of entry of the needle into the vein is covered by sterile towels, and is thus relatively inaccessible

The accompanying figure shows a standard blood-transfusion needle slightly modified to overcome this difficulty A hole is bored through the needle near its tip on the side away from the bevel If the bevel of the needle now comes to lie flat against the wall of the vein, the drip fluid is free to enter the vein via this alternative opening



This modified needle has been used by me for some months in the operating theatres here It presents no additional difficulties when it is introduced into a vein I have not yet had a case when using it where the drip has stopped owing to obstruction by the vein wall

The modification can be effected by any competent hospital-workshop technician The edges of the bored hole should be smooth, to discourage formation of adherent blood-clot round it

The work has kindly been done for me at the Radcliffe Infirmary in the workshop of the Nuffield department of anæsthetics by Mr R Salt and Mr R Corney

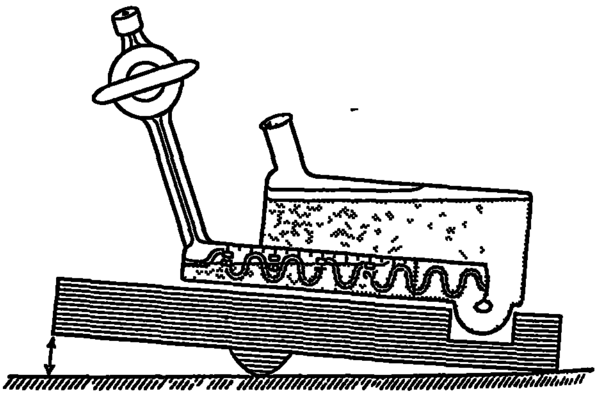
F K Boston
M A, M B Camb,
F F A R C S

Nuffield Department of Anæsthetics
Radcliffe Infirmary,
Oxford

AN OXYGEN ANALYSER

There is need for an oxygen analyser simple enough to be used by a nurse If such an instrument were available, the routine measurement of oxygen concentration in tents and incubators—obviously a desirable procedure—would probably become more generally practised Instruments depending on the magnetic properties of oxygen are costly, and those using a chemical absorbent have hitherto proved insufficiently reliable for routine use in hospitals

The instrument here described makes use of a chemical absorbent, 1 2 4-triacetoxybenzene (1 2 4-triacetylhydroquinone), which, unlike the agents previously in use (pyrogallol, hydrosulphite, and chromous salts), both absorbs oxygen rapidly and retains this property for a long time [1]



A horizontal glass tube of about 5 ml capacity is connected at one end by a short U-tube to a reservoir, the other end opening into a capillary tube with a tap A glass spiral is incorporated within the horizontal tube When the tap is opened, the absorbent fluid in the reservoir fills the horizontal tube and the capillary tube to a level just short of the tap The tap is closed, and the instrument is ready for use A layer of paraffin oil introduced into the reservoir will float on the surface of the absorbent fluid and prevent access of air to the latter

A sample of the gas to be analysed is withdrawn in a syringe, whose nozzle is connected by a short rubber tube to the tap, which is then opened A measured 3 ml of gas is delivered into the tube, after which the tap is closed

The instrument is mounted on a wooden stand fitted with a rocker, enabling the instrument to be rocked through a small arc on either side of the horizontal In this way the bubble of gas can be moved from one end of the tube to the other Absorption of oxygen is also facilitated by the glass spiral, which greatly enlarges the surface of fluid presented to the gas bubble as it traverses the tube When absorption is complete (a matter of about half a minute) the instrument is held vertically with the tap uppermost The level of fluid in the tube then registers the amount of gas absorbed, the tube being calibrated to allow the percentage of oxygen in the sample to be read off directly The whole procedure occupies less than a minute

1 2 4-Triacetoxybenzene (British Drug Houses Ltd) is used in 10 % solution in 15 % KOH Recharging of the instrument is required infrequently since one fill (10 ml) is good for several hundred analyses

The instrument is made by Camlab Glass Ltd 50a Burleigh Street Cambridge

Douglas Gairdner
D M Oxfd, F R C P

Addenbrooke's Hospital,
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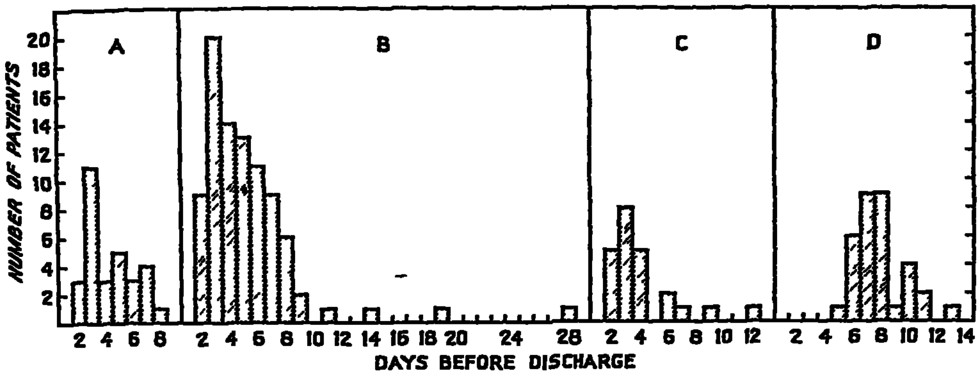
1 Devey J D *Scand J clin Lab Med* 1953 5 101



Time before discharge of patients with paronychia

A, 30 patients, aged 14 or over, submitted to combined surgical and physical treatment, without local aureomycin powder

B, 88 patients, aged 14 or over, submitted to combined surgical and physical treatment with local aureomycin powder

C, 23 patients, aged 13 or less, submitted to combined surgical and physical treatment with local aureomycin powder

D, 33 patients, aged 14 or over, treated by surgery and proflavine dressings only

The control series of 33 patients over 14 years of age (group D) treated by surgery and proflavine dressings were discharged after an average of 8 0 days

These results are summarised in the accompanying table and figure

Discussion

Patients treated by combined surgery and physical treatment (groups A–C) were discharged, on an average, three days before the group treated by surgery and proflavine dressings alone (group D) This confirms our clinical impression that in all types of superficial sepsis treated by combined surgery and physical methods, the results compared very favourably with treatment by surgical routines alone, in regard to speed of resolution of the lesions In the largest group (B) of 88 adult patients treated with combined surgical and physical treatment and application of starch powder containing 2% aureomycin, the average time of 5 3 days is longer than that for the group (A) of 30 adult patients treated in the same way but without local application of the powder We feel that the probable explanation of this slight difference was that the group B were more severely infected locally, with much pus present, and the aureomycin powder was used for this reason

The small group (C) of 23 children had very rapid resolution after surgery and physical treatment, some being discharged after two or three days The favourable factor in such cases is almost certainly the small area of the nail-bed involved, even though the young age group tended to soil dressings and the wound area to a much greater extent than did adults

The results indicate that, in cases of acute paronychia of the hand digits, treatment by surgery combined with physical methods leads to more rapid resolution of the lesion, and earlier return to normal work

RESULTS OF TREATMENT OF PARONYCHIA

Group	Age (yr)	No of patients	Nail removed	S W D twice daily	Local U V light	Local aureomycin powder	Average duration before discharge (days)
A	14 –	30	Yes	Yes	Yes	No	4 3
B	14 –	88	Yes	Yes	Yes	Yes	5 3
C	13 or less	23	Yes	Yes	Yes	Yes	4 1
D	14 –	33	Yes	No	No	No	8 0

S W D = short wave diathermy
U V = ultraviolet

Summary

141 consecutiv cases of paronych of the hand digi were treated b surgical removal (the nail combine with subsequent trea ment by physica methods

A control group (33 consecutive case were treated by surg cal removal of th nail only and dressing of 1 in 1000 proflavin hemisulphate

In the combinec treatment group ther was an average savin of three days in tim of disability befor discharge withou dressings and fit fo work

Our thanks are due to Mr R H Boggon, consultant i charge of the casualty department, St Thomas's Hospita for permission to report these cases and to the physic therapy staff who treated the majority of patients in th series

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LONG-TERM OXYTETRACYCLINE (TERRAMYCIN) THERAPY IN ADVANCED CHRONIC RESPIRATORY INFECTIONS

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WE have previously reported our experiences wit long-term oxytetracycline (terramycin) in advance chronic respiratory infections (Helm et al 1954) W describe here the later progress of these patients

Results

Chronic Staphylococcal Bronchopneumonia

Case A —This 4-year old girl with fibrocystic disease o the pancreas and staphylococcal bronchopneumonia remained greatly improved and led a normal life while oxytetracycline was administered but relapsed rapidly when administration was interrupted Her condition was maintained for nearly 3 years, but towards the end of this time resistant staphylo cocci began to appear in increasing numbers in her sputum, and, although the antibiotic still appeared to be essential for her survival, her condition began to deteriorate with recurrent

The design of the experiments was complicated but consisted broadly in treating anxiety as the independent variable in the first experiments, and in treating initial hippuric acid level as the independent variable in the second set of experiments Hippuric acid was chosen because earlier work by Dr Persky had shown that patients with free anxiety had a high hippuric acid excretion after intravenous injection of sodium benzoate

The investigation did not yield clear cut results Hippuric acid excretion, on which much of the work turned, was not higher in those who were judged to be under the greatest stress Glutathione level, however, dropped at times of severe stress, the maximum fall occurring ten hours after the stress In accounting for these unexpected findings, the authors emphasise their psychological observation that not only fear of physical harm through jumping but also fear of being shamed through failure played an important part in the man's anxiety this distinguished them from patients with anxiety, in whom high hippuric acid excretion had been found The psychological tests indicated that stress impaired the performance of tasks requiring perceptual discrimination and memory, but that a "stress tolerance test" which involved the response to vivid pictures of threatening events (such as falling with an unopened parachute), did not help to measure anxiety *In general, the biochemical findings discriminated* more effectively than the psychological ones

Though the work is presented in a wordy difficult form, it is a valuable and instructive attempt to observe under fairly rigorous conditions the changes that accompany an undeniable stress in real life

Atlas of Rœntgen Anatomy of the Skull

LEWIS E ETTER, M D, F A C R, assistant professor of radiology, school of medicine, University of Pittsburgh, Pennsylvania Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 215 £5 6s

USING a disarticulated skull with one bone at a time either removed or marked, Dr Etter gives a convincing demonstration of the part played by each bone in forming the radiographic image Most of the conventional projections are illustrated and described The book also includes Dr J B Farrior's material on the radiographic anatomy of the temporal bone, and a reprint of a paper on the skull of the newborn infant by Dr S Henderson and Dr L S Sherman

Most of the illustrations are clear, though not everyone will like the "new visual aid consisting of cutouts of the radiographs," when used for illustrating a book A black background, as used for many of the photographs, with white lettering would have been better Many of the illustrations would have been clearer had they been larger, even at the expense of the size of lettering used for the labels

Radiologists will find this collection convenient to use and few will be familiar with all it has to offer It will form a very useful work of reference, and, since the proof of its assertions is presented, a convincing arbiter of dispute

Moto-Kinesthetic Speech Training

EDNA HILL YOUNG and SARA STINCHFIELD HAWK Stanford Calif Stanford University Press London Oxford University Press 1955 Pp 176 40*s*

MRS Young and Dr Hawk have revised their earlier work, *Children with Delayed or Defective Speech* in the light of further research, and have produced a valuable textbook on speech training and speech rehabilitation What does "moto-kinesthetic" mean? The "moto" part is the teacher's use, in the three "dimensions" of place time, and direction, of pressure by the fingers on lips, jaw nose, throat, and waistline to induce the child to modify the air current so that desired sounds shall be produced Simultaneously, auditory and visual stimuli are offered The dust-cover depicts a teacher stimulating "shoe" with her right hand on the child's upper lip and jaw, while she shows him a picture of a pair of boots and says "shoe" He lies "relaxed on the speech table" while he learns by kinæsthesia feeling the actions and positions associated with the sound

In part I, Mrs Young concludes by stressing the need for research to show "*the facts relative to early muscular learning as affecting later speech*" It is obvious that her personal experience of a speech handicap has helped her to present with clarity and vision the moto kinesthetic technique In describing this method of sound stimulation, she first emphasises the need to understand fully the function of the air current as the basis of speech, and the way normal speech development may need encouragement to avoid subsequent defects

The book includes pictures illustrating the finger movements used to stimulate the enunciation of vowels and consonants Mrs Young does not suggest that her method is to be used exclusively for all problems, but she shows how it may be adapted to help even the more heavily handicapped such as the deaf, the blind, the cerebral palsied the aphasic, and the stutterer

In part II, Dr Hawk gives a careful analysis of speech disorders and describes the examinations and tests which have been used, and the conclusions drawn

How interesting will this book be to most medical doctors? To most, not very, to a few, absorbing while to those who see many children handicapped in all sorts of different ways it will be something to dip into now and again It will leave them feeling how much more they could do if they had the time, if they had not (in James Hilton's phrase) "the knack of putting first things second," as they hurry a patient in order not to keep the next one waiting

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Postgraduate Obstetrics and Gynæcology (2nd ed London Butterworth 1955 Pp 688 70*s*)—The first edition of this book appeared in 1950 and was based on the extremely popular postgraduate lectures given by Prof F J Browne in the years after the late war The text has now been revised, and father and son (Prof J C McClure Browne) combine to give the benefit of long years of experience and of more recent views The length of the book has been increased by some 35% although only a few new chapters have been added, and the policy is still to avoid repeating what is covered in the authors' book *Antenatal and Postnatal Care* Because of its origin the book is a series of essays rather than a standard text Each subject is treated in a readable yet authoritative way The illustrations and particularly the photomicrographs are excellent The reputation already enjoyed by this book will be enhanced by this new edition, and it will win new friends among postgraduate students and practising obstetricians and *gynæcologists*

Operative Technic in General Surgery (2nd ed Vol I New York Appleton Century Crofts 1955 Pp 973 $20) —The greater part of the first volume of this work (edited by Prof Warren H Cole, of the University of Illinois) is devoted to the surgery of the abdomen, which is dealt with authoritatively by acknowledged experts By contrast with the more coherent gastrointestinal section, the rather random order of subjects in the remaining chapters makes the volume uneven The endocrine glands suffer from separation, the thyroid and parathyroid joining company in one chapter, while the adrenals come as an afterthought to the pancreas and the thymus has got lost altogether Orthopædics receives its quota in chapters on amputations, on muscles fascial tendons, and bursæ, and on the hand and its tendons, but bone is excluded There is a chapter on the breast, while another on skin and subcutaneous tissue is thrown in for good measure (burns having been earlier considered on their own) without mention of plastic surgical technique Reliance is rightly placed on illustrations, which are variable in quality

Radium Therapy (2nd ed London Baillière, Tindall & Cox 1956 Pp 286 37*s* 6*d*)—Since the 1945 *edition of* this book by Mr C W Wilson, PH D, principal physicist to the Westminster Hospital London immense strides have been made in the field of radioactive isotopes, and the physical aspects have been incorporated in the new edition But radium therapy still remains the basis of the book Dr Wilson is to be congratulated on again producing an up to date and essentially practical book which is a 'must' for hospital physicists, radiotherapists, and students in need of a reliable basic text treatment could only be continued in fourteen (one with chronic staphylococcal bronchopneumonia nine with chronic bronchitis four with bronchiectasis) These are the patients whose subsequent course is reported here Only eight are still receiving the antibiotic, the duration of treatment ranging from $2^3/_4$ to $1^1/_2$ years In two other bronchitics, although progress was favourable, treatment was stopped in an attempt to prepare an autogenous vaccine

The ultimate death of the child with fibrocystic disease of the pancreas was presumably inevitable, since the staphylococcus fairly readily becomes resistant to antibiotics Nevertheless it does seem that her life was prolonged for some 3 years by continuous oxytetracycline

As regards the patients with chronic bronchitis and bronchiectasis, the original infecting organism was known to be *H influenzæ* in each instance Unfortunately, regular accurate estimates of the sensitivity of these organisms to oxytetracycline were not made but such information as we have indicates that resistance does not develop rapidly It is of considerable interest that one patient with bronchitis, whose response had been highly satisfactory for nine months, relapsed rapidly after a fortnight's interruption of treatment and subsequently failed to respond as well In this case a strain of *H influenzæ* isolated after a further 10 months' treatment was resistant to oxytetracycline From observations on other patients not included in this series we have the impression that it is often more difficult to obtain a satisfactory response if treatment is interrupted in this way than if it is continued without a break In addition as in the patient mentioned, we have seen others whose infection relapsed rapidly when therapy was discontinued, even if it had previously been given for many months This accords with the observations of Knox et al (1955) in patients treated for several months with antibiotics administered by aerosol These relapses are perhaps not surprising since *H. influenzæ* was isolated on occasion from several of our patients during chemotherapy indicating that the infection was not eradicated but merely suppressed

It is probable that the maintained benefit in these patients is due not only to the suppression of *H influenzæ* but also to the prevention of recurrent acute pneumococcal infections which are so common in the absence of chemotherapy In no instance in this series have pneumococci been isolated from the sputum of patients while on treatment and, since this organism appears unlikely to develop resistance, it is reasonable to hope that this effect at least may remain so long as treatment is continued

Although we feel that deterioration probably will occur ultimately, owing to development of resistant strains of *H influenzæ*, this has not yet occurred definitely in any case where treatment has been maintained without interruption How long treatment can be continued with benefit is still therefore a matter for conjecture and will probably be found to be variable and unpredictable There is no doubt however, that some patients are greatly benefited for long periods

Summary

A follow-up report is described of patients receiving long-term treatment with oxytetracycline for chronic non-tuberculous respiratory infections

Eight patients have remained on treatment with benefit to the present time for periods ranging from $2^3/_4$ to $1^1/_2$ years

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A NEW OPERATION FOR THE CONSTRUCTION OF AN ARTIFICIAL FALLOPIAN TUBE

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The theoretical basis for the operation described here is derived from embryological observations on the common origin of the peritoneum, the uterine tube, and the ovary The procedure consists of making an opening in the uterus, lining this opening with peritoneum, and utilising the round ligament and local peritoneal tissue in the construction of the tube

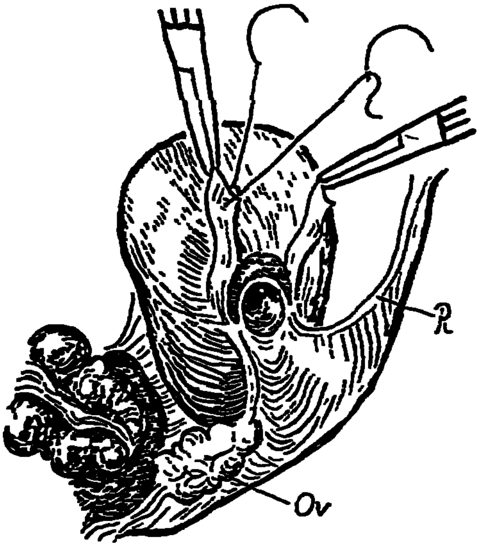


Fig 1—Peritoneal flaps raised around reamed aperture in uterus R round ligament, Ov ovary

Technique

The peritoneal cavity is entered through a median subumbilical incision The ovary, round ligament, and ovarian ligament on both sides are identified, and the uterus is pulled up

With a Green-Armytage reamer (9 mm) an opening is made into the uterine cavity at the site of the interstitial part of the tube, two flaps of peritoneum are fashioned from the anterior and posterior aspects of the uterus around the reamed aperture (fig 1) The free margins of these flaps are transfixed with a fine suture of 00 chromic catgut and by the Sturmdorf technique, the peritoneal flaps are drawn towards the uterine cavity thereby providing a peritoneal lining for the aperture reamed in

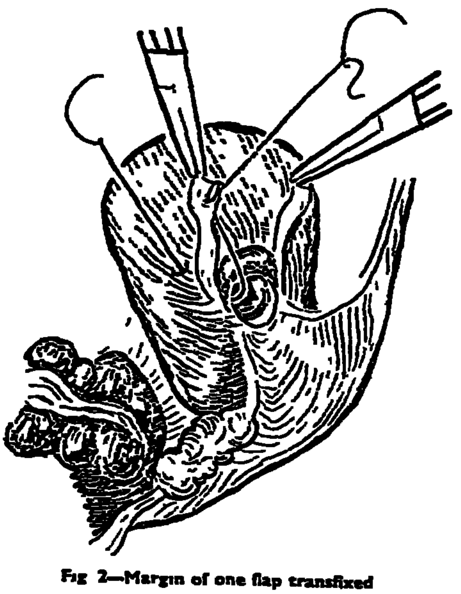
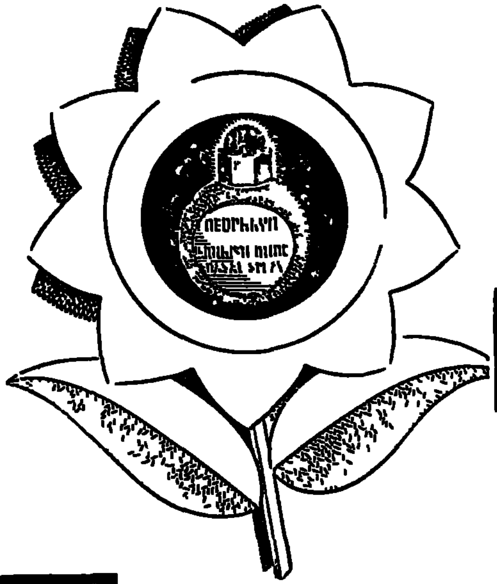


Fig 2—Margin of one flap transfixed

Symptomatic relief in hay fever, allergic rhinitis



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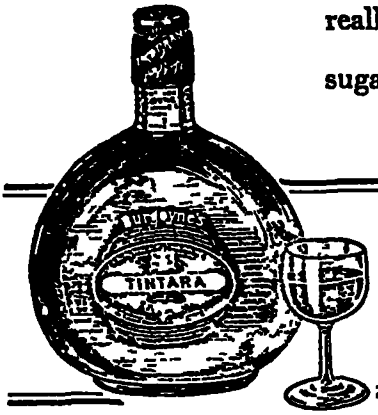

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CLASSIFICATION OF CARCINOMA OF BRONCHUS

Source	Bryson and Spencer (866 cases)	Walter and Pryce (1[illegible]9 cases)	Present series (171 cases)	
			Initial	Corrected for mucin production
Oat cell (%)	36.0	37.1	35.7	35.7
Adenocarcinoma (%)	4.9	28.3	15.8	22.8
Squamous cell (%)	6.9	20.1	27.5	27.5
"Squamoid" (%)	11.2	Nil	Nil	Nil
Polygonal cell (%)	40.2	10.7	21.0	14.0
Rejected (poor histology &c.) (%)	0.8	3.8	Nil	Nil

cell," or "squamoid" cancers. The term "squamoid" was used by Bryson and Spencer and is admirably descriptive; they used the term "polygonal" for the residue of undifferentiated carcinomas.

We eliminated the "squamoid" group and included all non-differentiated cancers in the polygonal cell group. It is obvious that this group must include anaplastic squamous cell and anaplastic adenocarcinomas, and we therefore tried to reduce the proportion of growths classified as "polygonal-cell" by demonstrating criteria by which they might be allocated to the squamous-cell or adenocarcinoma groups.

Variability of cell type is a feature of lung cancer (Willis 1948) and may be caused by metaplasia, which occurs commonly in adenocarcinomas and occasionally in oat cell tumours; it must be distinguished from differentiation in a predominantly anaplastic carcinoma. Areas of squamous metaplasia are common in small bronchi which are chronically inflamed and such bronchi may be included in the growth. It is also possible that, in some instances, a genuine mixed tumour results from the fusion of foci of differing cell types; we encountered 1 tumour of this nature in which large areas of squamous and oat-cell carcinomas were mixed. Cancer cells, of whatever type, often have a tendency to line spaces, and the lung alveoli provide an excellent basis for this pseudo adenomatous extension. This, however, is not true tubule formation and such tumours are not necessarily adenocarcinomas.

Our initial classification was:

(1) *Squamous cell carcinoma.* 'prickles' or keratin demonstrated; no oat cell or tubular growth.

(2) *Adenocarcinoma.* true tubular and mucinous cancers.

(3) *Oat cell carcinoma.* there is no difficulty about these, although, as well illustrated by Walter and Pryce (1955), half of them contain characteristic tubular structures.

(4) *Polygonal cell carcinoma.* these form a large residue and have none of the above characteristics.

The material analysed was obtained from necropsies; some of the growths were small and were studied by serial or interrupted serial sections. The study of secondary tumours, when present, shed some light in doubtful cases. The results are shown in the accompanying table; so far as the oat cell growths are concerned, our figures closely agree with those of Bryson and Spencer and Walter and Pryce. Certain factors undoubtedly influence the figures (e.g., cases considered operable were transferred elsewhere), but, allowing for these, there is still disagreement between the figures for the polygonal-cell group: in the initial classification of our series, 21% of the carcinomas were of the polygonal cell type, as compared with 40.2% recorded by Bryson and Spencer and 10.7% recorded by Walter and Pryce. Our figures for polygonal-cell carcinoma were undoubtedly raised by the discovery at necropsy of a number of small, unsuspected growths associated with lung scars (Raeburn and Spencer 1953); but "polygonal" is another way of saying "unclassified," and it is therefore desirable to diminish this group by any legitimate means.

Sections of all the tumours and of their secondary deposits in the polygonal cell group were stained for mucin; of the 36 tumours examined, 12 contained mucin and were therefore considered to be adenocarcinomas. In 10 cases there was copious mucin production; in the remaining 2, careful search revealed mucinous areas. A number of these tumours contained occasional small, cubical, strongly mucinous cells (unicellular remnants of destroyed mucous glands) which were easily distinguishable from carcinoma cells. 1 tumour which contained mucin in most of its cells looked very like a squamous cell carcinoma although true squamous characteristics were absent.

The corrected figures for the present series, after the growths had been stained for mucin and those containing mucin had been transferred to the adenocarcinoma group, are also shown in the table; the corrected figures for adenocarcinomas rose from 15.8 to 22.8%, and those for polygonal cell carcinomas fell from 21 to 14%.

Summary

Mucin can be demonstrated in some "polygonal-cell" carcinomas of the bronchus. These growths should be regarded as adenocarcinomas, and the residue of unclassified cancers will thus be diminished.

This work was aided by a grant from the British Empire Cancer Campaign.

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ARTIFICIAL SPONGES IN SURGERY

BRYAN WILLIAMS
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MATERNITY AND NORTH ORMESBY HOSPITALS, YORKS.

> "Only those surgeons who have operated without gloves and with soft marine sponges instead of gauze swabs can have enjoyed the pure delight of operating."—Grey Turner (1943).

FOR some time I have been using artificial sponges in obstetrical and gynæcological work. They are cellulose sponges made from wood pulp by the viscose process and marketed under the name 'Spontex'. When moistened they are soft, and they are highly absorbent. They can be easily washed after use and stand repeated boiling and autoclaving. Tests made by Dr. R. Blowers, director of the Public Health Laboratory (Medical Research Council), Middlesbrough, show that after autoclaving they are sterile both on aerobic and anaerobic culture. The material can be cut quite easily when dry, and various sizes of sponge have been tried. It has been found convenient to use a large size, about 3½ × 2½ × 1½ in., which will absorb about 4 oz. of water, and a smaller oblong size which can be held in a sponge forceps.

A great advantage of using these sponges lies in the resulting simplification of the swab count. It is possible to do a cæsarean section with only four large sponges in addition to the gauze ones used for skin preparation and the baby. The intraperitoneal part of a hysterectomy can be done with four small swabs; and the repair of the perineum or an episiotomy after delivery, which often needs the use of a considerable amount of gauze or wool if there is much bleeding, can be done with one or two small ones.

Another advantage of using the larger sponges is that, owing to their absorbing power, they are very effective in removing large amounts of fluid if a sucker is not available. Probably the regular use of such sponges in surgery would be an economy, because gauze is an expensive item in hospital budgets and may account for a third of the total cost of all dressings. These sponges myelitis, and all occurred during or shortly after the seasonal period of prevalence of poliomyelitis. The three British outbreaks [18 24 25] were in late summer, in contrast to the former peak incidence of encephalitis lethargica in the first three months of the year.[2] Five outbreaks took the form of dramatic localised epidemics, four of which were in nurses' homes. Dr RAMSAY and Dr O'SULLIVAN describe cases in the neighbourhood of one of these outbreaks, and HILL [17] had a similar experience in Durban. The attack-rate in closed communities is high. The onset in this group is usually acute with systemic prodromata such as are common in poliomyelitis. In contrast, fever is usually low and may be absent.[14 18 25] The course is generally two to eight weeks but occasionally symptoms may last for months. Relapses are frequent. Usually the immediate outcome is favourable but in a few cases paresis or mental sequelæ may be incapacitating for many months.[22 23 26] Depression, emotional lability, or irritability in convalescence have been a constant feature in all group-II outbreaks. Although previous experience has shown that a long period of observation will be necessary before the harmlessness of the disorder is assured, it can at least be said that the immediate mortality-rate of nil is in striking contrast to the epidemic infections of the nervous system previously described[4], and this in itself is very encouraging.

Among the more characteristic features of group II are the severe muscular pains, often accompanied by exquisite tenderness, which often dominate the clinical picture.[22–25] As WHITE and BURTCH [23] have pointed out, these pains differ from those of poliomyelitis in that they are not simply a short-lived precursor of paresis but may last for weeks. Most commonly they affect the neck, back, or limbs but there may also be Bornholm-like chest and abdominal pains.[17 18 23 25] Continuous or intermittent painful muscular spasms were noted in the outbreaks at the Middlesex and Royal Free Hospitals, and they are also reported by Dr RAMSAY and Dr O'SULLIVAN. In nearly every patient there are symptoms or signs of disease of the central nervous system, but the weight and site of the damage vary considerably from outbreak to outbreak. The Hampstead and Berlin epidemics illustrate this variation. The innervation of the eye muscles (diplopia and nystagmus) and the seventh and eighth cranial nerves (deafness, hyperacusis, vertigo, and facial weakness) suffer most commonly. Sensory symptoms and signs are common and pyramidal signs have also been observed. Some patients in Adelaide and Durban and at the Middlesex Hospital had retention of urine. The paresis, usually short-lived but occasionally persisting for weeks or months, is in itself an interesting problem for in many cases it is not accompanied by the classical disturbances of tone and reflexes which would point to damage in the anterior horn or pyramidal tract.[23 25 26] Pain, muscular spasm, and involuntary movements often make the degree of palsy difficult to assess. In this connection the striking electromyographic records obtained by Dr RAMSAY and Dr O'SULLIVAN are of great interest. Although they do not as yet point to the exact nature of the lesions, they may provide evidence of organic paresis in patients who might otherwise be suspected of hysteria, and in a disease at present so bereft of positive laboratory findings they may be a help in diagnosis in the future.

The outbreaks mainly differ in the severity and site of the damage to the nervous system but the lymph glands are another point of difference. Enlarged lymph glands, particularly in the posterior cervical triangle, were prominent in the Hampstead and Royal Free cases, and they were also noted in 4 cases by WHITE and BURTCH [23] and in the more doubtful Cumberland outbreak.[21] In retrospect lymphadenopathy was found to have been present in 2 of the 14 cases reported from the Middlesex.[27] Hepatitis and splenomegaly may also turn out to be part of the picture. It is doubtful whether the absence of these features in the other reports can be attributed entirely to observer error [27] and it must be accepted as a real discrepancy.

A study of the available material in group II shows sufficient common ground to suggest that this is a new clinical entity which may be expected to appear again here or elsewhere in the late summer and autumn. From the purely practical standpoint it would be useful to have a name for this syndrome. As the most helpful single feature in the recognition of this syndrome in the past has been the predominantly normal cerebrospinal fluid, the names which have already been suggested, "Iceland disease" [16 23] and "Akureyri disease," are not really appropriate. The objections to any but a purely descriptive name for a disorder without a known cause or established pathology are obvious. For this reason, the term "benign myalgic encephalomyelitis" may be acceptable. It in no way prejudices the arguments for or against a single or a related group of causal agents, and it does describe some of the striking features of a syndrome characterised by (1) symptoms and signs of damage to the brain and spinal cord, in a greater or lesser degree, (2) protracted muscle pain with paresis and cramp, (3) emotional disturbances in convalescence, (4) normal C.S.F., (5) involvement, in some variants, of the reticuloendothelial system, (6) a protracted course with relapses in severe cases, and (7) a relatively benign outcome. It remains to identify this syndrome more precisely, but we believe that its characteristics are now sufficiently clear to differentiate it from poliomyelitis, epidemic myalgia, glandular fever, the forms of epidemic encephalitis already described, and, need it be said, hysteria.

Antibiotic-resistant Staphylococci

IF bacteriologists are good judges of what is important, the direction and emphasis of much of their work suggests that it is high time we adopted whatever modifications of clinical practice are necessary to halt the spread of antibiotic-resistant staphylococci in hospital wards and outpatient departments. These infections in hospital are not only a cause of ill health, lost time, and wasted money, but also a source from which a veritable epidemic of staphylococcal infections may spread to the general community. There is no reason whatever to doubt the implications of ROUNTREE and RHEUBEN's [28] evidence that in December, 1955, 25·7% of 101 nasal carriers of staphylococci among 200 Sydney blood donors

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From October, 1955, she has injected streptomycin from the cartridges, giving up to 20 g daily with no untoward effects

Discussion

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It cannot be claimed, on the basis of only 2 cases, that the incidence of streptomycin sensitivity could be very greatly reduced, but the present cases seem to suggest that this may be so and that it would be advisable to conduct further trials, particularly on the already sensitised Then, if it is confirmed that sensitised nurses can continue to give injections by this method, the method should also be used to prevent contact sensitivity Care, however, should be taken that the ease of this method does not lull nurses into neglecting the aseptic precautions that should accompany the injection of antibiotics

Summary

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2 nurses with streptomycin dermatitis were enabled by this technique to return to giving streptomycin

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The sterile cartridges ('Viules') containing streptomycin were supplied by Boots Pure Drug Co Ltd

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HUMIDIFIER FOR USE WITH TRACHEOTOMY AND POSITIVE-PRESSURE RESPIRATION

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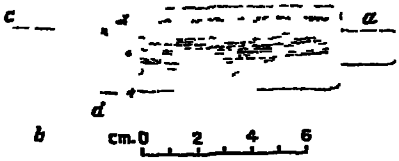
WHEN artificial respiration is applied by positive-pressure inflation of the lungs with a cuffed tube inserted through a tracheotomy stoma, the normal humidifying and warming function of the nose and pharynx are by-passed The nose and pharynx in a healthy person warm the air to body-temperature and humidifies it to 98% saturation at that temperature (Perwitzschky 1927)



Humidifying cartridge a to patient b tory tube c, expiratory tube d rubber seal

Experience with long-continued tracheotomy has shown that inhalation of air at room temperature and humidity leads to crusting bronchial secretions Humidification is needed to prevent this Marshall and Spalding (1953) have designed and used an apparatus which warms the inspired air to 35°C and humidifies it to 100% saturation at that temperature This apparatus has an electrical heating coil and an adjustable thermostat It is of substantial size Since treatment with positive-pressure respiration already needs much complex equipment, it was thought something simpler and less bulky might suffice

Apparatus

In view of the fact that the nose and pharynx present a large surface, warm and moist, to condition the inspired air, this humidifier was designed to incorporate these features It consists of a cartridge containing a roll of silver-plated copper gauze through which the patient breathes (fig 1) The expired air, passing over the gauze loses some of its heat and moisture, which are taken up by the inspired air The cartridge, which is also warmed by contact with the body, is a cylinder of 'Perspex' 2 5 cm in internal diameter The copper gauze has a mesh of 24 to the inch and is 45 cm long and 7 5–9 0 cm broad, the greatest width being used for patients needing large tidal volumes The gauze is silver-plated to resist corrosion Stainless steel would be more resistant but not so capable of holding heat The gauze is rolled to be a tight fit in the cartridge It can be easily taken out for cleaning, which may be required on alternate days, by pulling out the rubber seal which closes one end The volume of the air enclosed by the apparatus is about 38–45 c cm according to the size used The humidifier has been used in conjunction with the Clevedon positive-pressure machine (Macrae et al 1954), the small inspiratory and large expiratory tubes being connected to one end of the cartridge The other end, with the single outlet, is joined by a plastic tube 5 cm long to the cuffed endotracheal tube The cartridge is strapped firmly to the skin in the right or left infraclavicular fossa

The performance of the apparatus was first tested by a healthy person breathing through the mouth with the nose closed by a clip The performance was later tested with a patient being ventilated with a Clevedon positive-pressure respirator

Methods

The water content of the inspired air was measured by drawing off 40–50 c cm throughout the length of each inspiration to a total of 4000 c cm from the endotracheal junction and absorbing the water with dehydrated calcium chloride, weighed before and after (Perwitzschky 1927)

Temperature was measured crudely by intermittently inserting a mercury thermometer into the inspired air-stream The figures so obtained are likely to have been lower than the actual temperature

Pressure tracings (fig 2) were taken with a drum and tambour

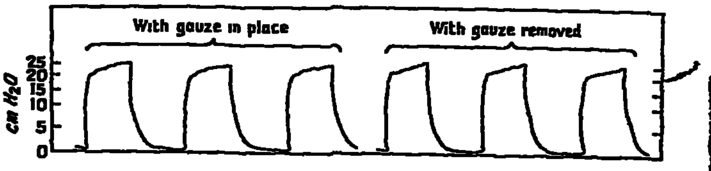


Fig 2—Pressure tracings with gauze in place and with gauze removed

effective dose, (6) bacteriological study before treatment of patients with chronic or mixed infections, (7) treatment for evidence of infection but not for the mere presence of bacteria, (8) remedy, where possible, of underlying anatomical, immunological, or metabolic defects, and (9) precautions against hospital cross-infection

Certainly it is time that we abandoned the naïve ignorance which underlies the apparently common assumption that the best thing a doctor can do for a febrile or potentially febrile patient is to "hit his bugs hard" Most of these miscalled creatures are harmless when they are left, among plenty of others of their kind, to the rich natural antibacterial resources of the human body If we were not so often and so uncritically anxious to do a bacteriological good deed where none is required, we should be far less likely to spread harm of a kind that it may soon prove impossible to control

Artificial Kidneys

SOON after the late war, various modifications of the KOLFF artificial kidney were used fairly intensively in special centres in this country, and in 1948 we reviewed this early experience[1] It was not on the whole very encouraging, and the pendulum soon swung to a conservative régime for the treatment of acute renal failure[2] [3] This can now be regarded as the standard treatment, and is in general use, with some modifications such as giving calories by vein rather than orally,[4] and delaying a rise in plasma-potassium by exchange resins in the sodium cycle[5] There seems little doubt that this practice is substantially sound, and it has saved many lives which might have been lost by ill-controlled attempts at active treatment by dialysis, which is generally recognised as requiring a trained team with frequent recourse to biochemical estimations But some recent reports of extensive work with artificial kidneys prompt the question whether we may not in this country have carried conservatism to a fault

Most of the artificial kidneys now in use follow the pattern of KOLFF, in which the patient's blood perfuses a 'Cellophane' tube round a rotating drum in a bath of suitable fluid BRUN in Copenhagen has now had long and favourable experience of a different type of artificial kidney,[6] in which blood is pumped between cellophane sheets which separate it from bath-fluid flowing in the opposite direction This apparatus has the advantage of containing a much smaller volume of blood without sacrifice of efficiency As MERRILL says, however, "the major factor in efficacy is the skill and experience of the operator and this cannot be incorporated in the design"[7] From his study of over 500 dialyses, MERRILL can speak with particular authority on the uses and limitations of the method The indications are clinical rather than biochemical, and he regards "nausea, vomiting, apathy, drowsiness and weakness" as the main evidences of 'a morbid state which cannot be relieved by the usual conservative method of management' To these, we might add uræmic twitchings and pericarditis This state of affairs is not usually reached in the first week of anuria, in civilian practice at any rate, but in traumatic surgery, with greatly increased tissue breakdown, it may appear in a day or two, and the artificial kidney was widely used in Korea, with dramatic relief of uræmic symptoms[8]

Early difficulties with the artificial kidney were largely related to disturbance of fluid and electrolyte balance, and they can be avoided by careful attention to the composition of the bath-fluid Moreover, the dialysis gives an opportunity of correcting such electrolyte disturbances as have appeared spontaneously or have been induced by evil practices such as overhydration This important function of the artificial kidney has been reviewed by HAMBURGER and RICHET[9] in the first number of a new journal, *Revue Française d'Études Cliniques et Biologiques*[10] In a series of 60 dialyses, they determined the concentration of plasma electrolytes before and at intervals after dialysis Of the cations, sodium concentration was normal or slightly reduced (others have found hyponatræmia more common in anuria, on régimes which do not restrict water intake as rigorously as that of HAMBURGER), potassium was sometimes increased, magnesium was increased more commonly than potassium, and calcium was always reduced Phosphate, sulphate, and organic acids were increased, while chloride and bicarbonate were reduced All these anomalies were altered towards normal by the dialysis, and this change was accompanied by clinical improvement "Au cours même d'application, une calme euphorie remplace l'anxieuse agitation ou la somnolence hostile de l'urémique" Faced with this complex of biochemical improvement, and adding to it the fall in blood-urea, HAMBURGER and RICHET are guarded in ascribing individual changes to specific biochemical alterations They suggest, however, that the raised magnesium concentration is related to drowsiness, and that the increase in phosphate and sulphate has not been sufficiently heeded as a cause of symptoms They claim that intestinal and peritoneal dialysis are less effective than the artificial kidney in removing phosphate and sulphate, and that these other types of dialysis are clinically less effective, in spite of a comparable effect in lowering the blood urea

As MERRILL points out, the use of the artificial kidney is based on the assumptions that it can be used safely and effectively in sick patients and that the medical state in renal failure can be improved by removal of diffusible substances from his six years experience he considers both these are justified The practical difficulty is to assemble and maintain, not the kidney itself, but a team who are competent to use it and not to abuse it Several centres in this country have now had time to appreciate both the general value and the occasional failures of conservative treatment, and some have turned to intermittent peritoneal lavage in selected cases[11] There may be a place for one or two groups to devote themselves to further study of the artificial kidney

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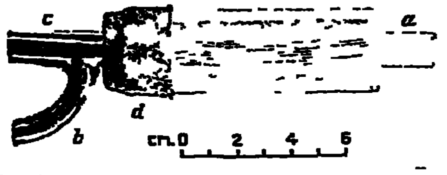

Fig 1—Humidifying cartridge a to patient b inspiratory tube c expiratory tube, d rubber seal

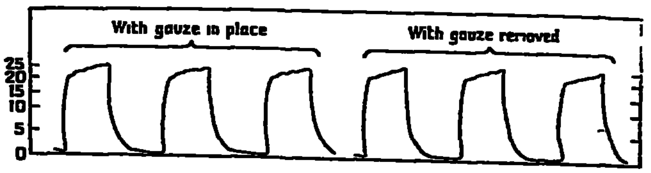

Fig 2—Pressure tracings with gauze in place and with gauze removed

When these lesions produce symptoms, discomfort in the knee often begins after a minor injury Pain and effusion are less common, and severe disability is rare "Catching" in the knee, due to the roughened patella surface, is an occasional feature (true locking indicates the presence of a loose body) Wiles et al[3] have pointed out two important physical signs pain on grating the patella against the femur, and tenderness over the articular surface of the patella, this can be elicited by displacing the patella laterally Karlson[2] attaches some importance to the presence of patella crepitus, but this sign may be misleading Radiographs are of value only in excluding other joint diseases Diagnosis should not be difficult, but associated lesions such as detachment of cartilage flakes, osteochondritis dissecans, and dislocation of the patella may also be present

Treatment may not be an easy matter When symptoms are slight, the condition tends to improve spontaneously, but rest and short-wave diathermy may help When disability is severe, the patella may be exposed and small areas of affected cartilage shaved off When there is extensive disease, either the whole articular surface of the patella may be removed or the patella itself may be excised Excision is usually indicated when the femur is also involved Although the smaller lesions usually respond favourably, the results of the more extensive operations are less satisfactory (Since these are selected cases, it is difficult to compare them with those treated conservatively) If, however, as Wiles believes, chondromalacia is a precursor of osteo arthritis, such operations may also be of prophylactic value

MR DODGSON'S MIGRAINE

WHEN he is awake, the normal person is aware of his body, its position in space, its size and shape in relation to other objects, the inter-relations of its various parts, and the continual changes in these relationships with bodily movements, or with growth and finally old age Since Paul Schilder in Vienna and Henry Head in this country elaborated their ideas of such a "body-image" or "schema," the subject has been of perennial interest to neurologists and psychiatrists The body-image is the resultant of a continuous stream of sensory impulses, both proprioceptive and exteroceptive, passing to the brain There is now much evidence from local brain lesions to suggest that these impulses are elaborated and coordinated in the posterior part of the parietal cortex in the region of the angular gyrus, which constitutes the "centre" for the body-image, but it is still a matter of argument whether the centre is represented exclusively in the non-dominant hemisphere or whether, as seems more probable *a priori*, there is some bilateral representation

This is the mechanism which mediates the normal smooth manipulation of the body in space As is often the case, the existence of such a mechanism becomes obtrusive only when its function is disordered When the body-image is severely disorganised by some gross lesion such as a vascular accident or tumour, the ensuing behaviour is bizarre To watch such a patient attempting to dress, to sit down in a chair, or to get into bed, will suggest at first a severe confusion or dementia, though subsequent examination may show that he is in fact fully orientated and his intellectual capacity in general is unimpaired

Perhaps of greater interest are the transient and episodic upsets seen in certain epileptic variants These represent focal fits originating in the posterior parietal cortex They range from some limited manifestation such as the sudden feeling that one limb is moving or has assumed some unusual posture, when it can be seen to be stationary or in quite a different position, to the hallucinatory experience of a complete image of the self (autoscopy) projected into external space, such as the famous instance of Goethe meeting his double coming towards him on the road to Weimar

Similar disorders of body image may be found in migraine, either as an aura to an attack or as a migrainous equivalent Lippman[1] drew attention to such phenomena and pointed out that the fantasies of altered bodily size and shape in *Alice in Wonderland* were very similar to the descriptions of their symptoms given by some migrainous patients Recently Todd[2] has described 6 further cases He emphasises that these symptoms may sometimes occur apart from the more usual manifestations of migraine, and will often cause much anxiety and fears of insanity Both he and Lippman point out that Lewis Carroll (C L Dodgson) himself suffered from migraine, and suggest, in Todd's words, "that Alice trod the paths and byways of a wonderland well known to her creator" If that is so, English literature is the richer for Mr Dodgson's migraine

PSYCHOSOMATIC RESEARCH

RESEARCH on mind-body relationships calls for the ability to recognise clearly a change in mental state and an acceptable method of measuring its consequences in the body Physiology may provide tested methods of measuring bodily changes, but psychology has not yet evolved ways of measuring changes of mental state These difficulties have not deterred investigators, and during the past half century a considerable volume of literature on the subject of psychosomatic relationship has accumulated This literature is candidly described by the editors of the newly published *Journal of Psychosomatic Research*[3] "Nowhere in medicine is there such a contrast between the wide span of theories and their narrow factual basis" This new international journal has been started with the admirable object of encouraging workers on psychosomatic relationships to apply scientific methods to their studies The editorial policy is to publish only the results of investigations in which hypotheses have been clearly formulated and tested by well planned experiments, and the scope of the articles published will be wide enough to include controlled clinical investigations, animal, human, or experimental work, and relevant studies from such related fields as psychology, sociology, and anthropology

The first two papers of the new journal, by Dr Brian Ackner, provide a good example of how psychosomatic relationships can be scientifically investigated The problem was to study the effect of anxiety on peripheral vasomotor activity Ackner considers possible methods of investigating vasomotor activity, and he concludes that the measurement of finger pulse volume is the most suitable technique Its advantages are that the apparatus is simple and unobtrusive, so that the subject's emotions are not aroused by the procedure, and it is sufficiently sensitive to define clearly the changes observed Patients were chosen from psychiatric inpatients who complained of constant anxiety and appeared anxious and tense throughout the day Observations made on this group were compared with observations on a second group of inpatients who were objectively and subjectively free from anxiety, and also with observations made on a group of normal persons Previous work had shown that the peripheral vasomotor tone is affected by many factors, and it was necessary for this investigation to show that the effects observed were solely attributable to anxiety The patients were observed in as basal a state as possible and then all emotional effects were removed by inducing sleep with quinalbarbitone ('Seconal') If anxiety produces abnormal digital vasoconstriction, sleep in

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[3] Wiles P Andrews P S Devas M B J Bone Jt Surg 1956 38B 95

[1] Lippman C W J nerv ment Dis 1952 116 316

[2] Todd J Canad med Ass J 1955 73 701

[3] Editor-in-chief Dr Denis Leigh Published quarterly by Pergamon Press Ltd 4-5 Fitzroy Square London, W 1

TABLE I—EXCRETION OF RADIO IODINE

Date	Activity (μc ¹³¹I)	0–8 hr (%)	8–24 hr (%)	24–48 hr (%)	Total (%)
t 18, 1953	30	33	2	1	36
21, ,,	10	16	3	1	20
23	17				
15, 1954	50	37	23	12	72
il 4, 1955	50	26	19	5	50

ected Unfortunately no marrow biopsy was done Whole od was transfused between April 6 and 27 1955, but hout any real benefit Cystoscopy and intravenous pyelo phy were done at the time The pyelogram, which suggested ease of the left kidney, proved a stumbling block and nporarily delayed a correct diagnosis On April 30 and y 7, 1955, the correct diagnosis was suggested by peri eral blood counts, which showed a low white cell count in first and large numbers of blast cells in the second On y 1, 1955, the patient developed a left sided hemiplegia, læna, and ecchymoses on the left cheek and buttocks She d on May 9, 1955

Necropsy showed a cerebral hæmorrhage and acute myeloid kæmia The thyroid contained many calcified and fibrous enomata, with a little pale pink colloidal thyroid tissue erspersed between the adenomata There were no leukæmic iltrations or deposits The bone marrow of the sternum, rtebræ, and upper two-thirds of the femora was soft and ldish green and had undergone myeloid leukæmic trans mation There was also leukæmic infiltration of the spleen, er, and renal pelves The last-named showed signs of ent hæmorrhage There was a minor degree of leukæmic iltration in the right occipital lobe of the brain, the mucosa the œsophagus and several lymph glands which were, wever all small and inconspicuous the largest measuring ×1 0 cm Dr J V Dacie reviewed the relevant necropsy aterial, and confirmed the diagnosis of acute monocytoid yelogenous leukæmia

Discussion

It would be improper at this stage to draw any conclu- on about the part, if any, played by irradiation in the duction of leukæmia in this particular case We merely eport the development of acute myeloid leukæmia in a oman treated for thyrotoxicosis with radioactive iodine ghteen months earlier Before treatment with radio odine she had been given carbimazole for ten weeks

TABLE II—RESULTS OF BLOOD COUNTS

Date	Findings
pt 14 1953	Hb 95%, white cells 5500 per c mm (polymorphs 60% lymphocytes 37% eosinophils 2% monocytes 1%)
pril 4 1955	Hb 80%, white cells 4500 per c mm
13 ,,	Hb 73%
19	Hb 63%
27 ,,	Hb 51%
30	Hb 50% white cells 1000 per c mm
ay 2	Platelets 80 000 per c mm
7	Hb 35% white cells 31 200 per c mm many primitive white cells on film (? myeloblasts)

Ionising irradiation has already been shown to be at ast a *contributory* cause of leukæmia in man under ertain conditions (March 1950, Folley et al 1952, Lange t al 1954, Court Brown and Abbatt 1955 Moloney and Kastenbaum 1955) Leukæmia has so far been reported n 5 other cases after radio-iodine (Delarue et al 1953, eidlin et al 1954, 1955, Blom et al 1955), but they were ases of carcinoma, in which much larger doses of radio- odine are given, and in 2 of them external radiation was lso given The cases of Pochin et al (1956) and urselves are the only ones so far reported in which eukæmia has followed the administration of the smaller loses of radio iodine necessary in the treatment of hyrotoxicosis It is important to emphasise that both ases were of acute leukæmia, a disease difficult to diag- nose without hæmatological facilities, and that therefore unrecognised cases could easily occur

It is not infrequently assumed that radiation in small doses—e g , in diagnostic X-ray examinations and in the radio-iodine treatment of thyrotoxicosis—does not damage enough tissue to initiate leukæmia But the ætiology of leukæmia remains unknown, and it is known that ionising radiation can play a part in its induction in certain conditions It is important to assess the risks of radio-iodine treatment as soon as possible by direct observation in man rather than by extrapolation from animals Such data can only be obtained from a large-scale survey of patients treated with radio-iodine and comparison with a suitable control group We suggest that the evidence is now good enough to warrant such a survey

Summary

A case is reported of a patient in whom acute leukæmia developed eighteen months after treatment with radio- active iodine for thyrotoxicosis

We wish to thank Dr J V Dacie Dr I Doniach and Dr S Robinson *for their help*

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INTERMITTENT POSITIVE-PRESSURE RESPIRATION

AN UNUSUAL COMPLICATION IN AN INFANT

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POSITIVE PRESSURE respiration introduced by Lassen (1953), has become an established form of treatment for certain conditions (*Lancet* 1955) but reports of its use (Macrae et al 1953, Smith et al 1954, Harries and Lawes 1955) refer only to adults or children, and we have found no description of its use in infants

We describe here *our* experience with an infant suffering from acute bulbospinal poliomyelitis who was treated by this technique

Case-report

A well nourished African infant aged 10 months, was admitted to the poliomyelitis unit in Nairobi on Sept 30, *1955 from an up country hospital* The patient who had been ill for six days, had been brought to the hospital originally because of inability to suck Notes taken on admission to the first hospital read as follows ' semi comatose, temp 101°F alæ nasæ working, respirations 60, diaphragmatic movement good some paradoxical movement of the upper chest, palate does not appear to move and the patient is unable to swallow

Investigations and Treatment

The cerebrospinal fluid contained 135 mg protein per 100 ml and 35 cells per 100 ml A stomach tube was inserted for feeding purposes Oximeter readings (mean of *six*) showed the arterial oxygen tension to be 94 6%, but this figure improved to 97% when oxygen was given From time to time suction of the nose and pharynx was needed to remove secretions The child s condition appeared to be maintained at a reasonable level without any respiratory aid We were unable to estimate the vital capacity or the pCO_2 Seven hours after admission the intercostal paralysis increased rapidly and paradoxical movement became more pronounced

The various combinations of filament size, weave, synthetic material, and its treatment which are now obtainable from the manufacturers are enormous, and it is obvious that much further research is needed to define the best type of tube. It seems likely, however, that improved fabrics will very soon be in use, and they may largely replace arterial homografts.

ALDOSTERONE

RECENT work has illustrated that our understanding of the syndromes associated with excessive secretion of aldosterone is by no means complete.[1] The chief problem at present lies in reconciling the clinicians' identification of a syndrome which they believe to be due to increased aldosterone secretion with the biochemists' failure to detect increased amounts of aldosterone in the urine or blood. This difficulty has arisen on at least two occasions. The first patient was described in our columns by Dr Chalmers and his colleagues,[2] and had the characteristic features believed to be due to excessive aldosterone formation: intermittent muscular pains, cramps, weakness, and paralysis; hypertension; polyuria, nocturia, and albuminuria; hypokalæmia and alkalosis. The second case (an even more difficult diagnostic problem) was described by Dr M. D. Milne to the section of endocrinology at the Royal Society of Medicine on April 25. An otherwise healthy woman complained of occipital headaches, was found to have hypertension, and was referred to hospital. A routine electrocardiogram revealed the changes of hypokalæmia which was confirmed by flame photometry. There was no muscle weakness or tetany, and no adrenal tumour was seen on X-ray examination, even after air insufflation and tomography. Nevertheless both patients were found at laparotomy to have adrenocortical tumours, removal of which righted the biochemical abnormalities, and in neither was there preoperative evidence of increased urinary excretion of aldosterone. One possible explanation for this paradox is that the tumours were secreting some hormone other than aldosterone but with similar physiological effects; or it may be that the present methods for estimating aldosterone are unsatisfactory. A similar difficulty has also arisen in the investigation of toxæmia of pregnancy. In patients with this condition increased amounts of a sodium-retaining substance are excreted in the urine, as judged by bio-assay procedures.[3,4] With justifiable speculation it has been suggested that this substance is aldosterone, but Dr J. D. Martin and Dr I. H. Mills reported, in a communication to the Society for Endocrinology on May 4, that they had failed to find any difference in the amounts of aldosterone excreted by normal pregnant women and patients with toxæmia. Venning and Dyrenfurth[5] have briefly reported similar negative results.

At the Royal Society of Medicine Dr J. F. Tait reviewed very clearly the methods, biological and physicochemical, for estimating aldosterone. Since the ratio of hydrocortisone to aldosterone secreted is about 60 to 1, the amount of aldosterone in the blood (0·08 µg. per 100 ml.) and in the urine is extremely small, and this is largely responsible for the difficulties of estimation. Nevertheless there remains a disturbing and unexplained difference in the quantity of aldosterone found in normal urine by British[6] and Swiss[7] workers. Little is known of the form or forms in which aldosterone is excreted. According to Dr Tait, the yield is increased threefold by hydrolysis at pH 1; Venning and Dyrenfurth[5] used both acid and glucuronidase hydrolysis. Failure to hydrolyse all the conjugates, as well as lack of knowledge about the metabolites of aldosterone, may therefore be in part responsible for the low urinary excretion in some cases of alleged hyperaldosteronism. Dr Tait suggested that the nephropathy caused by hypokalæmia[8,9] might result in diminished excretion of aldosterone in patients with hyperaldosteronism, but he emphasised that in the patient studied by Chalmers et al. the blood level was not raised. Dr I. Bush put forward a point in favour of regarding some cases of "hyperaldostéronism" as due, not to aldosterone, but to some unidentified hormone. He contrasted the large amounts of aldosterone excreted in secondary aldosteronism (cirrhosis, nephrosis, and congestive cardiac failure) and the much smaller or normal amounts in some cases of alleged primary aldosteronism. Until these questions have been resolved, diagnosis and management of primary aldosteronism must rest, as ably shown by Dr Milne, on the clinical findings and metabolic disturbances, without depending on the detection of increased amounts of aldosterone in the urine or blood.

ELECTROLYTES IN TUBERCULOSIS

ABNORMALITIES of the serum electrolytes have been described in tuberculous patients, both with and without antibacterial treatment. Hypokalæmia has been demonstrated during treatment with *p*-aminosalicylic acid[10-12] and with viomycin.[13,14] Low serum-sodium or serum-chloride may be found in untreated patients who are very ill with miliary, meningeal, or pulmonary tuberculosis, but no important changes in serum-potassium have been found.[15] Crofton and his colleagues[16] have lately reported 4 instances of low serum-potassium in patients with miliary tuberculosis having antibacterial treatment that included neither isoniazid nor viomycin. The serum-chlorides were also low in 3 of their patients. In all 4 there were severe symptoms of hypokalæmia with lethargy and profound muscular weakness, but in only 1 did the symptoms appear during the acute phase of the illness; 2 patients had symptoms during convalescence, and in another they were preceded by an attack of biliary colic and vomiting. Simple replacement therapy with sodium, potassium, and chloride produced considerable improvement, and in at least 2 patients it may have been life-saving. Crofton et al. conclude that the electrolyte disturbances were due to the cumulative effects, in severely ill patients, of decreased potassium intake (the result of poor appetite), and to increased potassium loss caused by mild diarrhœa and occasional vomiting, with, possibly, poor renal conservation.[17] It was not possible to examine the electrolyte balance in such gravely ill patients; but Crofton et al.'s paper is published at an incomplete stage of their investigations in order to draw attention to the condition. Electrolyte upsets in tuberculosis may be more common than published reports suggest; and it is possible that some who "just fade away" may in fact die from this remediable cause.

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a valve whereby air could be forced into the lungs but was prevented from escaping In the present case it was difficult to imagine a valve mechanism The possibility of erosion into the œsophagus, with the end of the endotracheal tube lying partly in the trachea and partly in the œsophagus, which might cause dilatation of the stomach or possibly some kind of valve mechanism, was considered but withdrawal of the tube had no effect Suction and squeezing produced no result this time, cyanosis became extreme and the apex beat could no longer be heard As the infant was rapidly dying a needle was inserted into the abdomen, without effect

When the apex-beat had not been heard for one and a half minutes an incision was made through the abdominal wall and as the peritoneum was incised air rushed out At first it was thought that the air had escaped from a puncture of the distended stomach, but a hurried search showed that this was not so The child's condition had improved by this time, cyanosis was less and the pulse could be felt at the wrist A catheter was quickly sewn into the stomach to prevent any further dilatation of the stomach, and the abdomen was sutured As the abdominal wall was being sewn the abdominal distension returned Cutting the peritoneal sutures relieved the distension by allowing air to escape It was now certain that the positive pressure respiration was forcing air into the abdominal cavity The infant was by this time moribund and died shortly afterwards

NECROPSY

Necropsy showed

1 Ulceration of the trachea on the posterior wall but not through to the œsophagus A large clot of blood was resting on the endotracheal tube above the taracheostome There was no sign of surgical emphysema round the trachea or œsophagus

2 Surgical emphysema of the right lung running into the mediastinum, which contained a large number of bullæ

3 Small bullæ running down the œsophagus from the mediastinum into the abdomen

4 Bullæ on the greater and lesser curvature of the stomach, some of these were about $^3/_4$ in in diameter

Discussion

Acute dilatation of the stomach is a fairly common complication of acute poliomyelitis, and fatal cases have been recorded (Hussein 1952, Perreau 1952) In this case the dilatation was severe enough to interfere seriously with positive pressure respiration and could be relieved only by squeezing the abdomen The radiograph taken after the third attack showed that there was no surgical emphysema at that time Presumably the operator during the last attack had allowed the inspiratory pressure to rise too high in an effort to overcome the resistance of the distended stomach, and as a result the alveoli had ruptured into the perivascular spaces and from there air had travelled back into the mediastinum (Macklin 1939, Macklin and Macklin 1944)

Mediastinal emphysema has been described as arising from air trapped in the peritoneal cavity during operations (Baggot 1952) and also as a complication of pneumoperitoneum (Towbin 1951), but we were unable to find any reference to pneumoperitoneum arising from mediastinal emphysema This was the first time we had employed finger respiration, and it is unfortunate that we did not incorporate a safety device in the system as we had done with the Radcliffe respirator

The danger of tracheal ulceration from an endotracheal tube in a small infant was recognised, but we were unable to obtain a suitable silver cannula with a chimney such as is used in Sweden (C G Engstrom, personal communication) These cannulæ have a more acute bend than rubber tubes and have a wider internal diameter

The blood-clot found in the trachea at necropsy was large enough to have completely occluded the trachea, and thus emphasises the need for laryngeal and tracheal toilet before removing the intratracheal cannula

Summary

A case of bulbospinal poliomyelitis in a 10 month old infant is described

The difficulties of intermittent positive pressure respiration in an infant are outlined Acute dilatation of the stomach may threaten life The positive-pressure system should include a safety device to prevent excessive pressures

In the present case death was due to surgical emphysema

We thank the Director of Medical Services, Kenya Colony, for permission to publish this article

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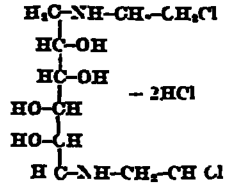
Preliminary Communication

CLINICAL TRIAL OF A NEW NITROGEN-MUSTARD COMPOUND

A NEW type of compound has been prepared by Dr L Vargha by linking a nitrogen mustard with mannitol to form 1, 6-bis (β chlorethylamino-1, 6 desoxy-D-mannitol) dichloride (B C M) (see formula), which strongly inhibits the growth of metastasising tumours and proliferating lymphocytes



$$\begin{array}{l} H_2C\text{–}NH\text{–}CH_2\text{–}CH_2Cl \\ HC\text{–}OH \\ HC\text{–}OH \\ HO\text{–}CH \\ HO\text{–}CH \\ H_2C\text{–}NH\text{–}CH_2\text{–}CH_2Cl \end{array} \cdot 2HCl$$

The recommended dosage of B C M is 1 0–1 5 mg per kg of body-weight administered intravenously on alternate days to a total of 900–1000 mg B C M is easily soluble in physiological saline solution and well tolerated when injected either intrapleurally or intra abdominally in man Intramuscular and subcutaneous injections should not be given The effect of giving B C M by mouth is being investigated No untoward side effect has been observed with a total dose of 1200 mg If that dose is exceeded, there is a risk of agranulocytosis (which, however, can be cured by treatment with corticotrophin)

We report here the results obtained clinically in various malignant disorders

CLINICAL TRIAL

Chronic Lymphoid Leukæmia

The best results were obtained in this disease in 6 of 7 patients an initial leucocytosis of 100,000 per c mm was reduced to normal In 1 of them severe skin lesions which had resisted all previous treatment regressed, and in 1 other a cervical lymph-gland as large as an apple disappeared All 7 patients put on weight, and several months after the end of the treatment they needed no further medication

Chronic Myeloid Leukæmia

In 3 cases the leucocytosis was reduced and the patients put on weight In 1 case the spleen became smaller In 3 other cases improvement was only temporary

Acute Leukæmia

In 2 cases pyrexia and the number of hæmorrhages were reduced, but in 2 other cases no effect was observed

TABLE II—SOURCES OF PATIENTS REFERRED IN 1954

—	No of persons referred	No of patients recalled as new cases for diagnosis	Recall rate (%)
'X ray only' sessions	6041	1106	18.3
New contacts of tuberculosis cases	965	22	2.2
Routine radiographs	197	97	49.2
Direct reference by general practitioners	280	280	100.0
From mass miniature radiography units	56	56	100.0
From other consultants	41	41	100.0
Tuberculin testing of children	831		
Patients with tuberculosis referred from other areas	85		
Total	8496	1602	

unclassified group were patients referred to find out if full resolution had taken place after a pneumonic infection and to exclude the possibility of an underlying carcinoma.

Bronchial carcinoma is becoming of increasing importance in chest work. In 72.6% of the 84 cases of bronchial carcinoma shown in table III the diagnosis was established pathologically by bronchoscopic biopsy, by finding of malignant cells in sputum or pleural fluid, by thoracotomy, or at necropsy. In most of the remainder pathological proof has not yet been obtained, because the patient's age and/or general condition makes surgery unadvisable. A thoracic surgeon attends on one afternoon a week to do bronchoscopy, operable cases of bronchial carcinoma being admitted direct to a thoracic surgical unit, and a follow-up examination of both doubtful cases and patients who have undergone resection is done in the chest clinic at a joint session held with the medical staff and the thoracic surgeon. Suitable inoperable cases of bronchial carcinoma are referred to the regional radiotherapy centre and then continue under clinic observation.

Respiratory tuberculosis is classified under three headings:

(1) *Notified cases* are those in which there is no doubt that an active lesion requiring treatment is present. The sputum in most cases is proved to contain tubercle bacilli either by direct smear or culture.

(2) *Observation cases* comprise patients who have radiographic evidence of tuberculosis but in whom there is doubt regarding the activity of the lesion, the sputum being negative and serial radiographs and observation being necessary for a final assessment of activity of the lesion.

(3) *Inactive cases* consist mainly of patients whose radiographs reveal calcified or hard shadows but who have no symptoms or physical signs.

TABLE III—DIAGNOSES IN THE 1602 NEW CASES

Diagnosis	Male	Female	Total	Average age (yr.)
Respiratory system				
Tuberculosis (notified)	98	54	152 (9.4%)	37
Tuberculosis (observation)	104	109	213 (13.2%)	38
Inactive tuberculosis	62	98	160 (9.9%)	54
Bronchitis and emphysema	110	42	152 (9.4%)	56
Bronchial carcinoma	76	8	84 (5.2%)	58
Spontaneous pneumothorax	11	0	11 (0.6%)	33
Pneumonia	137	47	184 (11.5%)	39
Sarcoidosis	6	0	6 (0.4%)	30
Bronchial asthma	14	14	28 (1.6%)	32
Pleurisy	24	16	40 (2.4%)	16
Bronchiectasis	19	20	39 (2.4%)	28
Pneumoconiosis	8	0	8 (0.4%)	58
Pulmonary embolus	1	4	5 (0.3%)	54
Lesion of upper respiratory tract	23	29	52 (3.2%)	20
Pertussis	1	3	4 (0.2%)	6
Congenital abnormality	5	7	12 (0.7%)	36
Fractured rib	0	2	2 (0.1%)	25
Hæmoptysis (no other abnormality)	40	32	72 (4.4%)	40
Unclassified	179	110	289 (18.0%)	15
Cardiovascular system				
Cardiac failure (including cor pulmonale)	16	10	26 (1.6%)	61
Hypertension	6	12	18 (1.1%)	56
Mitral stenosis	0	9	9 (0.5%)	31
Coronary thrombosis	6	0	6 (0.3%)	48
Miscellaneous	5	1	6 (0.3%)	30
Other systems				
Tuberculosis (notified)	10	6	16 (0.9%)	21
Miscellaneous	4	4	8 (0.4%)	50

Tuberculosis Contacts

All domiciliary contacts of both notified and observation cases attend the clinic both for chest radiography and a tuberculin test. In 1954 22 contacts were found to have a definite lesion when seen for the first time in the chest clinic, and 11 of them were notified as having active tuberculosis. There is an average of 4 domiciliary contacts for each case of tuberculosis. Continued follow-up of contacts is restricted to those in whom it is thought that there is some risk of subsequent development of tuberculosis, such as those in susceptible age groups and those in persistent contact with a patient with positive sputum. Where it is considered desirable, B.C.G. vaccination of young contacts is done. Despite selection of contacts requiring continued supervision there were 5314 attendances in 1954.

Treatment of Tuberculosis

We now have various methods of treating pulmonary tuberculosis and are only beginning to realise the great value of prolonged treatment with streptomycin, *p*-aminosalicylic acid, and isoniazid. As a result there has been a big drop in the death rate from tuberculosis, whereas the incidence of tuberculosis has decreased only a little. As a result all chest clinics have a bigger register of cases.

The Ministry of Health lays down that all patients must be followed up for at least five years from the time the tuberculosis becomes quiescent before they can be classed as recovered. Patients are usually seen at increasing intervals during this period and, unfortunately, relapses are discovered each year.

Before 1948 tuberculosis was one of the few diseases for which treatment was free and patients usually agreed to go wherever a bed was available. Since the introduction of the National Health Service Act there has been an increasing reluctance, and even refusal, of patients to go far away from home, with the ensuing paucity of visitors. The acute shortage of beds which existed up to two years ago led to the institution by chest clinics of domiciliary treatment, early admission to hospital being reserved for homeless persons living in lodgings and for those with poor housing conditions. Today the general standard of housing is much improved, and many patients prefer to have most of their treatment at home, being admitted to hospital only for minor collapse measures or to a special chest hospital for major surgical operations. Such a programme means that the patient remains mainly under the care of his own family doctor, and his progress is usually reviewed monthly at the chest clinic, transport being provided by the ambulance service, and streptomycin being injected by the district nurse.

Advice in the prevention of the spread of tuberculosis is given by the health visitors, who are employed by the local health authority (in this area the Middlesex County Council) and work from the chest clinic, so that they are in close contact with the medical staff. Some patients are admitted to the general hospital beds for various periods for assessment or for such procedures as induction of an artificial pneumothorax or pneumoperitoneum and the division of pleural adhesions. These beds are also essential for the admission of emergencies in patients treated at home and for patients with conditions which it is undesirable to admit to a general medical ward when there is a possibility that tuberculosis may be the cause.

Reviews of Books

Ophthalmology

A Textbook for Diploma Students P D TREVOR ROPER F.R C S, curator, department of pathology, Institute of Ophthalmology, London London Lloyd Luke 1955 Pp 656 75*s*

THE author set out to write a textbook of ophthalmology for those taking the diploma in this subject, and he has based its contents on the current teaching and practice of the Moorfields Eye Hospital and its related Institute of Ophthalmology Although the preface suggests an apology for the use of ' didactic and dogmatic diction,' this is quite proper, and indeed desirable and necessary, for a book of this kind containing the essentials in a short and well-written text enlivened by good illustrations

Three sections deal with the basic sciences on which ophthalmology rests Another devoted to optics has at its end a well illustrated chapter on methods of inspection The remaining two parts of the book are concerned with diseases of the outer and inner eye, and there is a final chapter on the visual pathways

Maintaining the high traditions of a distinguished literary family Mr Trevor-Roper's easy style and attractive composition are a pleasure to read Clearly this is a textbook which many postgraduates will want to have

Surgery in World War II

Vascular Surgery Editors DANIEL C ELKIN, M D MICHAEL E DEBAKEY M D Washington D C Office of the Surgeon General Department of the Army 1955 Pp 465

THIS volume was prepared by the Historical Unit of the United States Army Medical Service, under the editorship of Dr Elkin and Dr DeBakey It gives a reasonably complete account of the arterial complications of war-time injuries in Servicemen and the results to be expected with surgical and conservative treatment The U S Army wisely grouped into selected hospitals of the ' zone of interior " all their vascular cases under the supervision of experienced specialists As a result of this policy our knowledge of arterial injuries has been greatly extended, and the whole volume stands as a tribute to the meticulous documentation investigation, and surgery of the hospitals concerned The chapters are written by well-known authorities, such as Simeone, DeBakey, Freeman, and Shumacker, who were in active control of this work during the war, and the standard of presentation is exceptionally high

As a worthy successor to Makins's classical work, this book clearly reflects the progress that has been made during the two wars in the understanding and treatment of vascular injuries Without doubt it will become a standard work

Transplantation of Tissues

LYNDON A PEER M D, clinical and research director, Rehabilitation Center for Plastic Surgery St Barnabas Hospital, Newark, New Jersey Baltimore Williams & Wilkins London Bailliere Tindall & Cox 1955 Vol. I Pp 421 £5 2*s* 6*d*

THE author of this beautifully and expensively produced volume is a well-known plastic surgeon and authority on surgical research who has made important contributions to the fundamental technique of tissue transplantation He has a wide knowledge of the basic physiological problems of plastic surgery and this is the foundation of the work His own contribution to knowledge in the form of cartilage implants is seen in its many applications to facial and aural reconstruction He covers fully the other fields of tissue transplantation, with a very large bibliography A general pattern of animal and human operations has been followed and autogenous, homologous, and heterologous grafts are compared and contrasted Indeed, some may say that the book attempts too much

The chapter on cell preservation is almost an apologia, for there is no information of value in the remarks on tissue culture, and the section on freeze-drying technique is little more than a summary of some of its history The presentation of the problem of vital storage at very low temperatures is made without reference to the work of Parkes and Smith at Mill Hill though future applications of this work in Dr Peer's own department are mentioned

It is a little difficult to imagine for whom this book has been written. for the original experimental material which might have made a more opportune appearance as a formal monograph, is mingled with more speculative and practical matters concerning the clinical aspects of plastic and reconstructive surgery in general The book will, however, have a real value as a reference source

Cardiovascular Innervation

G A G MITCHELL CH M D SC professor of anatomy and director of anatomical laboratories, University of Manchester Edinburgh E & S Livingstone 1956 Pp 356 55*s*

UNTIL the publication of this book there was no monograph in English on the innervation of the human cardiovascular system Lazorthes's treatise is in French and descriptions by White Smithwick, and Simeone, and Kuntz are in works which are chiefly concerned with function and not structure Professor Mitchell's new book fills this gap He has selected relevant details from the extensive literature often confirming and augmenting them by his own investigations He has reviewed and occasionally modified existing hypotheses blending all into a composite picture, though first place has been given to Man Many topics are explained and illuminated by morphological embryological physiological, pathological, and clinical considerations But the provision of complete details in fields other than anatomy has not been the chief aim and an extensive bibliography is provided for those who want further information on specific problems

In a foreword, Sir Geoffrey Jefferson, F.R S, rightly observes that " this is a book on applied anatomy but a book with a difference—the difference being that the author is a vastly more erudite and better informed anatomist than the great majority of those who teach applied anatomy It is not only a comprehensive but a well-balanced account "

The Normal Child and Some of his Abnormalities

C W VALENTINE, D.PHIL. Harmondsworth Penguin Books 1956 Pp 291 3*s* 6*d*

WRITING for the intelligent reader untutored in psychology Dr Valentine describes the mental and intellectual capacity of children from babyhood to adolescence and their behaviour and development He sets out ' to stress individual differences as normal and to show that many things thought by some (psychiatrists especially) to be signs of serious abnormality are not so ' This he does relying partly on published observations, partly on observation of his own five children and of others known to him Family doctors and parents of sizeable families will find more confirmation of their own experience than surprises , but anyone with fears for the normality of a child under their care should read this book before concluding that the worst is in store

Anxiety and Stress

An Interdisciplinary Study of a Life Situation HAROLD BASOWITZ HAROLD PERSKY, SHELDON J KORCHIN and ROY R GRINKER London and New York McGraw-Hill 1955 Pp 320 60*s*

THIS informative study was carried out by four members (a psychiatrist, a biochemist, and two psychologists) of the staff of the Institute for Psychosomatic and Psychiatric Research and Training of the Michael Reese Hospital, Chicago They studied a group of paratroop candidates during the three strenuous weeks of their practical training Systematic observations were made to determine how visual perception, memory, intellectual control, and other psychological activities were affected by the stress of airborne training and at the same time hippuric-acid excretion plasma-glycine plasma-amino-acid blood-reduced-glutathione, and eosinophil levels were estimated

Special Articles

COMPOSITION OF FLOUR

THE panel appointed by the Government in May, 1955, to investigate the composition and nutritive value of flour[1] has now reported[2] Its main conclusion is as follows

> "Taking into account all the circumstances, and bearing in mind particularly the needs of the vulnerable groups in the population, the Panel concludes that the available evidence does not reveal any ascertainable difference between National flour as defined in the Flour Order, 1953, and flours of extraction rate less than National flour, to which vitamin B_1, nicotinic acid, and iron have been restored in the amounts specified in the Flour Order, 1953, which would significantly affect the health of the population in any foreseeable circumstances They believe, however, that differences between low extraction flour enriched as specified and low extraction flour not so enriched are significant"

Last week the Minister of Agriculture, Fisheries, and Food announced that the Government had accepted this conclusion (see p 810)

National flour is defined under the Flour Order, 1953, as follows containing the maximum quantity of wheat germ which, having regard to the type of milling, can be included in such flour, (2) not including any coarse or added bran, and (3) consisting of wheat flour, being either of 80% extraction or of substantially the same nature and containing substantially the same quantities and proportions of constituents as flour of 80% extraction

THE CONFLICTING VIEWS

The panel summarises two conflicting views

On the one hand, the Government's medical and scientific advisers and the Medical Research Council claim that, since bread contributes, on a national average, a third of the total calories of the diet, National flour of 80% extraction makes it virtually certain that the diet as a whole will provide enough protein, vitamin B_1, nicotinic acid, and iron, and that, in addition, such flour provides useful quantities of other essential nutrients for which the criteria of adequacy are less well defined If the extraction rate were lowered to 70%, there would be a loss of protein, vitamin B_1, nicotinic acid, and iron, and, even if these two vitamins and iron were restored by enrichment, a reduced intake of other vitamins might in some circumstances be reflected in nutritional deficiencies

The representatives of the milling industry, on the other hand, claim that between National flour of 80% extraction and whiter flour of lower extraction, enriched with vitamin B_1, nicotinic acid, and iron to the levels obtaining in National flour, any differences in composition are insignificant when related to the diet as a whole

TRIAL IN GERMAN SCHOOL CHILDREN

The panel refers to the trial in undernourished German children of flours with different degrees of enrichment and different extraction rates (from 70 to 100%)[3] The principals in this trial told the panel that their experience would lead them to believe that the difference between unenriched low extraction flour and higher extraction flours is less than was thought at the time of the Conference on the Post War Loaf[4] and is probably small enough to be ignored when the diet is otherwise well balanced

THE PANEL'S CONCLUSIONS

The panel concludes that a true 80% extraction flour will contain, as compared with flour of lower extraction-rate (taking 70% extraction as a reference-point) (*a*) more of certain essential nutrients, such as protein, vitamin B_1, nicotinic acid, and iron, (*b*) more of the other essential nutrients such as pyridoxine, pantothenic acid, biotin, and folic acid, and (*c*) a little more riboflavine It is, however, a simple process to add vitamin B_1, nicotinic acid, and iron to lower extraction flours so that the contents of these nutrients amount to or exceed those in 80% extraction flour, without impairment of technical quality The panel has an open mind about the significance of the other differences "The history of nutrition reveals many instances where the refinement or over purification of food has led to ill health and there is no reason to believe that this chapter of knowledge is closed"

The panel was particularly impressed by the fact that 10% of British children may pass their childhood in circumstances in which they depend on flour to supply certain essential nutrients in sufficient amounts "The panel is of the opinion that nutrition in such individuals would fall below the level necessary for good health if there were a return to the pre war practice of making bread from flour of extraction rates of 70 to 72 per cent to which vitamin B_1, nicotinic acid, and iron had not been restored" There is some evidence that the quality of the protein of 70% extraction flour is less than that of 80% extraction flour, but the panel believes that when 70% extraction flour is blended with the remainder of the diet its use is most unlikely to give rise to symptoms of protein malnutrition Lowering the extraction rate from 80 to 70% is very unlikely to lead to any nutritional disturbance from lack of pyridoxine, pantothenic acid, biotin, or folic acid

Compared with a 70% extraction enriched flour a true 80% extraction flour may give a more widely spread insurance against possible, but as yet unproved, deficiency in the rest of the diet, but 70%-extraction enriched flour gives a more certain cover against possible deficiency of the three "token" nutrients (vitamin B_1, nicotinic acid and iron) whose lack is associated with well recognised deficiency states

The panel was impressed by the evidence of demand, by millers, bakers, and public, for white flour and white bread There is a risk, the industry claim, that if people can obtain only bread made from 80% extraction flour they may eat less bread and more of other manufactured foods which may not be so nourishing

The panel precedes its main conclusion by expressing its belief that experience has demonstrated that "a policy of enrichment provides a realistic means of ensuring that the greatest nutritional benefit is derived from flour" But flours of higher extraction rate, containing no less nutrients than the enriched low extraction flours, should be also available The National Food Survey, it adds, should continue to be of great help in the periodic review of policy concerning bread

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[1] The members were Sir Henry Cohen F R C P (chairman) Mr A C Chibnall SC D F R S Prof J H Gaddum SC D M R C S F R S Prof R A Morton D SC F R S and Prof L J Witts F R C P

[2] Report of the Panel on Composition and Nutritive Value of Flour Cmd 9757 H M Stationery Office Pp 34 1s 6d

[3] Widdowson E M McCance R A *Spec Rep Ser med Res Coun Lond* 1954 no 287 See *Lancet* 1954 ii 1006

[4] Report of the Conference on the Post War Loaf Cmd 6701 H M Stationery Office 1945 See *Lancet* 1945 ii 759

HEALTH IN SCOTLAND IN 1955

EXPECTANT mothers, the newborn, and young children are singled out, statistically and traditionally, as in need of special protection against health hazards The report[1] of the Department of Health for Scotland suggests that to these vulnerable groups we should now add "men towards the latter half of middle age"

Last year the maternal and infant death rates each touched a new low record There were *43 maternal deaths* (compared with 70 in 1954) or 1 maternal death per 2200 births The infant death rate in 1955 fell to 10 7 per 1000 births, compared with 15 6 per 1000 five years ago The school medical officers found that infections were declining among their charges, while *growth* was more rapid and maturity attained earlier The major hazard to these children is now transport accidents

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[1] Reports of the Department of Health for Scotland and the Scottish Health Services Council 1955 H M Stationery Office *Pp* 157 5s

'Eminently suitable for medicinal purposes'

'In view of these analytical and general evidences, this brandy may be described as particularly suitable for medicinal purposes'

See Lancet, July 22, 1899, p 219

'The evidence both of analysis and taste indicates that the high standard of purity and quality has been maintained and that the brandy is eminently suitable for medicinal purposes'

See Lancet, May 7 1932, p 992

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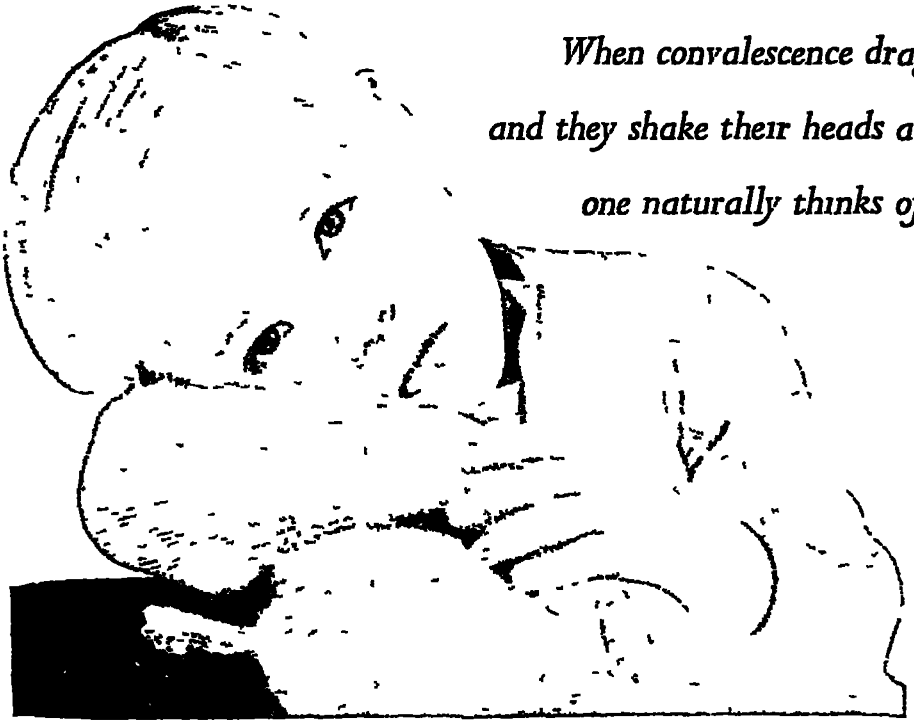

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of the periphery of the bone.[19] While changes in the sacro-iliac joints are usually the most readily demonstrable, characteristic changes may be displayed by special projections in the costovertebral and lumbar apophyseal joints.[20] Fusion of the sacro-iliac joints as the result of ageing processes is probably commoner than is generally realised,[21] and bridging by osteophytes in multiple disc degeneration is an obvious diagnostic trap. According to Mowbray et al.,[9] the disc spaces may be narrowed in ankylosing spondylitis unless they are buttressed by early ligamentous ossification. In adolescent kyphosis there is characteristically a compensatory exaggeration of the lumbar lordosis—in contrast to the flattened lumbar curve of ankylosing spondylitis.[4] Fluorosis can cause a crippling condition of the spine and pelvis which may mimic ankylosing spondylitis clinically,[22] producing fusion of vertebræ and calcification of the spinal ligaments at their attachments. Sclerosis of the bones in fluorosis is a characteristic distinguishing feature, and Steinberg et al.[23] found no excess of fluorine in the bones and soft tissues in a patient with ankylosing spondylitis. The intake of fluoride needed to produce these changes enormously exceeds the amount which could be derived from fluorinated drinking-water.

The diagnosis of ankylosing spondylitis is more difficult in women than in men, and sometimes involves the interpretation of the radiographic phenomenon of osteitis condensans ilii. This lesion, a triangular area of sclerosis in each ilium, with its base on the sacro-iliac joint, seems to be commoner in women, and to be associated with low back pains developing during pregnancy or the puerperium. Changes in the sacro-iliac joint itself are absent or inconspicuous. Thompson[24] reviewed 20 patients originally regarded as having osteitis condensans ilii, and concluded that 7 were actually suffering from ankylosing spondylitis. Like Tyson et al.,[25] he believed that ankylosing spondylitis occurs in a restricted or abortive form in women. In a very large number of patients treated with X rays Sharp and Easson[26] found that the response was distinctly better in typical cases of ankylosing spondylitis than in those with unusual features. The hands or feet were involved in 52.5% of "atypical" cases and in only 12.5% of the others. Tendinitis and tendon lesions were rare in the latter but were not uncommon in the atypical group. It seemed unlikely that the atypical group was composed largely of cases of rheumatoid arthritis, for the differential agglutination test was positive in only 12%.

From this atypical category Thomas[27] attempted to separate a group which were, he believed, examples of chronic arthritis due to repeated attacks of rheumatic fever. Recurrent severe attacks of pain in the back in these patients were readily relieved by salicylate. Some had changes in the peripheral joints of the type described by Jaccoud[28] and Bywaters[29] in rheumatic fever. Radiographically they showed very small erosions in the sacro-iliac joints, surrounded by spotty sclerosis, and in the spine irregularity and fusion of the interfacetal joints, narrowing of disc spaces, sometimes ossification within the discs and an increase in the height of vertebral bodies. Fusion of the sacro-iliac joints is fairly frequent in the arthritis associated with psoriasis and was commonly found by Birkin et al.[30] (together with the familiar high incidence of cervical spondylitis) in juvenile rheumatoid arthritis. Finally, ankylosing spondylitis, or something very like it, seems fairly common in non-specific urethritis.[31]

Treatment

Suggestive evidence that radiotherapy is not free from serious risk was published last year by Court Brown and Abbatt.[32] In a series of 9364 patients treated between 1940 and 1954, the observed deaths from leukæmia were at least five times, and possibly as much as ten times, the expected number (calculated from the male age-specific death-rate for leukæmia in England and Wales for 1953). The risk seemed to be greater if more than one course of treatment had been given. Court Brown and Abbatt quoted van Swaay's data on 7 patients who had died from leukæmia after X-ray treatment for spondylitis. There was some evidence that patients with ankylosing spondylitis may be unusually susceptible to leukæmia. On the basis of these findings, Court Brown and Abbatt concluded that it would be wrong to withhold X-ray treatment from those suffering from ankylosing spondylitis, but that treatment should not be given unless the diagnosis is unshakeable, and should be repeated only if absolutely necessary. Phenylbutazone has proved in many hands to be more effective in relieving pain in ankylosing spondylitis than in most other rheumatic diseases (except gout). This drug, too, has its hazards and in one series[33] produced toxic effects in 34% of cases, compelling its withdrawal in 6%. It should certainly be tried only if aspirin has been proved inadequate. Continuous treatment with corticotrophin was provisionally favoured by West and Newns[34] for those severely affected patients who received little benefit from radiotherapy. Adrenal stimulation should not be greater or maintained for longer than absolutely necessary. Immobilisation is rightly condemned nowadays as harmful, and prevention of crippling deformity is best achieved by prescribing a firm bed with a low pillow and the avoidance of prolonged stooping at work, or of heavy lifting with the spine flexed. Breathing exercises and extension exercises for the back are important measures. In severe cases with fixed kyphosis, spinal osteotomy[35 36] is occasionally indicated, and for badly affected hips the Batchelor operation has been helpful.[37]

The picture which emerges from Blumberg and Ragan's[1] study of the natural history of the disease warrants a more optimistic attitude than that induced by the exceptional case of severe deformity. In their words, "while the physical deformity and the confirmatory X-ray changes appear to proceed relentlessly with the passage of time, the manifestations of acute disease, i.e., the pain and E.S.R., are at their highest during the early phases and then decrease. The period of acute symptoms and signs is short, relative to the entire length of the disease. Systemic illness is not as common in this disease as in peripheral rheumatoid arthritis." In general, patients had an excellent occupational history. "The insulting agent, whatever it may be, does not appear to have a sustained effect, whereas the ankylosis of joints, presumably a reaction to the original insult, may take years to achieve completion. The patient is not placed in constant jeopardy of repeated devastating attacks which may lead to further acute injury to the joints (and viscera) as is commonly seen in peripheral rheumatoid arthritis." Very few patients were reduced to a bed and chair existence, and of 16 patients whose disease had been present for twenty-one to twenty-five years 13 were still in full employment.

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THE LANCET

LONDON SATURDAY MAY 26, 1956

A New Clinical Entity?

In 1917 von Economo[1] reported a small outbreak of an illness in which the main features were fever, stupor, and ophthalmoplegia 2 of his 13 patients died and at necropsy there was evidence of inflammation of the brain substance During the next two years a great many similar outbreaks were recorded and by 1921 the disease had reached epidemic proportions in almost every country in Europe[2] In spite of perplexing variations in the clinical picture from case to case locality to locality and even from season to season[2] it soon became clear that for practical purposes a new clinical entity had appeared[3] In 1924 5039 cases of encephalitis lethargica were notified in England and Wales alone,[4] but by the beginning of the next decade confirmed cases of this dangerous disease had become sporadic and by 1939 they were extremely rare[5] By the end of the late war, the centre of interest had shifted to poliomyelitis as by far the most prevalent and disabling infection of the nervous system The work of Ritchie Russell and others[6] focused attention on the importance of diagnosis in the pre-paralytic stage, and from other sources[7 8] there was evidence of a change in the epidemiology of poliomyelitis

Against this background of intense interest in poliomyelitis and its problems came reports of outbreaks[9–11] and isolated cases[12 13] which for one reason or another led to difficulties in diagnosis Broadly, these can be divided into those in which the cerebrospinal fluid (C S F) is abnormal and those in which it is normal Of the abnormal group (group I) only in the series described by Laurent[10] was no convincing causative organism isolated The conditions described by Kelleher[12] and Jennings[13] proved to be aberrant poliomyelitis and there was presumptive evidence of the same disease in the outbreak reported by Barrett[9] from Cambridgeshire in 1949 The Coxsackie group of viruses has also been implicated in this group[11 14] in such cases pleocytosis is the rule and signs of parenchymal damage to the nervous system are very uncommon Much more perplexing outbreaks are those in which no changes are found in the C S F (group II) Since we discussed these illnesses in 1954 under the non-committal title, Not Poliomyelitis[15] another epidemic with similar features has been reported from Durban[16 17] and two further outbreaks are described in this issue by Dr Sumner and by Dr Ramsay and Dr O Sullivan Only a brief description[18] has so far been published of the alarming outbreak at the Royal Free Hospital last year but there are arguments for including it in this group In none of these cases has it been possible to incriminate the poliomyelitis or Coxsackie virus, nor indeed has any other known infective agent been isolated

There seem good reasons in our present state of ignorance for placing in a third and intermediate group the epidemic which took place in Akureyri, Iceland, in the winter of 1948–49,[19] and about which Dr Sigurdsson and Dr Gudmundsson write on p 766 In all 8 cases examined the C S F was abnormal on the other hand the protracted course and mental symptoms described by Dr Sigurdsson are prominent symptoms in group II The outbreak in the nurses training school in the University of Pennsylvania in 1945[20] is also difficult to classify since it happened before the isolation of the Coxsackie viruses there was pleocytosis in 2 out of 5 cases The unusual epidemic reported by Wallis from Cumberland in 1955[21] has many features of group II —notably vertigo, diplopia, myalgia, cervical lymphadenopathy, and protracted convalescence with mental symptoms Unfortunately there is no information about the C S F The recorded atypical outbreaks can thus be grouped as follows

		Virus	*C S F*
Group I	Laurent[10] (1947)	Unknown	Usually abnormal
	Kelleher et al.[12] (1949)	Poliomyelitis	
	Curnen et al[11] (1949)	Coxsackie	
	Jennings et al[13] (1949)	Poliomyelitis	
	Barrett et al[9] (1952)	Poliomyelitis	
	Galpine and Macrae[14] (1953) and others	Coxsackie	
Group II	Adelaide[22] (1949)	Unknown	Normal in nearly all cases
	New York State[23] (1950)	Unknown	
	Middlesex Hospital[24] (1952)	Uncertain	
	Coventry[25] (1953)	Unknown	
	Berlin (1954) (Sumner)	Unknown	
	Durban[17] (1955)	Unknown	
	Royal Free Hospital[18] (1955)	Unknown	
	Hampstead (1955) (Ramsay and O Sullivan)	Unknown	
Group III	Pennsylvania[20] (1945)	Unknown	Abnormal 2 5
	Akureyri, Iceland[19] (1948)	Unknown	Abnormal 8 8
	Cumberland[21] (1955)	Unknown	Unknown

Of the 8 outbreaks in group II, all except that at the Royal Free were initially confused with polio-

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[22] Pellew R A A *Med J Aust* 1951 i 944
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[24] Acheson F D *Lancet* 1954 ii 1044
[25] Macrae A D Galpine J F *Ibid* p 350

Letters to the Editor

HOME CONFINEMENT

SIR,—May I, as a general practitioner, make a few comments in reply to Professor Russell's article in your issue of May 12?

I am surprised that he is so eager to increase the numbers of women admitted to hospital for confinement. To suggest that "normal midwifery only exists in retrospect" was no doubt purposely provocative, but this is unfortunately believed by many of our patients, and perhaps one of the important functions of the general practitioner is to explain to his expectant mothers that the processes of pregnancy and parturition are physiological rather than pathological.

Many primiparæ approach the time of delivery with a certain amount of understandable dread. This is not likely to be diminished by attending hospital clinics where they may not be seen by the same doctor or midwife on consecutive attendances. In the labour wards they are supervised by whoever happens to be on duty. It does not seem that the continuity which Professor Russell seeks is to be found here.

Professor Russell makes a passing reference to cross-infection in hospital. I think pædiatricians would agree that this is a very real problem in the care of the newborn in hospital: not only are these infections common but they are often caused by organisms resistant to all except the newer antibiotics. In my experience neonatal infections are rare in babies delivered at home.

The establishing of breast feeding is surely easier where the general practitioner is able to cooperate with the midwife. He will normally have a more detailed knowledge of the mother than has the hospital obstetrician. He should be more likely to anticipate the mother's worries and difficulties.

Professor Russell's suggestion that a general practitioner should not be allowed to attend delivery in the home seems to me particularly unattractive: if a general practitioner has not been trained to diagnose those emergencies and difficulties which require hospital treatment or specialist advice, then his training has been inadequate. Surely a doctor who is not aware of his limitations should not be practising at all.

I hope that these comments will help to justify the right of the general practitioners to continue practising obstetrics. Many patients will still need to be confined in hospitals or maternity homes on social grounds. Perhaps there is a strong case for increasing the number of beds available to general practitioners in maternity homes.

Bolton, Lancs. MICHAEL FASNACHT

SIR,—In your leading article of May 12 you reiterate the cliché that "if every [general] practitioner does only his own numerical share of obstetrics he will not have enough continuing experience to remain efficient." This is quite wrong. You should have written "if he deals only with that part of his share which is now left to him."

The ratio of general practitioners to births per annum is about 1 to 40 (and of practising midwives only 1 to 47). Four-fifths of pregnancies and labours are normal enough to be supervised by general practitioners. Any general practitioner who gives complete ante-, intra-, and post-natal care to 30 or more cases per annum will not only remain adequate in the type of obstetrics required in general practice, but will probably become more so.

Unfortunately many normal cases are delivered in specialist hospitals for a variety of peculiar reasons, and others are in the hands of self-reliant midwives. For the remainder the general practitioner is encouraged and paid to give only essential support to a midwives' service, and no more. Lack of experience and, when it exists, lack of interest are largely due to these limitations on the volume of general practitioner obstetrics; for, even under present conditions, only one general practitioner in six wishes to give up maternity work. Without these limitations, which are artificial, there would be no need for that artificial limitation of maternity practice—the obstetric list.

The service at present provided for "normal" cases is a midwives' service, supported by the general practitioner or the house-surgeon according to the place of delivery. It is a good service, but there is evidence that even better results can be obtained if there is closer cooperation between doctors and midwives, particularly at deliveries. To produce such a service, it is necessary to permit and encourage the practitioner to attend all his maternity cases, and to pay him to provide a complete service instead of a limited one.

If this were done your nostalgic picture of the family doctor and trusted friend bringing the son and heir into the world (or shall we say attending the delivery at which the midwife does so?) would not be anything like as unrealistic as you suggest. It is a vista greatly to be recommended to the committee now set up to inquire into the maternity services, for it has many advantages over the more impersonal arrangements. A maternity service based on the family doctor and local midwife working in close cooperation, with the specialist service at their disposal, is as likely as any to be that which best serves the interests of mother and child.

Gloucester. IVOR COOKSON

SIR,—I have read with interest Professor Russell's article. This is the latest in a long series by consultants in obstetrics which have sought to debase the general practitioner obstetrician.

In this district it is the usual practice for all primigravidæ to be delivered in hospital. In subsequent pregnancies some, if they have had a normal delivery the first time and prove to be progressing normally, are confined at home; others, if their medical and/or obstetric history dictates it, are confined in hospital. Such conditions as twin pregnancies and breech presentations are always referred to hospital. In this district also the local health authority allow the general practitioner obstetrician to do the antenatal work at the welfare centre, with the help of the health visitors, &c.

I myself do this and follow the antenatal session with an infant welfare clinic in which I see the babies routinely from about 14 days old to roughly 18 months. This, I find, adds to the interest of general practice enormously. At the first visit the expectant mother is examined fully, blood is taken for Wassermann reaction and ABO and Rh grouping, and arrangements are made for routine radiography of the chest. Relaxation and mothercraft classes are also held at the clinic, which each mother is encouraged to attend. So at first with monthly visits and later with weekly visits her health and the progress of her pregnancy are watched and her education is completed.

I agree that theoretically, from the purely obstetric viewpoint, it is desirable for every confinement to take place in hospital. There are, however, some objections, the gravest to my mind being the antibiotic-resistant bacterial population of every hospital, and the risk of infection—particularly infection of the newborn. I cannot see that the standard of antenatal care given by general practitioner obstetricians who are interested and keen is as low and as dangerous as is made out. I hope that it is not, as numbers of women will have to be confined at home for some years to come unless more money can be allotted for new building.

I agree that Professor Russell's students need not go into the home to learn the simple operative techniques that are all the general practitioner obstetrician should attempt, but having learnt them in the hospital let them harboured penicillin-resistant strains—twice as high an incidence as in 1954 In his article last week Dr Fairbrother concluded that one removable cause of the trouble was the habit of using penicillin indiscriminately for all forms of trivial infection His plea that "a stricter control of penicillin therapy is urgently required" will doubtless find many supporters, but it is probable that the only available control will be such self-control as doctors can bring themselves to exercise in their own use of penicillin and other antibiotics The arguments for such self-control have often enough been repeated in these columns the dangers of sensitisation of patients, of severe toxic reactions, of diminishing usefulness of antibiotics in serious infections, and of such grave superinfections with resistant organisms as, for example, an often fatal form of enterocolitis All these things have been said so often by so many writers that it is now becoming difficult to repeat these exhortations without wearying those who heed them

In this situation, however, it may still be worth commenting on some of the evidence about the adaptability and versatility of the staphylococcus Fairbrother, for example, now shows—contrary to what was at one time believed—that penicillin-sensitive and penicillin-resistant staphylococci isolated from the same lesion may quite often be of the same phage-type In 25 cases in which such pairs of staphylococci were isolated, the resistant and sensitive organisms were of the same phage-type in 11 Barber and Burston[29] regarded the penicillin-resistant organisms as the variant or mutant strains, but Fairbrother thinks it possible that *Staphylococcus aureus* formerly led a wild existence in which it produced penicillinase and that this function was later largely, but not entirely, lost by prolonged adaptation to the human nares This interpretation means that the penicillin-sensitive staphylococci are mutants derived from penicillinase-producing penicillin-resistant strains In support of this idea, Fairbrother found it easy to derive penicillin-sensitive variants from penicillin-resistant penicillinase-producing strains by growth at 44°C, but he was unable to accomplish the opposite change Fairbrother's speculation gains some added interest from Dr Phyllis Rountree's observations, which we also published last week, on the staphylococci harboured by the Wabaga, a primitive self-contained race inhabiting a remote part of New Guinea and thus isolated from outside contacts and so from antibiotics and those who might carry antibiotic-resistant organisms 23 of 120 Wabaga were nasal carriers of strains of *Staph aureus*, none of which was antibiotic-resistant Among 110 strains of non-pathogenic (coagulase-negative) staphylococci found in nasal swabs from the Wabaga, 87 conformed to Shaw et al's[30] definition of *Staph saprophyticus*, and of these, 6 were penicillinase-producers 2 of these strains were resistant also to chloramphenicol, 1 strain was resistant to streptomycin, chlortetracycline, and chloramphenicol, and 1 penicillin-sensitive strain was resistant to chlortetracycline Much experimental evidence is quoted by Eagle and Saz[31] in their authoritative review on antibiotics, all of it pointing, like Rountree's findings, to the conclusion that the antibiotic-resistant variants, now so common, are in fact preformed mutants which grow out selectively in the presence of the antibiotic The only difference between this and Fairbrother's view is that Fairbrother would regard such resistant forms as the begetters of the race which are being restored to their original position by our malpractices

True, we may derive some comfort from the fact that many bacteria are less able than the staphylococcus to produce resistant forms—a point stressed by Finland[32] in three recent papers on the emergence of antibiotic-resistant bacteria Thus, with penicillin we have no resistant forms of group-A hæmolytic streptococci, pneumococci, gonococci, or spirochætes It is probably true that tubercle bacilli and staphylococci create the greatest clinical problems so far posed by antibiotic-resistant forms of pathogens, but we must not forget the gradually increasing clinical importance of such naturally antibiotic-resistant genera as, for example, proteus pseudomonas, and aerobacter and of the non-hæmolytic streptococci and enterococci Against any comfort we may get from concluding that only a few genera of micro organisms are involved, we must set the evidence which suggests that staphylococci are responsible for an ever rising incidence of clinical infections of some severity in man In their article this week Dr Disney and his colleagues quote findings which, if they are of general application mean that any child of less than 2 years with clinical signs of pneumonia or of fluid has more than three chances to one of being infected with *Staph aureus* Among the staphylococci isolated by lung puncture from these infants, 20 strains were tested for sensitivity to antibiotics and 14 were found to be resistant to penicillin Moreover, on p 771 Dr Duncan Evans and Dr Myrddin Evans show that staphylococcal infection of the lower respiratory tract in adults may produce a severe and often fatal illness during influenza epidemics In these cases the cause of death appeared to be the rapid and abundant production of staphylococcus toxin in the lungs

Brodie et al[33] recently emphasised once again their view that in any particular hospital the important staphylococci may belong to only a few types carried in the noses of the staff In exactly such circumstances Rountree et al[34] report success in controlling neonatal staphylococcal infection by treating the noses of the staff with an ointment containing bacitracin and neomycin—a procedure following the method introduced by Gould and Allan,[35] whose choice of oxytetracycline, however, was in some ways less likely to be satisfactory for such a purpose Lepper[36] suggests nine methods of dealing with the problems we have discussed (1) combinations of drugs, (2) introduction of new drugs, (3) diminishing the use of a drug against which many resistant infections have appeared, (4) reduction in the use of all antibiotics to a minimum, (5) use of drugs of limited antibacterial spectrum and their use in their minimal suffering from repeated attacks of epilepsy and we were unaware of the history of head injury, the patient being admitted for investigation as a case of possible cerebral tumour The 5th patient was a young adult who again was decerebrate on admission

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[29] Barber M Burston J *Lancet* 1955 ii, 578
[30] Shaw C, Stitt J Cowan S T *J gen Microbiol* 1951, 5, 1010
[31] Eagle H Saz A K *Ann Rev Microbiol* 1955 9, 173
[32] Finland M *New Engl J Med* 1955 253 909, 969 1019
[33] Brodie, J, Sommerville T, Wilson, S G F *Brit med J* March 24, 1956 p 667
[34] Rountree, P M, Heseltine, M, Rheuben, J, Shearman, R P *Med J Aust* 1956 i, 528
[35] Gould, J C Allan, W S A *Lancet* 1954 ii 988
[36] Lepper M H *Arch intern Med* 1955, 43 299

As you point out, the development of unilateral fixation and dilatation of a pupil, although a valuable lateralising sign, is invariably a late sign and one of danger, indicating that speedy measures will have to be taken to relieve pressure on the brain stem

It is clearly impossible for all these cases to be saved, but I feel that a recovery-rate of 75% should be our aim When it is remembered that a tentorial pressure cone may develop and result in decerebrate rigidity within a matter of twenty to thirty minutes or less, then it is manifestly unwise to subject a patient suspected of suffering from this condition to an ambulance journey of perhaps fifty to sixty miles In its common form, this condition is one of the few surgical emergencies in which minutes really do count, and in my opinion these patients should be operated upon at the nearest hospital

Morriston Hospital
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NORMAN WHALLEY

PLASMINOGEN IN AGAMMAGLOBULINÆMIA

SIR,—It is well established that a proteolytic enzyme is present in normal blood in the form of an inert precursor, plasminogen, which is attached to the globulin fraction (Cohn fraction III 3) An inhibitor, plasmin, is present in excess in the albumin, and in the α_1 and α_2 globulin fractions

We have found repeatedly that plasminogen was associated with the γ globulin fraction, which was obtained by treating 0 4 ml of serum with 9 6 ml of saline ammonium sulphate The yield of γ globulin was estimated photo electrically using Weichselbaum's biuret reagent (90 g Rochelle salt in about 400 ml of $N/5$ NaOH, 10 g $CuSo_4 5H_2O$, 10 g pot iodide, made up to 2 litres with $N/5$ NaOH) The purity of this fraction was confirmed by paper electrophoresis

Recently in a woman with "agammaglobulinæmia" there was nearly complete absence of γ globulin and comparatively normal levels of albumin and α_1 and α_2 globulin fractions Despite this, normal proteolytic activity of serum was observed on activation by streptokinase

Department of Pathology,
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E WILDER
R S PARSONS

MEDICINES FOR HOSPITAL OUTPATIENTS

SIR,—After being seen at an outpatient clinic of one of London's children's hospitals a mother collected from the dispensary a bottle of over one hundred capsules for her child The child was unable to swallow these and the mother asked me whether she should destroy them in case they were dangerous There was no indication on the bottle of the nature of the capsules but after much inquiry I was informed that they were an antibiotic preparation—cost, nearly twenty pounds Luckily in this case I was able to prescribe a more suitable form of the antibiotic for the child and to return the capsules to the hospital With a perhaps less intelligent mother, the twenty pounds' worth of medicine might well have gone down the drain

This experience is not an isolated one, by any means Is it really necessary for hospitals to supply medicines to their outpatients? Would it not cause less strain on short staffed hospital dispensaries, be more helpful to patients and their family doctors, and be much less wasteful if hospitals confined their prescribing to in-patients? For outpatients a short note to the family doctor suggesting the treatment required is surely the procedure of choice

St Mary Cray, Kent

E TUCKMAN

MENTAL DEFECT AND HYPSARRHYTHMIA

SIR,—I am distressed to find sectarian jargon appearing in one of your annotations Under the above title in your issue of April 28 I read that "the children had salaam attacks," and that "Ounsted has shown that the phenotypic expression of the convulsive genotype is rapidly overcome by maturation" It is often difficult to understand the many papers which have been written jointly by three or four workers in different fields, and your more simple readers look to the annotations for clear explanation and comment

St Mary's Hospital
London, W 2

R G HOWELL

G M C ELECTION

SIR,—I was very glad to read the letter from Dr Whiteside and Dr Dillon (May 12) I completely agree with them about the evils of an electoral procedure which allows pressure groups to keep independent candidates out of the G M.C

The B M A sent to the profession at large a card urging it to poll for seven names No mention was made of the two other candidates, and, if this card did not create the impression that no more than seven existed, it certainly helped to exclude the two youngest Not content with influencing its own members, the B M A made it a self appointed obligation to canvass tho that stay out of the association

I voted for Dr Whiteside and Dr Dillon to the exclusion of the B M.A nominees I hope that at the next election the B M A will show more tact, and perhaps, then, young unsponsored candidates will be more successful

Thames Ditton, Surrey

L R CHRISTIN

BACTERIAL RODENTICIDES

SIR,—Dr Taylor's article (May 5) provides useful reading on laboratory findings, and controversial opinions on rodent control economic practice

The article details objectionable methods never or no longer used in this country It is well established in practice that, under proper safeguards, the use of bacterial cultures of the right kind is a safe and important contribution to the war against rodents, themselves of much greater danger to mankind

Statutory Rules and Orders made it obligatory from Oct 1, 1945, that—inter alia—no liquid virus should enter into retail trade, and no *Salmonella enteritidis* var *jena* should be manufactured No case is recorded by Dr Taylor of human illness attributed to anti rodent virus up to the time when those Orders were revoked in 1950

In 1951 the Working Party on Toxic Chemicals was asked to investigate rodenticides—including virus The working party reported in 1953 The Ministers of Agriculture, Food, and Health and the Secretary of State for Scotland considered the recommendations in this report, and after consulting the trading interests affected announced—via the Minister of Agriculture—that the firms had agreed to collaborate with the Departments, "it being borne in mind that these preparation which are not on sale to the general public have been in use on a considerable scale for many years" It was recorded that of the four specific recommendations made two were already in current practice, and the remaining two were accepted with minor modifications The future collaboration envisaged was as to the adequacy of the agreed safeguards in practice Since these arrangements were made no untoward incident has been brought to notice

Table III of Dr Taylor's article refers to jena having been isolated in 1948–49 No human illness was involved The firm concerned supplied voluntarily to

Annotations

PREVENTION OF INDUSTRIAL ACCIDENTS

Of some 7 million workers employed in factories in this country over 450 are killed and about 160 000 injured each year. In addition over 250 workers are killed and more than 20,000 injured in workplaces other than factories subject to the Factories Acts. Though these figures are lower than the toll of accidents on the roads and in the home they have far-reaching social and economic consequences—and all are preventable. In its recently published report,[1] the industrial safety subcommittee of the National Joint Advisory Council reviews the whole subject of industrial accidents and makes important recommendations for future action. The National Joint Advisory Council comprises representatives of the British Employers' Confederation, the Trades Union Congress, and the boards of nationalised industries under the chairmanship of the Minister of Labour and National Service, and it advises the Government on matters in which employers and workers have a common interest. The recommendations should therefore carry great weight with both sides of industry.

Accident prevention is not new, because the Factory Department and voluntary organisations have paid close attention to it for many years. The subcommittee has, in fact, nothing very original to say on the subject, but it describes how organised action in this field developed out of common law relating to masters and servants and out of statutory protective legislation. In the first place, it was concentrated more on the provision and maintenance of safe physical working conditions than on the human side of accident prevention. This is true even today, and the subcommittee, by implication, does not seem to think that the medical profession (though naturally it has to deal with the results of accidents) has a large part to play in accident prevention. The report points out that most accidents arise from ordinary everyday causes such as handling goods, using hand-tools, or falls; in nearly all cases there is some failure of the human element. No reference is made to the fact that doctors could give much greater assistance than they are at present called upon to do. Admittedly, the subcommittee says that team-work and coöperation are essential "first of all in the workplaces between employers and workers, and between industry and the Factory Department, research organisations, voluntary organisations, teaching bodies and many others such as architects and doctors." But it seems that the emphasis is a little out of perspective.

The subcommittee's recommendations in general constitute a plea for more of everything except accidents. Both employers and workers should take more interest in the subject, and accident prevention should not be subordinate to production; there should be more safety officers and works safety committees and more training of workers, especially of young workers. Firms should insist upon getting premises and plant with "built-in" safety. Full use should be made of available knowledge and experience in the works and as necessary information and advice should be sought from outside the works—in particular from Her Majesty's inspectors of factories, the Factory Department publications, the Industrial Health and Welfare Centre, industrial organisations, specialist firms and consultants, and voluntary organisations.

Hitherto industrial research organisations have usually concentrated on production problems, and it is hoped that safety research will now be accepted as a function of these organisations. Voluntary organisations such as the Royal Society for the Prevention of Accidents, should continue to develop opportunities for the exchange of information and experience, and arrangements for the dissemination of information and publicity material. The subcommittee thinks that, though the official Factory Department publications are excellent within limited fields, they are inadequate both in kind and range. As well as more technical papers for specialists there is a great need for relatively brief and practical publications for employers and workers. The report recommends the production of films about safety in industry (though the present Government policy precludes direct expenditure of public funds on the production of such films), and arrangements are encouraged whereby such films could be made widely available through the Central Film Library.

In the matter of training, the education departments, local education authorities, colleges, and schools should examine the possibility of further developing safety-training as a part of general education. For this purpose there should be liaison between the schools and colleges, industry, H.M. inspectors of schools, and H.M. inspectors of factories. Another point in the report is that the Factory Department should intensify its work on accident prevention with which it has been concerned for more than a hundred years, and the subcommittee comments on the future rôle of the department in the light of its recommendations. The contribution of the inspectorate will be no less important in the future than it has been in the past, both in its enforcement functions and in the advisory work which often arises out of enforcement. As industry shows itself capable of achieving higher standards, it is hoped that there will be a further shift of emphasis in the work of the inspectorate from enforcement of the law to the giving of advice. It is important, however, that the standards of inspection should be high, and that the number of qualified inspectors should be maintained and increased as necessary.

Finally, the report urges that all concerned should examine afresh every possible means of helping to promote higher standards of safety in industry, both directly and indirectly, and take the opportunities they have to increase their contribution. A standing national committee, including representatives of Government and industry, should be established to keep under constant review all aspects of industrial safety, including research.

CHONDROMALACIA OF THE PATELLA

Fissuring and flaking of the articular cartilage of the patella (chondromalacia) is one of the commonest forms of degenerative change seen in joints. Owre,[1] in a series of post-mortem examinations, found these changes mostly in persons over the age of 20, but they are relatively rarely associated with symptoms. Since it seems that nearly all adult knees show changes of this type, it is hard to assess the natural course of the condition. The cases studied by Karlson[2] suggest that chondromalacia, even when associated with symptoms referable to the knee, does not necessarily progress. Of 71 patients treated conservatively, only 20% were substantially disabled by the knee. Arthritis deformans seemed to be a relatively uncommon development, and in this series it was never severe.

Chondromalacia of the patella begins as a nodular swelling of the articular cartilage, which becomes opaque. The lesion is localised and is associated with a decrease in the condroitin-sulphate content. Fissuring and flaking may follow later, and may involve the whole articular surface. The flaking often produces scales which may result in cartilaginous loose bodies. Marginal osteophytes can later develop and the femoral condyles occasionally show "mirror" lesions.

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[1] Industrial Accident Prevention. Report of the Industrial Safety Sub-Committee of the National Joint Advisory Council. H.M. Stationery Office. Pp. 36. 1s. 6d.

[1] Owre, A. *Acta chir. scand.* 1936, 77, suppl. 41.

[2] Karlson, S. *Ibid*, 1940, 83, 347.

observation was being made Perhaps the plump male or postpartum female who goes on a diet of apples is in as much danger as those of us who over eat modern foodstuffs (innocently being starved of some essential food factor) I have been assured (without reference) that the cholesterol in the bile of the starved is increased

The rise in the incidence of hospital cholelithiasis in Scandinavia is staggering, the disease appears to be more fulminating than in this country In Gothenburg in the main hospital nearly 1000 gall bladders were removed in 1954 (pre-war about 200) Clinical talk has it that the increase in the disease started in Finland after the war, the intensity is now maintained all over Scandinavia While I have had (without any facts) suspicions concerning manufactured foods such as margarine for some time, I was intrigued to see the powerful research machines in these centres being turned towards this very subject Sjovall is studying the effects that diet has on the metabolism by the liver of cholesterol and bile salts [4] (Scandinavia, by the way, lives on margarine, the butter being exported)

It may well turn out that starvation (including the essential fatty acids) and overfeeding in the fully grown (including the wrong fatty acids) are equally dangerous to our welfare We must aim for unadulterated freshness in food and guard against excess of any kind This may be the unthinkable answer, so we must spend fortunes and many lives to prove it, and when the pudding is done, who will want to eat it ? Perhaps the most that will happen will be a sudden increase in pamphlets and wealth of pharmaceutical firms turning out essential food factors (alas for medicine and the patients—they have jumped the gun already !)

This letter may be considered threadbare and no windbreak to the gusts which rush and flutter around Dr Sinclair's edifice, yet threads there are, and strong

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A J H Rains

Sir,—I was glad to see in your issue of May 12 the widening response to your leader of April 28

Since my previous letter appeared (May 12), Prof H Malmros has kindly sent me samples of the artificial milk used in his experiments, in which a considerable amount of corn oil is incorporated I am glad to find that it has a very pleasant taste, and I hope that food manufacturers in this country will soon market similar products, including cheese and ice cream

London, W 1

Z A Leitner

OBSERVER ERROR

Sir,—In the report of their investigation of observer error in M M R film readings Dr Eley and Dr Paxon (April 21) are not justified in their conclusion that "the number of truly active cases missed by A was around 5% and by B 7%" They derive this conclusion from their observation that Dr A missed 8 5% and Dr B 13 5% of all cases, and the presumption that only half of these would be active, for they have halved the numerator of the equation

$$\frac{\text{Total cases missed}}{\text{Total cases}}$$

but left the denominator alone In the experiment of Yerushalmy et al, to which they refer, the proportion of sputum positive cases missed was greater (42 5%) than the proportion of inactive cases missed (30%) The same was true of "active" cases in the investigation by Clayson et al [5] and may well be true of the cases in their own experiment—or it may not The case against the importance of observer error cannot be made by faulty arithmetical manipulation A follow up of the cases could provide a correct assessment of the proportion of active and sputum-positive cases missed

Dr Eley and Dr Paxon have only shown the amount of error between two readers (who may happen to have had very similar methods and abilities) Yerushalmy et al took great care to ensure that their "positive cases" were all the undoubted positives agreed upon by ten readers in consultation Among the 10,000 films read by Drs A and B there may have been some positives which they both missed and which are not included in their "error" In this sort of work the size of the sample of readers is as important as that of the sample of films that is read

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C M Fletcher

A SHORT WAY WITH *TÆNIA SAGINATA*

Sir,—Dichlorophen (2 2′-dihydroxy-5 5′ dichloro diphenyl methane) a white, almost tasteless solid, is an established veterinary remedy for *tæniasis* of dogs and cats Its action differs from that of other tænifuges in that it has a direct lethal effect upon the worms which after being killed, are subjected to the digestive process of the intestinal secretion, so that the parasite is evacuated in a hardly recognisable state

The earliest reference to its veterinary use is in a careful paper by Craige and Kleckner,[1] in which they reported success rates, in dogs infected with *Tænia pisiformis* and *Dipylidium caninum*, of 75% with doses of 50–100 mg per kg body-weight and of 90% with a dose of 200 mg per kg They investigated the mode of action of the drug by examining dogs killed at various intervals after dosage, and found that after thirty to forty minutes the tapeworms were detached from the intestinal wall and were passing along the ileum After two hours the worms were in the colon and were markedly degenerate The minimum lethal dose for dogs lies between 2 and 3 g per kg body weight

The results obtained in the first six cases of *T saginata* infection I treated by this remedy were as follows

Case no	*Dose (g)*	*Result at 16 weeks*
1	6	Cured
2	3	Recurrence *after 10 weeks*
3	4 5	Cured
4	6	Recurrence *after 11 weeks*
5	2	Cured
6	6	Cured

Each of these patients was admitted to hospital for convenience of observation No preliminary starvation or subsequent purgation was used The dose—0 5 g per 16 lb (7 25 kg) body weight—was given, all at once, at about 10 A M After two or three hours most of the patients experienced mild colicky pains and passed two or three loose motions These were carefully examined, but nothing of the worms could be found except varying numbers of more or less disintegrated mature segments It was not possible, therefore, at the time of treatment to know whether the scolex had been destroyed and the patient cured *T saginata* takes not more than twelve weeks to grow from a scolex to the point where the host begins to pass segments The patients were therefore followed up for at least sixteen weeks

The cure rate in this small series of cases is reasonably satisfactory The explanation of the two failures may be that, because of the drug's laxative action its contact with the scolex was too fleeting for its lethal effect to operate It may well be that by giving repeated smaller doses over a period of twenty four to thirty six hours a more certain action will result, and I have lately tried the effect of giving a total dose of 6 g in three equal amounts at intervals of twelve hours anxious persons should be associated with an increase in finger pulse-volume, whereas untroubled patients, or normal people, would show no such change. The findings showed that the three groups studied differed significantly both in the size of the pulse volume during the resting state and in the increase in pulse-volume during sleep. The increase in finger pulse-volume in the anxious patients clearly distinguished them from the other two groups. The findings therefore indicate that anxiety is associated with an increased level of peripheral vasomotor activity.

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[4] Sjovall J Ekdahl P H *Ibid* 1955, 34 2
[5] Clayson C Lees H W O McIntosh D G McWhirter J G McKinlay P L Stein L *Brit J Tuberc* 1955 49 81

[1] Craige A H Kleckner A L N *Amer Vet* 1946 27 [illegible]

Other somatic manifestations of anxiety—tachycardia, increased blood-pressure and respiration-rate, and changes of skin electrical resistance—were found to be unreliable as measurable indications of anxiety. Further work may indicate whether the degree of anxiety is related to the amount of pulse-volume change as sleep ensues; if it does so, then we would have an objective method of assessing the degree of anxiety at different times in any one patient. It is very unlikely that the method could be used to assess by how much the degree of anxiety in one patient differs from that in another.

After this good beginning, standards are not quite so high in the other papers in this new journal. If the "narrow factual basis" of psychosomatic research is to be widened, somatic manifestations and psychological disorders must both be clearly defined and described in specific terms. "Mixed neurosis," "social inadequacy," "neurodermatosis" or "-itis," and "social isolation" are not precise terms. Control groups must be impartially investigated, and the tests used must be such that, when they are repeated in the same subject, the difference is less than the differences between normal and abnormal subjects. It seems likely that secure progress cannot be made in psychosomatic medicine until a better knowledge of psychosomatic physiology is available. Psychosomatic research needs the work of investigators comparable to Harvey, Claude Bernard, Starling, Dale, and Lewis, and one of the new journal's aims will be to encourage this fundamental work.

CAROTID THROMBOSIS IN THE YOUNG

SEEMINGLY spontaneous carotid thrombosis in the young adult has been known as a rarity for fifty years or more. Carotid angiography has more recently uncovered a surprising number of such cases. The finding poses afresh the problem of ætiology, because the usual degenerative factors held to contribute to thrombosis do not apply at this age. A few thromboses can be clearly classified as traumatic. Blows to the neck in boxing, for instance, may occasionally be responsible; the nature of the local injury and the timing of symptoms leave little doubt about the causal link. In one or two cases the circumstances suggest that some upset in water or electrolyte balance is the cause. Thrombo-angiitis obliterans and giant-celled arteritis are uncommon in any form, and even rarer as a cause of carotid obstruction. Ill-defined constitutional factors, such as operate in families more than usually susceptible to thrombosis in general, presumably play a part; but in most cases the cause and even the occasion remain obscure.

In 1942 Cairns[1] first suggested the possibility that damage to the carotid at some distance from the site of blockage may start a local thrombosis which then extends spontaneously. He described a closed head injury with thrombosis at the carotid syphon. Sedzimir[2] reconsidered the matter recently and gave details of 6 cases in which blunt injury to the head seemed to precipitate carotid thrombosis, starting intracranially and spreading down into the neck. In the 4 cases where the diagnosis was confirmed by necropsy or angiography the injury was frontal. In 1 there was an associated atheroma which probably contributed to the thrombosis. In all 4 some time elapsed between injury and the onset of signs of thrombosis, and in 2 this amounted to several days. Some of these cases undoubtedly confirm the view that head injury may initiate a spreading carotid thrombosis. Such a cause must therefore be carefully considered in apparently spontaneous carotid thrombosis in the young. The relationship may the more easily be missed since not all the recorded cases had severe head injuries and there was a variable interval between the trauma and its effects. At a time when thrombotic disease seems to be on the increase, any information about the factors causing or favouring its production has a general interest and application.

SYNTHETIC ARTERIES

THE replacement of diseased or blocked arteries by human homografts is undoubtedly one of the major surgical triumphs of recent years. Large series of successful transplants in the distal aorta have been recorded by DeBakey and Cooley[1] and Bahnson[2]; more recently Holmes Sellors[3] has described 3 patients with coarctation of the aorta associated with a proximal aneurysm in which both lesions were resected en bloc and continuity restored by an arterial graft. We recently suggested[4] that the by-pass operation for femoral-artery blocks holds great promise. Admittedly, despite many experiments with the preservation and sterilisation of homologous vessels, there remain many objections to their use. It is not always easy to obtain a sufficient number and range of young homologous aortas or smaller arteries, and their sterility may be difficult to ensure. Freeze-dried or quick-frozen arteries are non-viable and depend essentially on their elastic fibres to prevent the dilatation and disruption which is occasionally reported.[5,6] Even so, the results of homologous arterial transplantation are good, although sufficient complications and difficulties have been described to make safer replacements desirable.

Blakemore et al. suggested[7] that fabric tubes might be used as an alternative, and they later demonstrated that 'Vinyon N' cloth, folded and stitched longitudinally in a tube, was in fact capable of acting as a scaffolding for the ingrowth of fibroblasts. Many technical questions immediately presented themselves, some of which are gradually being answered. Impermeable tubes are less satisfactory than a mesh weave which allows fibroblastic ingrowth for the surrounding host tissue to form a new intima; but if the mesh is too big, with holes of larger than 50–100 μ, then there may be uncontrollable and fatal oozing through the wall.[8] Hufnagel[9] used 'Orlon' and 'Dacron' cloth because their water-repellent qualities limit this type of bleeding; others have used 'Ivalon' sponge and polyvinyl sheets. A serious objection to all fabric grafts is the possibility of kinking with subsequent clotting if the insert material is too long or if the graft crosses a flexion area such as the groin, axilla, or popliteal space. To overcome this "wrinkle" thrombosis Edwards and Tapp[10] have experimented with crimped or "concertinaed" nylon tubes, which are treated with silicone to discourage bleeding through the open mesh. This design has the advantage of allowing the graft to take up slack and pass round sharp angles without wrinkling. The rough corrugated inner surface to the crimped tubes causes much turbulence in the blood-flow; but although one might suspect that this would encourage postoperative clotting, this was not in fact so, even with tubes of a diameter of 0.5 cm.

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[2] Bahnson, H. T. *Ibid*, 1953, 138, 377.
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[5] Brock, R. C. *Guy's Hosp. Rep.* 1953, 102, 203.
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[8] Wesolowski, S. A., Sauvage, L. R. *Ibid*, 1956, 143, 65.
[9] Quoted by Edwards and Tapp (ref. 10).
[10] Edwards, W. S., Tapp, J. S. *Surgery*, 1955, 38, 61.

A little solemn, I thought—but then, of course, you were addressing a man old enough to be your father

The plain truth is that I must not make a virtue of necessity I retire at sixty-five, and that's that I am not a special case Thanks all the same for your friendly advice which I shall try humbly to follow It has been such fun since you wrote

Yours truly,
J M MACKINTOSH

Parliament

Capital Punishment

ON the committee stage of the Death Penalty (Abolition) Bill in the House of Commons on May 16 an amendment, moved by Sir Hugh Lucas-Tooth, a former under-secretary to the Home Office, providing for the retention of the death penalty where murder is committed by prisoners already serving a life sentence, was carried by 4 votes—198 to 194 The amendment was supported by Major GWILYM LLOYD-GEORGE, the Home Secretary, who said that Parliament had already thought it right to protect prison staffs against attack falling short of murder by preserving corporal punishment for offences of this kind It seemed right that prison staffs should have analogous protection against attacks that killed Mr SYDNEY SILVERMAN, the promoter of the Bill, described the amendment as the greatest nonsense in the world What he asked, had this to do with an offence which everybody conceded had never happened in living memory in any country? The committee were being asked to retain the death penalty, with all its solemnity of the gallows, the black cap, and the rest, for a purely imaginary danger

QUESTION TIME

Nutritive Value of Flour

Replying to a question, Mr D H AMORY, Minister of Agriculture, Fisheries and Food, said that the main conclusion of the Panel on the Composition and Nutritive Value of Flour was that the available evidence did not reveal any ascertainable difference between National flour as defined in the Flour Order, 1953, and flours of extraction rate less than National flour, to which vitamin B, nicotinic acid, and iron had been restored in the amounts specified in the Flour Order, 1953, which would significantly affect the health of the population in any foreseeable circumstances

The Government had decided to accept this conclusion as a basis for action The present Flour Order provided for the restoration of the three nutrients to all flour of an extraction rate below 80%, and to that extent was already in accordance with the main recommendation of the panel This Order would continue in force until the bread subsidy was abolished on Sept 29, 1956, when it was proposed to replace it by regulation under the Food and Drugs Act, 1955, and corresponding Scottish legislation, providing that all flour should contain not less vitamin B_1, nicotinic acid, and iron than the quantities laid down in the present Flour Order

The Government had decided to invite the Food Standards Committee to consider whether, in addition to requirements as to the content in flour of vitamin B_1 nicotinic acid, and iron, more extensive regulations governing the composition of flour and bread were needed to protect the consumer

Advice on Smoking

Replying to a question, Sir DAVID ECCLES, Minister of Education, said that a new edition of the Ministry's handbook on health education, containing suggestions for teachers, to be published shortly, would include a passage regarding advice to school children of the dangers associated with smoking

School Milk

Replying to a question Mr DENNIS VOSPER, parliamentary secretary to the Ministry of Education said that most pupils taking school milk at weekends were at independent boarding schools Very few children from other schools attended the special centres open on Saturdays and during holidays, and these centres were expensive to administer There was no good reason why pupils in nursery schools should have a larger allowance than pupils under five in nursery classes and ordinary classes

N H S Working Parties and Committees

In answer to a question, Mr R H TURTON, Minister of Health, gave the following list of working parties and committees due to report on the National Health Service

Mileage Committee —A report is in draft

Committee of Inquiry on the Rehabilitation of Disabled Persons —Report is expected later this year

Working Party on the Recruitment and Training of Health Visitors —Report has been received and will be published shortly

Committee on Hospital Supplies —An interim report is expected in June

Joint Subcommittee on the Control of Dangerous Drugs and Poisons in Hospitals —Report is expected before the end of the year

Study Group on Maintenance of Building Plant and Grounds —Report is expected shortly

Committee on Medical Manpower —Not yet known

Committee on Recruitment to the Dental Profession —Report is expected this summer

Working Party on Social Workers —Not yet known

Study Group on Application of Electronic Devices to Hospital Accounts and Costing —Not yet known

Committee on Maternity Services —Not yet known

Obituary

JOAN GRAEME MALLESON

M B Lond

THE news of the death of Dr Joan Malleson in a drowning accident in Fiji on May 15 was received in London last week To her work at University College Hospital and for the Family Planning Association and to her writing and broadcasting, she brought a clear unprejudiced mind and a ready yet discerning sympathy

Joan Billson was born at Leicester in 1900 and educated at Bedales, where she was head girl She qualified from Charing Cross Hospital in 1925, and after holding a house-appointment there she became medical officer to the comprehensive clinic at Holborn and later clinical assistant at the West End Hospital for Nervous Diseases Her experience in these posts and in the general practice which she ran for a number of years with the late Cecile Booysen convinced her that much of her patients mental and physical ill health was caused by sexual difficulties due to ignorance She believed that health education on marriage and the special problems of women would be the most useful contribution she could make to medicine, and her success in this work led her gradually to give up her general practice to spend all her time in this specialty Outside her consultant practice she was medical officer to the clinic for sexual difficulties of the Islington Women's Welfare Centre, and to the dyspareunia clinic at the obstetric unit of University College Hospital As a member of the executive committee of the Family Planning Association she gave evidence to the Royal Commission on Population and started the association's seminological centre She also wrote many of their pamphlets Under the pseudonym of "Medica" she wrote books addressed to women and married couples, notably *Change of Life* and *Any Wife or Any Husband*, and she gave an excellent series of talks in *Woman's Hour* on the problems of the menopause Her contributions to scientific journals included a paper in our columns in 1951 in which she suggested that in many affective disorders there were remediable endocrine factors For some years she had continued to work despite ill health, and last January she sought recuperation in an exchange of practice with a New Zealand woman doctor She was on her way home from this successful experiment, of which she had lately written cheerfully and happily to friends in this country

M C N J writes

'More than thirty years ago Joan Malleson and I—Joan Billson as she was then—were fellow students at University College in Gower Street, but we subsequently went to different hospitals and did not meet again for many years by which time we were both wives and mothers and back in medical practice Joan was in partnership with that forthright pacifist Cecile Booysen, by whom she was greatly influenced and to whom she was devoted Cecile's untimely and tragic death was a great blow to Joan and left a gap in her life which was never quite filled Not long afterwards she gave up general practice for consultant work of a kind in which her great gifts of sympathy and gentleness brought untold comfort to the many couples who came to her with their marital

Public Health

THE WORK OF A CHEST CLINIC

R. GRENVILLE-MATHERS
M.A., M.D. Camb., M.R.C.P.E., F.R.F.P.S.
MARGARET SHELDON
M.B. Lond
PHYSICIANS, HARROW CHEST CLINIC, MIDDLESEX

THE work of any institution must depend primarily on the demands made on it We therefore attempt here to describe the work of a chest clinic from the organisation of a particular clinic and from all the new cases seen there in 1954, in much the same way as has been done by Avery Jones (1953) for a regional hospital and by Gibson (1955) for a geriatric unit In this way, we hope, a composite picture of the function of the various units of the health service will gradually be painted

Patients

The patients seen in a chest clinic can be succinctly divided into tuberculous and non-tuberculous The chest clinic since 1948 has seen two simultaneous processes (1) a decrease in responsibility for non respiratory cases of tuberculosis (although contacts and other environmental factors are still dealt with), and (2) an increase in the number of patients with respiratory symptoms from any cause referred to the clinic The increase in the latter has greatly exceeded the decrease in the former

TABLE I—INCREASE IN NUMBER OF PATIENTS SEEN FROM 1950 TO 1954

—	1950	1952	1954
New patients referred to clinic	2264	5846	8496
No of persons radiographed	8121	13 813	18 877
No of X ray examinations (units)	21 612	29 917	39 285
Sessions held	988	1420	1630

Table I shows the increase in numbers referred to the clinic from 1950 to 1954 (when the attendances numbered 31,066)

Equipment

Since the chest clinic is increasingly being regarded as an outpatient department dealing with all respiratory diseases, it is usually equipped to deal with such diseases Thus, the building of the Harrow clinic, which serves a population of about 225,000 consists of a waiting-room, 18 dressing-cubicles, 3 consulting-rooms, and rooms for the radiological department general clerical staff almoner, health visitors, clinical investigations, and records

Radiography now plays a vital part in chest work, and the clinic has a four valve set with rotating anode tube, a tilting couch with tomographic attachment, and an 'Odelca' mirror camera for miniature radiography, Placed between two of the consulting rooms and accessible from each is a screening-room containing a separate X-ray screen, so that films of the patient can be supplemented by screening when necessary

The clinic also has spirometers for testing respiratory function and an electrocardiogram for differential diagnosis

Staff

The clinic staff consists of a medical team comprising a whole time consultant physician, assistant physician, registrar, and two part-time assistant physicians who between them hold five sessions a week in the clinic The whole time medical staff are also responsible for the ward care of patients in the associated hospitals, Edgware General and Colindale The remainder of the clinic staff consists of one whole-time radiographer, one part-time radiographer, a dark-room assistant, a trained almoner, four health visitors, an administrative officer, two medical secretaries, four other clerks, and a receptionist

Referral of Patients

Patients seen and examined by the medical staff may be referred by direct appointment by their general practitioners or come via the "X ray only" sessions (Trenchard and Grenville Mathers 1952) General practitioners are naturally reluctant to refer patients to a consultant for an opinion where respiratory symptoms are minimal or of short duration, but they welcome the opportunity for having a chest radiograph taken of the patient without the necessity for making an appointment

These radiographic sessions are held daily and usually last thirty to forty-five minutes Two views are taken of each patient with an odelca camera producing an image measuring 70 × 70 mm The films are read the following day, and a report is posted to the general practitioner Where abnormalities are seen an appointment is sent to the patient, and the referring practitioner is notified accordingly

This latter system of reference to the chest clinic, originally started as an auxiliary system, has now become the principal way by which patients are referred and is particularly valuable in detecting early cases of respiratory tuberculosis and bronchial carcinoma Thus, in 1954, only 280 patients were referred direct by their general practitioners, whereas 6041 were first sent to the "X-ray only" session

Whereas the mass miniature radiography units are now finding only 2 cases of pulmonary tuberculosis per 1000 adults radiographed, this session in 1954 yielded 17 cases of pulmonary tuberculosis, and 5 cases of bronchial carcinoma per 1000 adults radiographed, with an incidence of 62 per 1000 in men aged more than 45

In addition to the above methods of reference patients are seen in domiciliary consultation at the request of the practitioner In view, however, of the need for a chest radiograph in many of the latter patients, the practitioner concerned often arranges by telephone for the patient to attend the clinic by ambulance and stretcher

Such a system of working means that the work of seeing patients for the first time is quite onerous because the great majority have already been through a radiographic sieve and therefore usually have some definite radiographic abnormality

Other patients seen for the first time in the clinic include those referred by the directors of the mass miniature radiography units (56 patients in 1954) and those referred by colleagues in other departments

The full radiographic facilities of the clinic are also used for routine chest radiographs—e g, pre employment radiographs of management committee staff, annual radiographs of nurses, and radiographs of school entrants found to be tuberculin-positive At the request of the school medical department tuberculin testing of children is also done in addition to the routine tuberculin testing of all children referred to the clinic for the first time by general practitioners and school medical officers

New Cases in 1954

1602 new cases received full clinical and radiographic investigation in 1954 in addition to 965 new contacts of tuberculous patients Table II shows that 8496 patients were originally referred to the clinic and the number in each category of reference requiring to be recalled to the clinic for further examination The various diagnoses made in the 1602 recalled cases can be seen in table III, which shows a large group of unclassified cases, mostly in children The children were mainly referred for an opinion after a respiratory infection during the course of a specific fever Many of the adults in this most capable and intelligent young people Yet farming is an interesting, though hazardous, life Nature still largely governs the growth of crops and animals frost and tempest, drought and floods, inflict heavy loss, diseases and pests attack plants and animals Natural hazards are always upsetting the farmer's plans, and on occasion may ruin him They have not been and probably never will be controlled as closely as manufacturers can control their output The biological processes of gestation, birth, growth, and maturation take a long time, and crops and livestock production cannot be suddenly turned or stopped to meet market changes Farming is more than an occupation it is a family enterprise and a mode of life, which cannot be rapidly adapted

As this F A O booklet points out, farming and industry are not essentially in competition They are indeed partners In nearly every country, if industrial incomes are high, so are farm incomes, but, when industrial incomes are low, farm incomes are lower But whether a country be rich or poor, agriculture does not receive a "fair" share of national income If agriculture is to keep pace with the growth of increasing industrial populations, it must have both financial capital and intelligent leadership for its development

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University of Cambridge

On May 12 the following degrees were conferred

M D—B A J Chodak Gregory R G Orr, C M B Pare, Matthew Wilkinson

M Chir—P F Jones

University of London

On Nov 23 the hon degree of LL D will be conferred on Sir Harold Himsworth

Mr J H Birkinshaw, D SC, reader in biochemistry at the London School of Hygiene and Tropical Medicine, has been appointed to the university chair of biochemistry at the *school* Dr B S Cardell, senior lecturer in morbid anatomy at King's College Hospital Medical School, has been appointed to the university readership in morbid anatomy at the school

University of Sheffield

Dr R A Caldwell has been appointed lecturer in pathology, Dr R S Duff lecturer in medicine, Dr J P Green, Dr A Simpson, and Dr R A James demonstrators in anatomy, Dr F J Flint part time clinical teacher in medicine, and Mr A A Jefferson part time clinical teacher in neurological surgery

University of Leeds

Dr C E Lumsden has been appointed to the chair of pathology

Dr Lumsden graduated M B in the University of Aberdeen in 1936 and later held house appointments in the Royal Infirmary there In 1938 he was awarded a Garden research fellowship in the university and he remained in Aberdeen until 1951 as an assistant lecturer and finally senior lecturer in the department of pathology He was released from the university at his own request in 1940 and served in the R A M C in India and Persia In 1948 he took the degree of M D with honours and in 1949 with a senior Rockefeller fellowship visited American medical schools In 1951 he was awarded the Royal Society's Henry Head research fellowship which he still holds The first six months tenure of the fellowship he spent working in the cytochemical division of the Carlsberg Laboratory Copenhagen He then joined the Institute of Neurology of the University of London and created at the Maida Vale Hospital for Nervous Diseases a small independent unit for research in experimental neurocytology

Faculty of Ophthalmologists

The following have been elected officers of the Faculty for 1956–57

President Dr John Marshall, vice presidents Mr J R Wheeler Mr L H Savin hon treasurer Mr A McKie Reid hon secretary Mr T K King

Symposium on Arteriosclerosis

The Swiss Academy of Medical Sciences is holding a symposium on arteriosclerosis at Basle from Aug 8 to 10 Further information may be had from Prof A Gigon Petersplatz 13 Basle, Switzerland

Nuffield Burns Unit

On May 12 this unit was opened in the plastic surgery department at Stoke Mandeville Hospital Aylesbury, by Sir Harold Gillies Immediately before the opening ceremony Lord Nuffield put the last screw in the plaque on the door of the unit which bears his name

Hunterian Society

The gold medal for this society's essay competition in 1955 has been awarded to Dr John Fry

Beit Fellowship

A junior Beit fellowship has been awarded to Dr R J Shephard

National Blood Transfusion Service

There were 759,371 donations of blood in 1955 compared with 700,202 in 1954 116,410 people gave their blood for the first time, and at the end of December the donors' panel was 591,204, compared with 540,389 a year before To meet the ever increasing demands for blood, the service needs at least 650,000 regular donors to make sure that supplies of blood are adequate Anyone who is in normal health and between the ages of 18 and 65 is welcomed

Dental Man-power in the Forces

The Ministry of Health and the Department of Health for Scotland, in consultation with the dental profession have appointed a Dental Manpower Committee to advise on the allocation and recruitment to the Forces of dentists liable for National Service Mr J P Dodds, of the Ministry of Health, is to be the chairman, and the medical members are Sir William Kelsey Fry, Mr F G Gibbs, Prof W E Herbert, Prof R V Bradlaw, Dr T H J Douglas, and Dr A T Wynne

Maternity Services Committee

This committee, which was set up by the Minister of Health under the chairmanship of the Earl of Cranbrook, to review the organisation of the maternity services in England and Wales held its first meeting on May 17, and decided to invite written evidence Invitations are being sent to selected organisations and the committee will also consider evidence submitted from any other source Any person or organisation wishing to submit views should write to the committee's secretary Mr J S B Butler, Ministry of Health, Savile Row, London, W 1

Treatment Centre for Spastics

On May 16 Miss Patricia Hornsby Smith, parliamentary secretary to the Ministry of Health, opened at Prested Hall Feering, Essex, the National Spastics Society's first residential treatment centre for adults The centre will take 30 men and women with cerebral palsy, between the ages of 25 and 40 The staff includes 2 physiotherapists, 2 occupational therapists a speech therapist, and house parents, under the guidance of Dr A G Mackenzie and Dr Nicholls Palmer Miss Hornsby Smith said that the society's record was a proud one In a comparatively short time they had opened 4 national school and residential centres and, in cooperation with local health authorities, 29 local schools and centres There was she believed, immense scope for voluntary effort on specific and numerically limited problems such as this "Anyone who imagines that the health service can do everything at once, is living in the realms of fantasy, and with the many vast problems with which we have to deal we can only fix our priorities and try and solve them within the limits of the financial allocation which Parliament allows us

Appointments

THOMAS R G, M B Lpool D I H deputy S A M O [illegible] R H B

Colonial Appointments

ANASTASSIADIS I N M B Athens district M O Cyprus
HARRIS, F C M R C S D C P specialist pathologist Gold Coast
JONES L G G M R C P I M O grade A venereologist Trinidad
KOTHARI P C, M B Bombay M O Sierra Leone
LOW A D M R C S district M O St Lucia
PRENDIVILLE K P L R C P I asst M O Bahamas
THOMSON, M J C L M S S A resident M O Uganda
VOLLICH B M D M O northern region Nigeria

Births, Marriages, and Deaths

BIRTHS

TURNER—On May 6 at Redwood City California to *Joan* wife of Robert G Turner F R C S a son James brother to Peter and John

Some patients are treated for respiratory tuberculosis ithout ever being admitted to hospital, although it is esirable that all patients should have a period in a hest hospital, at least during the time of up grading, n addition to those admitted for major surgical operaions In recent years there has been a decline in the opularity of minor collapse measures in the treatment f respiratory tuberculosis in favour of more permanent ollapse therapy, which obviates, for upwards of three ears, any need for weekly attendance for refills In pite of this the attendances at the refill clinics in 1954 ere 9262

Resettlement

In chest medicine the resettlement of the patient is utomatically considered as a routine part of treatment Fowler 1955), and whenever fresh employment is equired it is arranged through the resettlement clinic Grout 1952) The greatest difficulty is found in attempting to reable patients with chronic bronchitis and mphysema

Summary

An account is given of the staffing, equipment, and work of a chest clinic

The attendances in 1954 and the various types of chest diseases found are analysed

Attention is drawn to the striking increase in the number of attendances during the past five years and of the way in which the chest clinic is increasingly being regarded as an outpatient department dealing with all diseases of the respiratory tract

REFERENCES

Fowler P B S (1955) *Lancet* i 467
Gibson K B (1955) *Ibid* p 960
Grout L J (1952) *N A P T Bull* 15, 875
Jones F A (1953) *Lancet* ii, 556
Trenchard H J Grenville Mathers R (1952) *Tubercle*, 33, 20

Centenary Celebrations

The centenary celebrations of the Society of Medical Officers of Health, held in London last week under the presidency of Dr C F White, included an oration by Lord Adrian, O M, an exhibition arranged by the Wellcome Historical Medical Museum, and a dinner given by the Corporation of London

LORD ADRIAN'S ORATION

Lord Adrian surveyed past achievements—work that cannot be fully indicated by statistics, since it has not only prolonged but also transformed our lives—and looked into the future, pointing to new fields for endeavour Much remains to be done, he suggested, in the field of mental welfare

"The problems raised by the village idiot the tramp, the feckless mother, and the idle apprentice have exercised social reformers and lawgivers without number Mental defective children must have been given a training more or less adapted to their capacity long before there were intelligence quotients and special schools with medical officers to send them there But past attempts to deal with social misfits have little to tell us about the kind of research we should undertake now Most of them were aimed more at the welfare of the community than at that of the individual With a more stable society we can afford to be more sympathetic to mental inadequacy, and we have come to doubt the efficacy of punishment in this world or of the threat of it in the next as a deterrent to faulty behaviour "

The results of mental-health measures were seldom as clear-cut as those of measures for physical health Reports on the former must be based much more on general impressions, and these would have little value unless they were made by someone with knowledge of mental hygiene and the time to study it There was a danger that, by too much insistence on measures that had not been well considered and by too much official visiting and advice, the mental health services might forfeit the coöperation without which they would certainly fail—cooperation from the general practitioners, the schoolmasters, the parents, and the public at large There was also a danger that too much insistence on mental health would raise a new standard of good—or rather of uniform—behaviour "We must aim at a stable and contented society but not one without the reformers and critics and eccentrics, the people who will not conform and are a nuisance to their fellows We must allow some revolt because our nature, as beings with human brains, ensures that we shall sometimes be discontented however wisely we are brought up, even though we are steered through infancy and adolescence with just the right amount of parental affection and the schooling which will make us responsible units in a democratic society "

EXHIBITION

The exhibition, at the London School of Hygiene and Tropical Medicine, is mainly retrospective, showing the society's progress over the past hundred years, but such retrospection is vastly rewarding From the first tentative beginnings in Liverpool, where the medical officer of health had to struggle not only with the immense difficulties of his task but also against personal poverty and public indifference, the exhibition traces, by means of pictures, diagrams, memoranda, diaries, and newspaper cuttings, the path to the modern health service Mr Punch's outbursts over the years—humorous, scathing, or indignant—are displayed to good effect

This admirable exhibition will be on show from 10 A M to 5 P M on Mondays to Fridays until further notice No doctor will fail to find here some item of interest to him

CITY'S DINNER

At the dinner, on May 15, the Lord Mayor observed that the post of M O H for the city, from which the society's president had just retired, was first occupied by Sir John Simon The Lord Mayor reflected that throughout the ages men had sought the right thing to say about doctors The work of those in public health was less spectacular than that of clinicians, but they could take pride in important achievements—for example, in the control of diphtheria and tuberculosis, and in promoting the health of children Dr White, replying for the society, admitted that Simon was not the first M O H his appointment in 1848 was just preceded by that of an M O H for Liverpool, but he would not hazard a guess whether that was because Liverpool was more enlightened or because it was dirtier Mr S E Cohen, chairman of the public health committee, proposed The Guests, and Mr R H Turton, the Minister of Health, and Prof C Fraser Brockington replied Mr Turton thanked doctors in the public health service for their cooperation in the programme for vaccination against poliomyelitis, but expressed concern at the unsatisfactory rate of immunisation against diphtheria As Minister of Health he was not concerned with all the M O H 's activities, for in 1951 (before the days of the garden of Eden) the Ministry of Housing and Local Government had been set up, and now he was not responsible for water or sewers The Lord Mayor responded to the toast of The Lord Mayor and Corporation proposed by Sir Allen Daley

Epidemic Keratoconjunctivitis on Clydeside

Since last November an outbreak of keratoconjunctivitis has caused considerable disability among workers in heavy industries on Clydeside The number of cases increased rapidly at the beginning of January, when there was a minor epidemic in a large shipyard, and the disease has since spread to involve other shipyards and industries Complement-fixation tests with the A P C group virus antigen showed significantly rising titres in 5 out of 7 paired serum samples taken in the early and convalescent phases of the illness Tests on 52 sera taken on the same day from cases of different durations, ranging from 1 to 112 days after onset, showed predominantly high titres after the 14th day but low titres before the end of the second week

These findings suggest that a virus of the A P C group is responsible for the outbreak Attempts to isolate and identify the serological type of virus involved have not yet succeeded hopelessly hurried and crowded, this experience has become dedicated to the 2nd M B It is no longer a foundation, either for practical purposes or for an education Preclinical teachers struggle hard against the difficulty of their scant numbers and their increasing separation from clinical work More enlightened perhaps than many of their predecessors, they try to inculcate an understanding of science and to stimulate their students' minds But outside the older universities and the schools that provide facilities for a B SC degree, these efforts influence only a minority of students Even where attempts have been made to reduce and select the content of the preclinical curriculum and where integration in teaching has been achieved, the examination is still the student's main objective and incentive, and unfortunately the student's concept of the examination is very different from the examiner's

I regard the second professional examination as one of the main reasons for our failure to adapt medical education to changing conditions and requirements It presents an official barrier to the integration of clinical and preclinical studies It imposes a time limit on preclinical studies so that the introduction of new basic disciplines such as psychology and social science is impracticable It prevents a reduction in factual and non-essential teaching such as is necessitated by dissection of the whole body Integration with the basic premedical sciences is likewise prevented, and this in turn has led to over-teaching of these subjects in the period which should still be devoted to general education The most serious indictment, however, lies in the attitude of mind it produces in the majority of students Because so many facts have to be assimilated in so little time, leisure has been eliminated If there is no leisure there is no time for thought, and if there is no thought there is no meaning in terms of subsequent experience *Too* many students still believe and hope they have "finished" with anatomy and physiology after passing the 2nd M B

But science itself has ignored the rigid barriers of the educational system Though medicine has not and never will become an exact science, it is now impossible for its practice to be good without the application of scientific method The effectiveness of this application will always depend on the doctor's understanding, imagination, sympathy, and moral integrity, but these attributes cannot make up for the absence of a scientific outlook Thus, to cope with the increasing complexity of medicine over the past twenty-five years, a sound clinical training demands a preclinical education, not merely as good as in the past, but considerably better

Clinical teaching —In clinical medicine factual teaching cannot be neglected or even selected to the same extent as it may be in the preclinical stages, for pathology, diagnosis, and treatment have a large factual content, and the student must at some stage strive to become acquainted with the whole truth in the branch of medicine he proposes to follow Yet some selection must be made, since nobody can now familiarise himself with the whole of medicine Professional competence and the advancement of knowledge both demand specialisation, and postgraduate training is therefore necessary for any kind of medical practice—including general practice which is one of the most difficult (and important) specialties

We might have expected, therefore, that for all forms of practice clinical training would have been separated into undergraduate and postgraduate stages, but there has been no real effort to make clear what should be done in each In face of a dual need of a more scientific approach and of more selective presentation of factual knowledge the undergraduate curriculum appears to have had only one consistent objective—to remain comprehensive

Specialisation Breeds Comprehensive Training

The reason for this is not hard to find So long a medical education adheres to the structure and organisation of fifty years ago, specialisation will continue t enforce an increasingly comprehensive training Almo every specialty claims some portion of the student time, and the process is cumulative because there is le and less overlap between special departments Thus th student's clinical experience is increasingly fragmented and though it is superficially wide it is seriously lackin in depth

From this stems a further trouble fragmented an distorted clinical experience, combined with an increa in teachers but a decrease in supervision, steadily under mines the apprenticeship system on which depends no *only* the vocational study of medicine but also th technical training in clinical method

It is frequently said that, if presented with a wid field of clinical experience, the good student will select for himself But there are different types of experienc appropriate to different stages of development Th student naturally feels that he would like to know everything, and the comprehensive final examination —for many students an external one—leaves him with little choice of what to leave out

It is apparent, therefore, that in both the preclinical and the clinical fields rapid expansion of knowledge, with all the consequent changes in medical practic have produced serious changes in medical education largely because our system of teaching and our method of examining have by comparison remained static

The Past Twelve Years

These observations are not new About a decade ago there appeared a number of detailed and objective assessments of the state of medical education All stressed the same things—the need for a basic rather than a comprehensive curriculum and the need to give undergraduate students an education, not merely a training, in medicine

Few reports have made this more clear than that of the 1944 Planning Committee of the Royal College of Physicians[3] "Medical Education" said this report "is directed towards two objectives which may be termed educational and vocational"

> In education we seek to train the student so that he can collect, analyse and interpret facts for himself, to observe and to understand what he observes *It is an objective* common to all University education in natural science and in pursuing it, medical education is peculiar only in selecting material for study that is relevant to the *problem of dis* The goal of this aspect of medical education is to produce men who are equipped to learn both by *their own experience* and that of others and who will continue to develop even when they have left the school in which they were taught Vocational training, on the other hand, aims at giving the student such a basis of knowledge as will enable him to practi Medicine on his own account It seeks to ensure that the medical graduate knows enough to *recognise* the *common* forms of disease and how they are treated

This committee drew attention to the inevitable conflict between the two objectives Describing the overcrowding *of the curriculum* by the attempt to include it in all knowledge before qualification, it said

> The result is that to an increasing degree during th clinical period the student's time and energy are taken up in absorbing an enormous mass of facts, *so that he can giv* no thought to the scientific principles underlying Medicine Students of exceptional ability may survive the ordeal with no more serious consequences *than fatigue* but the average man usually seeks the easiest way *out of* his impasse and accepts that the primary *object of* his training is to absorb as much information as possible"

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[3] Royal College of Physicians Planning Committee's Report o Medical Education 1944

The other group of people whose health is endangered by our present way of living is men of 45 to 64 Coronary thrombosis and cancer are "the leading causes of death" among these men Illness among employed people has increased steadily since 1952, and the figures for 1955 show an increase of 9% over 1954 Tuberculosis was still the most important cause of loss of time at work, though notifications continued to fall—to 128 per 100,000 of the population, which is a reduction of 7% on the rate for 1954 The number of people on the waiting-list for admission to sanatoria had fallen from 515 in 1954 to 148 at the end of 1955 This fall is not matched by the fall in notifications, and the improvements in the hospital position is partly due to the increasing efficacy and use of domiciliary and outpatient management

The blue-book also includes the report of the Scottish Health Services Council and its standing advisory committees

Occasional Survey

ANKYLOSING SPONDYLITIS

In a comprehensive review Blumberg and Ragan[1] remind us that this disease was first described by Bernard Connor Born in Ireland in 1666, Connor published in 1691[2] a description of a skeleton with spondylitis—an "extraordinary humane skeleton, whose vertebrae, the ribs, and several bones down to the os sacrum, were all firmly united into one solid bone, without joynting or cartilage" From the time of this description the emergency of ankylosing spondylitis as a specific entity was retarded by confusion with other conditions, notably with degenerative joint disease of the spine with senile kyphosis In the United States the disease being generally regarded as a form of rheumatoid arthritis, goes under the name of "rheumatoid spondylitis" In this country most clinicians prefer "ankylosing spondylitis," and would agree with Hart[3] that "in the meantime it is, perhaps, more profitable to study these disorders as different unsolved problems than to put them all into one diagnostic cauldron" The syndrome, by whichever name it is known, still lacks complete uniformity and atypical cases have quite recently been distinguished Buckley[4] held that the predisposition of ankylosing spondylitis to attack men more than women, its characteristic tendency to produce bony ankylosis, its centrifugal spread. and its failure to respond to gold, made it unlikely to be a variant of rheumatoid arthritis To these points may be added the responsiveness of ankylosing spondylitis to treatment with X rays (at any rate in terms of relief of pain) and the rarity of a positive differential agglutination (Rose-Waaler) test (which was positive in only 3 of Ball's 203 cases[5]) The only good evidence for the opposite view is that peripheral joints may be involved and that the histopathology of the diarthrodial joints of the spine is strikingly similar to that of rheumatoid arthritis Cruickshank[6] found certain minor differences, there was a greater liability to haemorrhage in ankylosing spondylitis (perhaps a result of the earlier formation of adhesions and their rupture by movement) and a tendency to thickening of small vessels, usually in the form of endarteritis obliterans He argued that the histopathology of rheumatoid arthritis is not entirely specific, and that a similar picture in ankylosing spondylitis need not imply a common aetiology Subcutaneous nodules—lesions much more specific for rheumatoid arthritis—are unknown in ankylosing spondylitis van Swaay[7] proposed a different view of the pathogenesis of ankylosing spondylitis, believing that the essential process in the sacro iliac joints is a proliferation of new cartilage, which replaces the old without evidence of inflammation The joint-space is finally ossified.

The cause of ankylosing spondylitis remains unknown Various agents have been suspected, including tuberculosis, brucellosis, and gonococcal infection These conditions can certainly produce lesions in the sacro iliac joints which in some ways resemble those of ankylosing spondylitis, but they cannot be accepted as aetiological agents Parathyroid dyscrasias, genito-urinary disease allergy, and metabolic and hormonal factors have all been put forward, but none has been convincingly established Several groups of workers[8–10] have failed to confirm the finding of Davison et al[11] that the excretion of 17-ketosteroids is increased in ankylosing spondylitis Inheritance is known to play a part, and Hersh et al[12] decided that the factor involved was an "autosomal dominant which has about 70% penetrance in males and about 10% or slightly greater in females"

Diagnosis

In many cases the diagnosis of ankylosing spondylitis is not difficult, and a story of pain or stiffness in the lower back or buttocks (perhaps with sciatic radiation) in a young man raises immediate suspicions The lumbar segment of the spine should be examined for flattening and loss of movement, and the chest for impaired expansion[13] X-ray examination of the sacro-iliac joints is essential and a normal erythrocyte sedimentation rate should not be accepted as excluding the diagnosis There are, however, important deviations from the classical picture In Hart's series[3] the earliest symptoms in 13% of patients were in the peripheral joints, and there was swelling of these joints in over 20% The knees and ankles are most commonly involved and the distribution of affected joints is rarely that of classical rheumatoid arthritis For example, the wrists were involved in only 7% of Blumberg and Ragan's cases and the hands usually escape Iritis may be the presenting sign, and this again helps to differentiate ankylosing spondylitis from rheumatoid arthritis, in which lesions in the eyes, if present, are those of episcleritis or keratoconjunctivitis sicca In Blumberg and Ragan's series 25% of patients had one or more attacks of iritis during the course of their disease, and this complication was often the only reason for admission to hospital and for treatment with hormones In this country iritis has been observed in 6–24% of cases[14–17] Pain over the angle of Louis is not uncommon, and Savill[18] described a sequence of radiographic changes starting as erosions of the bone ends and ending in bony ankylosis Changes in the manubriosternal joint may however, be found in rheumatoid arthritis Among other features of ankylosing spondylitis, tenderness over bony prominences notably the ischial tuberosities and iliac crests is common[10], and the radiographic accompaniments are irregular lytic defects with a punched out appearance, irregular zones of increased density and "whiskering" or ' fringeing" to say whether this has improved the quality of medical students There is in fact no means of comparison Almost all the factors affecting students have changed, and I personally believe that we have very little accurate information about the students in our schools

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[1] Blumberg B Ragan C *Medicine Baltimore* 1956 35 1

[2] Connor (or O Connor) B Lettre écrite à Monsieur le Chevalier Guillaume de Waldegrave Paris 1691 See Dictionary of National Biography

[3] Hart F D *Ann rheum Dis* 1954, 13 186

[4] Buckley C W *Brit med J* 1943 ii 4

[5] Ball J *Ann rheum Dis* 1952 11 97

[6] Cruickshank B *Ibid* 1951 10 393

[7] van Swaay H Spondylosis ankylopoietica een pathogenetische studie Leiden 1950 p 182

[8] Pond M H *Ann rheum Dis* 1954 13 67

[9] Mowbray R Latner A L, Middlemiss J H *Quart J Med* 1949 18 187

[10] Hart F D Robinson K C Allchin F M Maclagan N F *Ibid* p 217

[11] Davison R A Koets P Kuzell W C *J clin Endocrin* 1947 7 201

[12] Hersh A H Stecher R M. Solomon W M Wolpaw R Hauser H *Amer J hum Genet* 1950 2 391

[13] Hart F D Bogdanovitch A Nichol W D *Ann rheum Dis* 1950 9 116

[14] Birkbeck M Q Buckler W. St J Mason R M, Tegner W S *Lancet* 1951 ii 802

[15] Campbell A M G *Ibid* 1947 i 406

[16] Simpson N R W, Stevenson, C J *Brit med J* 1949 i 215

[17] Buckley, C W *In* Textbook of the Rheumatic Diseases London 1955, p 336

[18] Savill D L *J Bone Jt Surg* 1951 33B 56

Although selection has been widened in one way it has been restricted in another The academic requirements for entry into universities have been raised, and the average student does not complete them until the end of his school career after a two-year course of study For almost all who wish to take up medicine, this study is limited to subjects of the 1st M B examinations, for not to limit it in this way would prejudice the student's chances of passing the 1st M B, even after a year's course at the university But studying even two scientific subjects up to advanced level in the General Certificate of Education seriously reduces the opportunities for studying any other subjects Although the scientific sides of all public schools and grammar schools have been strengthened since the war, it is difficult for these schools to provide classes in which general education can remain balanced and at the same time the examination requirements be satisfied

Moreover, it is natural for boys and their parents to argue that if two thirds of the 1st M B examination can, and virtually must, be passed from school, then the only sensible course is to complete the 3rd part also, and thus avoid a year at the university devoted to the study of one subject In consequence it has become common practice for future medical students to devote the last two years of their schooling to chemistry, physics, and biology almost exclusively Direct entry to the preclinical department of the medical school is now common and is increasing For twenty years it has been the standard procedure at the University of Cambridge, which requires that these parts of the 1st M B should be passed before entry

The importance of a good general education to those who are to be doctors has been stressed repeatedly Although some have wished to exclude science, the majority regard a good education as a *balanced one* The deplorable fact is that medical students now have a less balanced general education than ever before Many in fact cease to have any non scientific education at all after the age of 16

This unrelenting demand for a high examination standard in the premedical sciences has hampered good scientific education Except in schools with an unusually large science staff, it is almost impossible for the average boy to gain a sound scientific understanding and at the same time acquire the amount of factual knowledge required to take three (in London University until recently four) subjects at advanced level The premedical examination is, however, an inflexible criterion of selection, and it ensures that, from the age of 16, prospective medical students are conditioned to factual teaching for factual examinations At each later stage of the curriculum this conditioning process is continued and reinforced

I am unaware of any figures showing what proportion of candidates selected by medical schools on grounds of character and personality are later refused for failing to pass the 1st M B I doubt whether anyone can assess what some of those who pass and enter have forgone in their last two years at school in order to get through —the athletic activities that have been given up, the general reading that has been abandoned, the prefectships that were not taken up or not taken seriously Positions of responsibility at school are of inestimable value to boys who are destined to have very little responsibility in the later years of their professional training

Grants and Examinations

The majority of medical students are to some degree State supported by grants With these grants and family help some are comparatively well off while others manage moderately well with part time paid employment Others are quite comfortably supported financially by a combination of a grant and a wife who is earning A comparatively small number, with no grant or only a minor one, exist at subsistence level only In all cases, however, the financial implications of examination failure are very serious

Most grant giving authorities are, in my opinion, very sympathetic to their medical students, but some naturally have difficulty in realising that a degree course in medicine is not comparable with a degree course in, for example, history There is no honours degree course in medicine it is a matter of pass or fail in the examinations, and during the past five years the failure rate in London University's final M B —an external examination—was between a third and a half of those making their first attempt The situation is not much different with the external qualifying examinations of other licensing bodies Thus for a not inconsiderable proportion of medical students the clinical curriculum is prolonged for six months beyond the accepted course—even if they pass the examination at the second attempt

To the grant giving authorities this high failure rate is both baffling and expensive, and at least one county council has notified students that failure in the examination will be immediately followed by withdrawal of the grant This situation inflicts a grave injustice on many students, and, apart from the anxiety occasioned, it has further repercussions For a large proportion of grant aided students take the Conjoint diploma in addition to the university degree as an insurance against M B failure and loss of grant This procedure not only adds to the financial strain but also interferes seriously with the third year of clinical training, for the idea that students take these extra examinations merely for practice, without specific preparation and without undue concern is, in my experience, largely a myth There is no more lamentable facet of medical education in this country than the double external qualifying examination

The Student's View

With this atmosphere of learning in mind, it is worth trying to envisage the medical curriculum as it may appear to an average student

He comes to his medical school armed with whatever general education he had acquired on reaching the age of 16—to which he has added remarkably little since either from learning or from experience of the world He has spent up to three years on the study of chemistry, physics, and biology He then spends about two years on isolated study of anatomy, physiology, biochemistry and (if he has to pass an examination in it) pharmacology He often gains no knowledge of psychology except that given him by his own experience and his inherited intuition

When he comes to clinical studies, he rarely has any knowledge of pathology, he has seldom acquired the art of learning (being accustomed to the acquisition of knowledge by memorising, and relying mainly on didactic lectures and textbooks), and his critical faculty has seldom been awakened He is enormously relieved that he has no further important examinations to face for nearly three years and he is prepared to take things more easily Nevertheless he starts his clinical work with enthusiasm This, he thinks, is the real thing he *is going to deal with people*, and he usually believes that work will now be much more stimulating and much less difficult The stimulation of the live patient lasts for some time, but medicine soon begins to appear extremely vague and muddling and often most disappointing There seems to be no sure basis for it all Pathology, which might give him this, seems to him (if indeed he meets it at all in the early months) a very strange subject with a terminology that he does not

In England Now

A Running Commentary by Peripatetic Correspondents

MOST people think that working in an international organisation is an opportunity for learning foreign languages But how many realise that it is also an opportunity for rebuilding one's own ? For these organisations are laboratories in which the English of the future is being designed In their documents new words are continually being coined, tested and then either adopted or discarded Did not the word " global " itself (as opposed to globular) spring from the United Nations ?

Some words fulfil an obvious need What could be neater than ' two suitcases were completely unreusable,' " the recruitment of a nurse is being pended for the time being," or " supplies and equipment were still packed in their cases and no head or tail could be made out of them " What could be more natural than that a statistical report should be submitted for ' multiplying " ?

But telegraphese is less attractive, and I hope that the English language will never accept such concise phrases as " please onforward the finalised planops or ' in view of criticisms by the Government of article v the plan of operations is returned herewith for refinalisation " Undoubtedly international medicine is an etymological paradise

* * *

Bed rest has enabled me to plan the sanatorium of the future, full of happy patients, dedicated doctors, and satisfied administrators

The large main block will face south, overlooking a large lawn, sloping away to a background of trees In the centre of this is a circle of stone seats enclosing two large flat stones, with, to the south a double archway arranged so that the sun, striking through it, falls on the two stones at the summer solstice and at the vernal equinox Every patient's bed would have a direct view In the admission block, the patient will be prepared for entering the community Brain washing coupled with the gradual severing of family ties and the discontinuance of visiting will take place simultaneously with the provision of a suitable substitute for the family inside the sanatorium—for example, for father, the physician, for mother, the ward sister, and for mother in law, matron A sibling of the same sex would be an up patient, while the trained sublimation of sex will be a major source of strength to the community

At each full moon there would be an initiation ceremony, at which the neophytes, sponsored by their new family, would enter the community and be conducted to their new bed in the main block Details of the ceremony could be varied in each sanatorium, but the style would be a mixture of the best of Wilfred Pickles and Aimee Macpherson At monthly psychi surgi soma therapy ceremonies patients who needed a decision as to treatment would sit round the circle, holding their latest film. Presiding at this, as at all big moments in the community life, will be the archetypal figure of the fully gowned and masked thoracic surgeon. As each patient holds up his film, he will cast different coloured stones on to the ground out of urns placed on the flat stones, and will interpret the message they give Thus, for example

> This is the treatment we dictate
> For the patient admitted to room number eight
>
> Three months horizontal he will stay
> Bar using a bedpan once a day
> Lower his head and raise his toes
> Thus his cavity will close
> Daily strep and INAH give
> To keep his T.B sensitive

Once a year, at the vernal equinox, at a ceremony of rebirth, patients will be chosen for discharge They will immediately change their up uniform for their own clothes and be withdrawn to the discharge-block, there to undergo the reverse of the admission process For instance, the thoracic surgeon would appear to them for the first time in ordinary clothes The umbilical cord chaining them to the community would thus be cut, and visits from families encouraged On midsummer day a maypole would be erected, and at the moment of the solstice, the ribbon cut by the chairman of the management committee Patients for discharge would dance with their children to symbolise the reunion, and at the end of the day would return home.

Let no-one think the Medical Research Council is forgotten Its statistical committee could control the colours of the stones in the urns, and a controlled series of surgical cases, alternately chosen by the oracle or by the physician, would give rewarding results

* * *

The other day while using that Middle Eastern instrument, the shuftiscope, to inspect the mucous membrane of the distal colon, I was idly speculating on the -scope end of the word and wondering how the stethoscope came to be so named What did stethos mean ? Despite a highly prized classical education up to VI form standard, I had not met this obviously Greek word as far as I could remember A little research in *Chambers's English Dictionary* told me that it meant ' breast " Obviously, the early single-tubed instrument was not really suitable for inspection of the breast, as the small hole would give a limited monocular view and some time would be needed for a proper inspection of the whole area It would of course be an admirable instrument for patients who expect a full examination through the aperture made by undoing one button It was then found I suppose, that one could listen to heart and chest sounds while carrying out this tedious inspection Some inventive fellow, no doubt, then thought out the instrument with two ear-pieces, increasing the efficiency of inspection of the breast by allowing the use of binocular vision over a larger area than was possible before and also making feasible auscultation of heart sounds at one and the same time

I feel that as its secondary use as an aid to hearing rather than vision now takes precedence it should be renamed, and I shall rename mine a cardiophone On second thoughts I am really much more interested in gastro enterology, and as the first to draw attention to this obvious misnomer, I shall claim the right to have it called a borborygmiphone More impressive in front of the patient, too, and—better still—a Greek ending on a Latin stem. There's too much of this rampant Nationalism these days I'm all for coexistence

* * *

Wallpaper blisters when it is applied by the amateur, even when one of the new plastic substitutes for flour-paste is used exactly according to the maker's directions Most of the blisters disappear spontaneously as the wall dries out, but a good-quality embossed paper in the drawing-room let us down badly It wasn't only blistering the edges lifted where they should have stuck firmly There was consternation and disappointment in the house, but from the depths of despair the ' needling technique " was born

A 3 c cm. syringe with an exploring needle can be filled with plastic substitute if the plunger is pulled hard The long needle slips under the lifted edges of the paper and the required amount can be injected easily A moment's pressure and a wipe from a clean rag sclerosed the first blister beautifully, so the remaining lesions were treated to a surgical approach.

The technique was one of subcutaneous infiltration From one puncture, adhesive could be infiltrated between paper and wall over most of the separated area and it was found that 2–3 c cm was required for the larger lesions Pressure was applied by junior members of the family and a flat smooth surface was the first result Tomorrow we shall know if there has been recurrence or relapse

* * *

My long preparation for the final M B has resembled an Orwellian brain-washing, for I have been conditioned to accept oft-quoted dogma Thus I carefully palpate for the inferior epigastric artery, sagely oscillate the vertex in vertical polarisation, and, following the lead of the Professor of Surgery, I say " Yes, Sir, direct I think " I had become reconciled to the specious self-deception involved in the detection of such outlandish signs But now, the awful truth is revealed the course of brain-washing is utterly complete Today the Professor of Surgery invited me to palpate, and clearly and unmistakably I felt the inferior epigastric artery 1984, and I have arrived

* * *

Patient When I swallow, food seems to stick in my sarcophagus

Doctor Well that's your funeral

The other major reform, and one of very great educational potentialities, is the institution of the preliminary-registration year of hospital appointments under supervision This year is now an officially recognised part of the undergraduate curriculum During the three years of its operation, however, no serious attempt has been made to integrate the special experience of this period with the rest of medical training In effect, the qualifying examination forms a barrier to educational continuity at *this* stage just as effective and as harmful as that which the 2nd M B interposes between clinical and preclinical teaching It must be remembered that, although the universities have the responsibility for approving these posts and for certifying that the student carries out his preliminary-registration training satisfactorily, it is the hospital authorities that make the appointments and pay the salaries Between the two there is at present no adequate liaison, and in making the appointments and deciding the character of clinical experience which they provide, the needs of hospitals for "pairs of hands" play a far greater part than any educational considerations

In short, the primary reforms which have been made in the past ten years, in face of rapidly changing conditions, have been well conceived and were potentially effective, but they have not brought any appreciable relief because the system itself is outworn In the apt words of Prof Clifford Wilson "The old tree creaked before, its branches were overgrown and its roots insecure It needed drastic pruning and the fertilisation of new enthusiasms and ideas Instead it was given a number of grafts and they have not taken very well"

Medical Education in America

It was against this background that I visited last year a number of American medical schools, and from what I saw I should like to single out some features which seem particularly relevant to our present situation Although the growth of medical education has been much more rapid and diversified in the United States than it has here, we have much in common in our aims and methods of thought—largely because of the constant interchange of ideas between our two countries

In the first place I was impressed by the intense awareness of the problem of medical education In the individual schools both staff and students are actively interested in its improvement, and the great foundations are stimulating and supporting research into educational methods

As far back as 1924, a situation in many respects comparable to our own of today led the Association of American Medical Colleges to establish a national Council on Medical Education Serious problems had arisen through the combined effects of rigid controls and excessive specialisation At its first meeting the council decided that the immediate need was "to secure relief, if possible, from the restraint and burden of external regulations"[5] It is no doubt this early conviction which is responsible for the striking differences which now exist between the American medical schools and our own in the opportunities and freedom to experiment Not only have there been radical and novel experiments in certain centres, but even the older and more conservative schools have been able to make big changes when the need arose One of these has been the virtual abolition of the final examinations at the end of the clinical course Educational continuity is thus encouraged, and is further supported by the considerable efforts at integration in the earlier stages Throughout, joint teaching sessions and conferences are far more numerous than in this country

A most important factor is the proportion of his time and energy which the clinician spends in hospital In the U S A the "geographical full time appointment" has been deliberately encouraged and is now common in the main teaching centres Thus clinical conferences, combined rounds, and group discussions offer far greater opportunities than we enjoy for the exchange of ideas and information No less important is the much closer personal contact between student and teacher The student is taught as an individual rather than as a member of a heterogeneous group, and individual assessment of progress is made periodically before he proceeds to the next stage He is, of course, older than his counterpart in this country having had a longer premedical education, and he has at least that added maturity which develops so rapidly at this period This partly accounts for the fact that he works much harder than the English medical student, shows far more interest, and is more critical in his approach He is given time for special study of his own choosing and often undertakes minor researches Examinations play a very small part in his incentives, which seem to derive mainly from a genuine and active interest in his work

Experiments in medical education are difficult to assess and easy to criticise Whatever they do or do not achieve, they bestow an undoubted benefaction on a medical school in the enthusiasm and sense of joint endeavour they produce in both students and staff A study of medical education in the United States at the present time can be most rewarding It helps us to recognise more clearly what we must do to retain and strengthen what is good, and to eradicate what is bad, in our own system

(To be concluded)

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[5] Commission on Medical Education final report of 1932 New York

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PARITY AND THE INCIDENCE OF DIABETES

D A PYKE
M B Camb, M R C P
SENIOR MEDICAL REGISTRAR,
RADCLIFFE INFIRMARY, OXFORD

It is a common observation that more women than men have diabetes mellitus In youth there is little difference in sex incidence, but after about the age of 45 a preponderance of women appears, and from that age onwards women outnumber men by at least three to two (Harris 1949, Joslin et al 1952) Various reasons have been suggested for this difference, in particular that it may be because more women than men are fat, and that it may be related to the menopause (Joslin et al 1952 Bartels 1953)

I report here a survey of the patients attending the diabetic clinic at the Radcliffe Infirmary in relation to

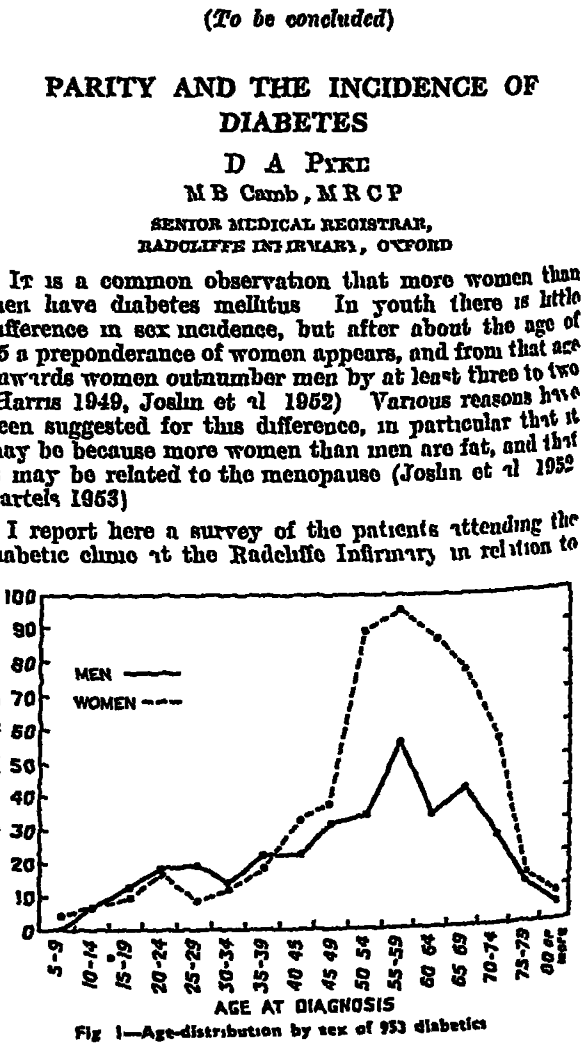

Fig 1—Age-distribution by sex of 953 diabetics

practice them in the home and they will realise how their education has been lacking

Castle Bromwich H M KENT

SIR,—I should like to congratulate Professor Russell on his article This must be an encouragement to the many who are struggling to cope with these problems, which are becoming increasingly acute

May I underline one pressing problem? There is a nation-wide shortage of trained midwives, which may be fatal to a service which is based on the work of this important group of women I do not myself subscribe to the concept of the midwife working in "glorious isolation," but regard her as a key member of the obstetric team As such, her status, privileges, and pay should be such as to support her pride in herself and her work Urgent attention needs to be given to this matter

Ashton under Lyne General Hospital T B FITZGERALD

REVISION OF THE CURRICULUM

SIR,—From reading the memorandum and correspondence in your columns, and attending meetings where medical education is discussed, the uneasy feeling emerges that most teachers and all administrators are taking themselves too seriously They ignore the proportion of the burden of learning which is carried by the student himself, teachers may make it easy or attractive for him to learn, but make him learn they cannot (neither for that matter can they stop him so doing) The essential personal nature of interchanges between teacher and student can be little altered by juggling with the times at which they meet, and thus playing about by administrators also obscures the real crisis facing medical education in the next few years—are we attracting a high proportion of the most capable and intelligent schoolboys? This vital problem is not controlled by selection, which filters out the worst If we do not attract the best, no change in the curriculum will matter much in the face of this defeat, if we do attract them, the student quality will be such that it will be immaterial what the curriculum is like

Is it the wisest approach to the new curriculum to turn the world upside down because there are unsatisfactory regions of it? It is doubtful whether the G M C will willingly surrender their authority, or in other words surrender us to the pleasure of a small group of enthusiasts (some would say fanatics or cranks), the names of the members of the R C P committee were not given in your summary of their memorandum, but one has doubts how widely representative this body is of, on the one hand, the basic sciences and, on the other, of the medical schools outside London The memorandum too asks for the blankest of cheques—the intentions of the new schools are not even sketched out in outline Even if the G M C surrenders, there are university and medical college boards to be circumvented, how will students belonging to two schools—the Oxford and Cambridge students doing their clinical work in London—be catered for if there is a difference in plan between these places, as is not unlikely? Are 57 varieties of medical education to be allowed, some of them canned?

Surely the wisest and quickest and least disturbing course is to seize on all commonly agreed points and act on them—good strategy to reinforce strength "Basic training" is not so agreed (is it principles, or general practice?), neither is a "good doctor" (should he be all head, is it permissible for him to be all heart, or must he be both?) But the synchronisation of related studies and the reduction of factual knowledge as such can be achieved inside the present G M C framework by discussion and arrangement between the individual subjects concerned I do not believe, either, that the present professors in preclinical subjects do in fact demand gross factual knowledge, this excessive demand for facts exists more in the imaginative memories of clinical professors than it does in real life Even so, some strenuous learning in the preclinical phase does not seem quite out of place, if only as an exercise ground and a selection hurdle

A further point arises from the loose use of the term "experiment" This word implies an investigation trimmed down to one essential point, at the end of which an accurate quantitative evaluation will emerge, preferably answering the question "yes" or "no" No rat is killed except for such an answer, but no such evaluation of the results of medical education is feasible, and we cannot write off five years and a batch of medical students in a proceeding for which we would not kill a rat Instead of experiment it were fitter to use the term "trial", it has two meanings

I should not write this except that as a pathologist I see a good deal of both the clinical and preclinical sides, and as a very young teacher myself I have not entirely forgotten or lost contact with students There are *too* many elderly men only too ready *to* dictate in matters which the present generation of teachers and students are perfectly capable of taking in their stride, as we did ourselves not so very long ago The present G M C rule may be somewhat inert and imperfect, but it is not illiberal, but the busybody goes about with a net of iron

London Hospital, E 1 J W LANDELLS

EXTRADURAL HÆMATOMA

SIR,—I read your annotation of May 5 with interest There are certain points, however, which I consider ought to be stressed with regard to this condition

The diagnosis of surface clot compression of the brain is essentially a *clinical* diagnosis In those cases where there has been a latent period, the development of severe headache with mental confusion, drowsiness, or giddiness should at once arouse suspicion of intracranial hæmorrhage, whether associated with bradycardia or not The quality of the headache in extradural hæmorrhage is unmistakable

Lumbar puncture and spinal manometry should be unnecessary in the ordinary case It is a dangerous procedure It is of value only in those few cases which develop slowly and insidiously over many days or weeks, with minimal neurological signs and little or no alteration in consciousness

Radiographs of the skull are useful only if they can be obtained quickly, the chances of survival are jeopardised by delay from any cause Delays in hospital can be just as serious as delays in transportation Speed is the keynote in the handling of this type of case

Local bruising of the scalp is one of the most valuable lateralising signs, provided the possibility of contra coup hæmorrhage is borne in mind, it does occur, as do bilateral extradural hæmorrhages

If for any reason operation cannot be performed under local anæsthesia, then general anæsthesia will have to be employed Unskilled anæsthesia which gives rise to increased venous congestion of the brain may precipitate a tentorial herniation

Rowbotham's figures[1] and my own[2] show a recovery rate of approximately 80% in this condition In the past five years I have seen a further 31 patients with extradural hæmorrhage in the neurosurgical service here 5 of the patients died, and thus the recovery-rate was over 80%

2 young adults died during transportation to hospital A young baby was decerebrate on admission and died after operation Another patient had a posterior fossa clot which had been developing over two weeks, the patient was

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[1] Rowbotham G F Acute Injuries of the Head Edinburgh 1945

[2] Whalley N *Brit J Surg* 1949, 37, 212

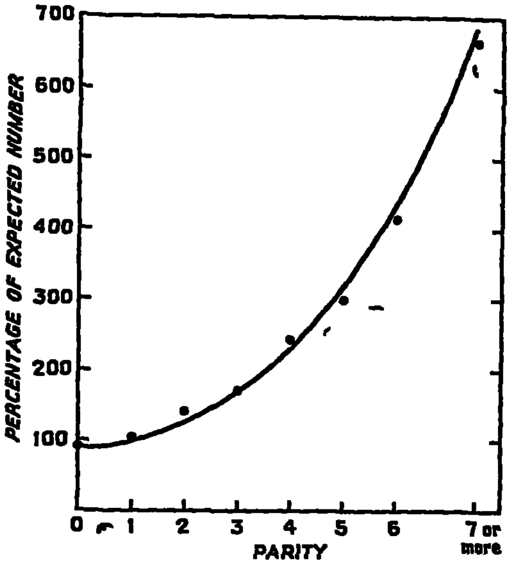

Fig 2—Increase of incidence of diabetes with parity in women aged 45 or more

This figure increases to nearly 50% for women who have borne two children but thereafter remains roughly the same for the higher parity groups. The difference between the nulliparous and highly parous women *expressed in this way is much less than the difference* between their relative incidence of diabetes.

Furthermore, as shown in fig 3, the relative increase of women diabetics with age is as pronounced among the normal and underweight as among the overweight.

Discussion

That the sex difference in the incidence in diabetes is confined to married patients was observed over twenty years ago by Mosenthal and Bolduan (1933), who attributed it in part to "the injurious effect of pregnancy upon the carbohydrate tolerance." Joslin et al (1936) confirmed this observation and attributed the difference mainly to a greater tendency of married women than single to become fat. They thought that the increased incidence of diabetes among middle aged women "reflects the strain on the endocrine system during menopause."

TABLE VII—INCIDENCE OF OVERWEIGHT IN RELATION TO PARITY

Parity	No of women	Percentage overweight
0	91	31
1	69	36
2	89	46
3	58	53
4	44	16
5	27	58
6	25	61
7 or more	60	41

Munro et al (1949) found that the large excess of women over men among their patients aged more than 40 (719 women, 239 men) was confined to married women, and that the difference could be "related, at least in part to previous childbearing," because they found more mothers of large families among their patients than were expected. These workers thought that marriage and childbearing did not affect the age of onset of diabetes or its severity, judged by tendency to ketonuria.

The present study suggests that the effects of parity are alone enough to account for all the true difference in the sex incidence of diabetes. This finding is in harmony with the views of Hoet (1954) and Jackson (1955), who regard pregnancy as an important provoking factor in a patient who is potentially diabetic. It is curious, if this is true, that pregnancy should lead to the development of diabetes, or rather its diagnosis, only some decades later, and that parity does not lead to the earlier appearance of diabetes. Nor does parity explain the apparent increase of diabetes among women in this century (Harris and McArthur 1952).

The greater tendency of multiparous than nulliparous women to become fat does not appear alone to be enough to explain the large number of multiparæ, because (1) there is a preponderance of women diabetics aged more than 45 even among those of normal weight and those under weight, and (2) the number of multiparæ who are overweight, though greater than the number of nulliparæ who are overweight, does not appear to be enough to explain the large difference in the incidence of diabetes among multiparæ and nulliparæ. Figures for weights of normal women also show a relatively small increase with parity (O'Brien and Shelton 1941).

That the menopause is not an ætiological factor of importance is suggested by the fact that there are no more nulliparæ aged more than 45 among the diabetics than are to be expected among the general population. If the menopause were a significant factor, an excess of women would be found in all parity groups, including the nulliparæ.

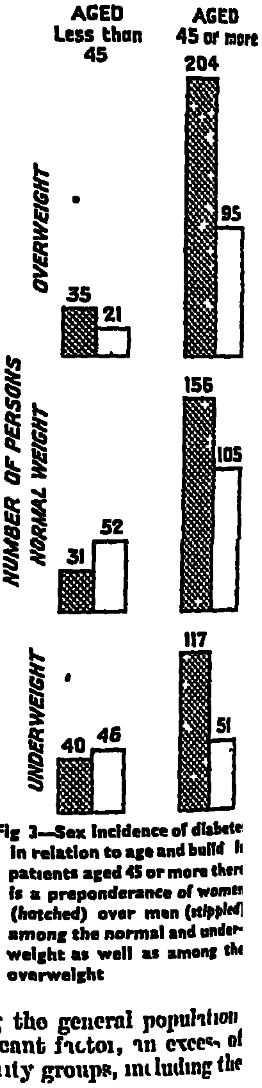

Fig 3—Sex incidence of diabete in relation to age and build I patients aged 45 or more ther is a preponderance of wome (hatched) over men (stippled) among the normal and underweight as well as among th overweight

Summary

An analysis of 953 diabetics shows an approximately equal sex incidence under the age of 45 but a preponderance of women over 45.

Part of this difference is due to the excess of women in the general population. The rest of the difference can be explained by the effect of parity. The excess of women diabetics is confined to women who have borne children and rises with increasing parity. A woman who has had five children appears to have about three times as great a chance of developing diabetes as a woman who has had none; but parity does not lead to the earlier appearance of diabetes.

This effect of parity cannot be due merely to a slightly greater tendency of multiparæ to become fat, since the preponderance of women diabetics is found among those who are of normal weight and the underweight.

Likewise, if the menopause were an ætiological factor of importance, an excess of women diabetics would be expected in all parity groups, but this is not the case.

I wish to thank Dr A M Cooke for help and advice, Mr B Merry and Mrs M Eastway for hours of laborious clerical work, Mr J H Luck, records officer of the Oxford Regional Hospital Board for analysis of clinical data, and Mr A Barr for statistical advice.

References at foot of next column

medical officer of health for testing two unopened ampoules supplied by an independent laboratory On receipt of the disquieting analysis they terminated the contract and ceased to use this material in 1949

W McAuley Gracie
Formerly Director of Infestation Control,
London S W 1   Ministries of Food and Agriculture

PARAPLEGIA FOLLOWING SPINAL ANÆSTHESIA

Sir,—In their article (May 12) Dr Payne and Dr Bergentz express doubt on the judge's most carefully considered opinion (in a recent High Court action) that the paralyses which occurred in two consecutive surgical patients resulted from the contamination of ampoules of cinchocaine hydrochloride, injected intrathecally, by the carbolic solution in which they had been stored The cause may have been something else, but (1) I have it on first-hand information that the intrathecal injection of this carbolic solution into higher animals resulted in apparently identical lesions, and (2) I have myself seen that the contents of an ampoule can be contaminated, with a coloured solution in which it is stored, through flaws in the glass too small to be detected by ordinary means

I have just returned from a five weeks' tour of hospitals in West Africa In many the doctor has to tackle practically any situation single-handed, and, if only on this account, spinal anæsthetics flourish My notes show that thousands are given annually, and a striking fact is that in answer to repeated inquiries I did not hear of a single case of resultant paralysis Fortunately the pernicious practice of immersing ampoules of local-anæsthetic solutions in antiseptics is not followed in that part of the world

Pembroke College
Oxford.   R Macintosh

MEDICAL EVIDENCE

Sir,—I was most interested in your leading article of April 14, and I am sure it must have been welcomed by many practitioners who have appeared in court as expert witnesses and by those whose interest in medicolegal cases is purely academic Few will disagree that the methods of giving medical evidence are unsatisfactory in many respects

The value of a doctor's testimony should depend not on his adroitness as a witness, but on his knowledge and experience as a medical expert Far too often, however, the effect of important medical evidence is lost as a result of the failure of experts to withstand the cunning manœuvres of skilful counsel who are rightly permitted a great deal of licence in court Experts should not be brow-beaten, ridiculed, or disparaged, nor have their sincerity, character, or qualifications assailed with the object of undermining the value of their testimony Surely the object of a court case is to establish the facts, and it is incompatible with justice that established facts should be open to rhetorical distortion

There should be no question of doctors being on one side or the other either in civil actions or in criminal proceedings They should be impartial, and any means of obtaining an objective picture of the medical evidence should be welcomed by all concerned in litigation in which medical evidence features

In order to avoid arguments and discussions on medical evidence in court, in which, after all, lay persons —no matter how brilliant—are scarcely competent to participate, independent experts should be appointed by the Royal colleges to establish the medical facts and state them to the court

Litigants or accused persons should be able to select expert medical witnesses from an approved list to adjudicate on their cases Inevitably they would be confronted by experts selected by the other side The selected experts should, before the case is heard, consider the medical evidence, in the presence of a specially appointed medicolegal chairman, and present to the court their agreed findings as a report At the trial one of the appointed experts would be available to answer questions posed by the judge and or members of the jury in order to leave them in possession of a clear picture of the medical facts

As things are, if the diagnosis of one expert is not agreed by another, surely the only conclusion which the court can reasonably draw is that one of them is not an expert This is a ridiculous situation and brings medical evidence and doctors into disrepute.

London W 1   Ellis Stungo

FATS AND DISEASE

Sir —Dr Sinclair's letter of April 7, with the responses by such figures as Dr Ancel Keys and Professor Yudkin followed by a lecture from the latter, do I think invite a contribution concerning the etceteras that Dr Sinclair may have in mind It may surprise you to receive this from a surgeon

It is hard for a man to give his "vision" words Dr Sinclair has such a difficulty, for a surgeon it is even more apparent Yet there is such a communion with the construction of thoughts, constituting Dr. Sinclair's almost bursting edifice, that from one who is engaged on an etcetera—the formation of gall-stones—words of support must come For the past two years the thoughts have been there. but I have considered it most irregular to put them into words based as they are on meagre experimental and clinical data

The experiments concerning the formation of gall-stones have a centre in the study of the physicochemical properties of bile-salts [1] The characteristics of the molecular arrangement play a significant part in the solubility of cholesterol in the bile, leading to experiments which study the queer and unstable cholesterol/bile salt relationships pH plays a significant part in this. the influence of fatty acids in different forms is about to be studied

This train of thought for future research was accelerated by a visit abroad last year Christensen and Dam in Copenhagen have demonstrated the formation of gall-stones in hamsters [2,3] To me, two things were of special interest Firstly the gall-stone-producing diet is a poor almost starvation, diet Secondly, prevention of gall-stones in hamsters lies in some factors present in certain seeds and nuts which are not subjected to mutilation and possible hydrogenation Brewer's yeast seems particularly efficacious Christensen has noticed the skin conditions that these creatures may also suffer from, and its prevention by these fresh foods He also showed me alteration in the colour and texture of the affected animals' hair, which reminded me of the clinical adage "fair. fat and forty"

Fair, fat, female fecund and forty" is proving to be an uncertain guide, for in surgical practice we are seeing increasing numbers of elderly thin, often male sufferers Perhaps safer anæsthesia has increased the numbers that nowadays come to the surgeon It is plain that thin and fat, old and middle-aged people get gall stones It is difficult to go into the dietary habits and histories of patients with gall-stones, for people cannot remember what they eat However, I have been impressed by a number of patients (well covered) who have disclosed their attempts to diet by periods of near starvation While I was in Scandinavia I found that the same

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1 Rains A J H *Gastroenterologia Basle* 1955, 83, 18
2 Dam, H Christensen F *Acta path microbiol scand* 1952 30 236
3 Dam H Christensen, F *Acta physiol scand* 1954 31, 75

TABLE IV—RESULTS OF EXAMINATION FOR TUBERCLE BACILLI

Group	At start		At 3 mos		At 6 mos	
	Total patients	No +ve	Total patients	No +ve	Total patients	No +ve
Males						
Inpatients	34	29	34	9	23	6
Outpatients	33	30	33	9	22	4
Females						
Inpatients	37	33	37	9	22	4
Outpatients	37	33	37	10	24	5

respectively 2 1 and 1 4 lb of the weight they had gained at three months It is worth noting that 18 of the 37 female outpatients were married and the majority continued to run their households throughout treatment, whereas 28 of the 33 male outpatients, although ambulant, remained off work for at least the first three months

Bacteriology

Each patient was asked to submit specimens of morning sputum on three consecutive days immediately before the start of treatment and at three monthly and six monthly intervals These specimens were examined for tubercle bacilli by direct microscopy Bronchial lavage (Lees et al 1955) was also performed at these times and the specimens obtained were examined by direct microscopy and cultured The results are shown in table IV

TABLE V—ZONES OF LUNG INVOLVED RADIOGRAPHICALLY AT START OF TREATMENT

Group	Number of lung zones involved						Total patients
	1	2	3	4	5	6	
Inpatients	13	28	18	12			71
Outpatients	11	14	26	15	3	1	70

A positive result signifies the finding of the tubercle bacillus by either sputum or bronchial-lavage examination or both Some patients were unable to submit enough sputum for adequate examination, but a satisfactory specimen was always obtained by bronchial lavage The inpatient and outpatient groups were well matched as to bacteriological status at the start of treatment, and the proportions in the two groups showing sputum conversion at three months and at six months were almost exactly the same

TABLE VI—ZONES OF LUNG CLEARED AFTER THREE MONTHS' AND AFTER SIX MONTHS' TREATMENT

Group	After 3 mos		After 6 mos	
	Total patients	Zones cleared	Total patients	Zones cleared
Inpatients	71	20	45	32
Outpatients	70	2[illegible]	46	27

Radiography

The radiographic appearances were assessed by a radiologist who was unaware to which group the patients belonged Table V shows an analysis of both groups o patients according to the number of lung zones involve It will be seen that in many cases the lungs were widel affected and that the outpatients, as a group had mo extensive disease Table VI gives the number of lun zones which cleared in each group of patients after thr months and after six months If anything, more zon had cleared in the outpatients than in the inpatient but the outpatients, as a group, had more zones involve initially

TABLE VII—CAVITY CLOSURE AFTER THREE MONTHS' TREATMENT

Group	Total no of patients	No with cavitation at start	No with cavity closure at 3 mos
Inpatients	71	43	13
Outpatients	70	44	12

Cavitation

In assessing the position as regards cavitation, t cavities were measured at the start and again at thr months and six months Table VII shows the number o patients with measurable cavitation at the start an after three months' treatment, small, multiple cavitie are not included

TABLE VIII—CAVITY CLOSURE AFTER SIX MONTHS' TREATMEN

Group	Total no of patients completing 6 mos treatment	No with cavitation at start	No with cavity closure at 6 mos
Inpatients	45	31	20 (64 5%)
Outpatients	46	33	15 (45 4%)

43 of 71 inpatients and 44 of 70 outpatients had measurable cavities at the start of treatment, and afte three months cavity closure had taken place in 1 inpatients and 12 outpatients

TABLE IX—CLOSURE OF INDIVIDUAL CAVITIES AFTER SIX MONTHS' TREATMENT

Group	Total no of patients	No of cavities at start			No of cavities closed at 6 mos
		Total	<2 cm	> 3 cm	
Inpatients	45	36	17	19	26 (7
Outpatients	46	44	23	21	26 (59

Table VIII shows the number of patients who, having completed six months' treatment, showed cavity closure

At the start 31 of 45 inpatients and 33 of 46 outpatients had cavitation, and after six months' treatment 20 (64 5%) of the inpatients and 15 (45 4%) of the outpatients showed cavity closure

The cavity position in the patients who completed six months' treatment is further analysed in table IX

TABLE X—OVERALL RADIOGRAPHIC ASSESSMENT

Group	Deterioration	No significant change	Improvement			Total patients
			Slight	Moderate	Excellent	
At 3 months						
Inpatients	1	4	8	26	32	71
Outpatients	1	2	11	24	32	70
At 6 months						
Inpatients	2	4	2	18	19	45
Outpatients	2	5	6	10	23	46

This shows that the 45 inpatients had 36 cavities (17 of 2 cm or less in diameter, and 19 greater than 2 cm), whereas the 46 outpatients had 44 cavities (23 of 2 cm or less in diameter and 21 greater than 2 cm) After six months' treatment 26 (72 2%) of the inpatients' cavities had closed, compared with 26 (59%) of the outpatients' cavities

Over all Assessment of Radiographic Changes

The radiographic appearances at three months and at six months were assessed in the categories of (a) deterior

The particular advantage of this method of treatment is its extreme simplicity, which eliminates all the discomforts and inconveniences of starvation and purging necessary when mepacrine or male fern are used, and enables the patient to be treated in his home with little or no interruption of his ordinary activities.

Dichlorophen was supplied by Dr Robert Forgan, of Messrs May & Baker Ltd.

Liverpool School of Tropical Medicine D. R. SEATON

BURNS AND SCALDS

SIR,—The dermatologist, whose opinion is sometimes sought by a surgical colleague, will read with interest and benefit your leader last week.

Most dermatologists, however, would disagree strongly with this recommendation to the family doctor: "Before the development of blisters an anti-histamine ointment may minimise the reaction." It is the experience of many dermatologists that the anti-histamine ointments are rapidly displacing topical sulphonamides and penicillin as the commonest cause of treatment-induced contact dermatitis.

In those cases of burns which can be treated at home, or by a casualty department, a 1% greasy hydrocortisone ointment combined with neomycin is a pain-relieving and safe application. If used early it may prevent blister formation and should guard against secondary infection. It has proved to be a most useful first-aid application in a casualty department where dermatological advice was requested on this problem.

Hove, Sussex PATRICK HALL SMITH

TREATMENT OF TETANUS

SIR,—Professor Lassen and his colleagues are to be commended for their interesting paper (April 28). It is only within recent years that cases of severe tetanus have survived long enough to exhibit bone-marrow depression, which has been reported in a number of recent papers.

There are three factors that are most likely to be responsible: the tetanus toxin, muscle relaxants, and sedatives, including nitrous oxide. In their paper, Lassen et al. present us with some interesting, although inconclusive, evidence that nitrous oxide may be the causal agent.

This problem can be elucidated further only by attempting to separate these three factors. For this reason, I wish to mention a case of a man, aged 49, with infective polyneuritis (shortly to be reported in full).

This patient received intermittent positive pressure respiration for seventeen days until his own respiratory efforts were adequate. Throughout this period narcosis was maintained with nitrous oxide in concentrations varying from 50% to 75%, with oxygen. At no stage did his peripheral blood counts exhibit any signs of bone marrow depression.

I am sure that other workers may have similar cases where neither a toxin nor muscle relaxants need be considered. Such cases should be reported so that the dangers of nitrous oxide can be evaluated.

Meanwhile, I feel that neither the muscle relaxants nor the tetanus toxin itself can be completely absolved as a cause of the bone marrow depression reported in some recent cases of tetanus.

Department of Anæsthesia,
Royal Melbourne Hospital,
Victoria, Australia. PATRICIA WILSON

RESIN-REINFORCED PLASTER CASTS

Mr N. P. NEWTON, of Smith & Nephew Ltd., writes:

With reference to the last paragraph of the letter last week from Mr D. F. Thomas, it is not the intention of my company to withdraw from the market 'Gypsona' or 'Glassona.' Gypsona 'Extra' polymer reinforced plaster of paris bandages are complementary to our other splinting materials and not necessarily a replacement.

Personal Papers

TWENTY-THREE YEARS AFTER

IN his essay on child guidance in Old Age,[1] Professor Mackintosh mentioned that in his early 40s he wrote himself a warning letter not to be opened until his 65th birthday. When that day came, he duly unsealed the envelope; and this is what he found:

6th March, 1933.

My dear MACKINTOSH,

I hesitate to call you by your Christian name, because I do not know you well enough. All the same, I think you may profit by a few words of friendly advice. Certain undesirable tendencies in your character and outlook are already apparent; and I have little doubt that they will become more marked as you grow older.

In the first place, you will become more talkative. Do try to curb this fault, because it is the early sign of unwillingness to learn from younger people. It will lead you to a final inability to learn anything. Try to be a good listener as you grow older: it is well worth your pains. But you must *really* listen—not just turn your head and make gestures which have become automatic.

Secondly, do not get suspicious of people and their motives; and avoid especially prying into the affairs of young folk, even on the plea (for self-justification) that you can help them. If they ask for help in time of trial, give it in full measure, but don't imagine that the so-called wisdom acquired by you from experience will help *them*, unless they feel the need. They have to live their own lives. They have *their* souls to keep.

Thirdly, do not try to attract sympathy to yourself. Do not pose as the dear old man, in the hope of hearing affectionate murmurs that you are young in spirit. For God's sake be a real person, with a valuation that does not need artificial boosting. There are three qualities that you can develop as you grow older; they are courtesy, tolerance, and integrity, which together make an understanding spirit. By integrity I simply mean that wholeness of spirit that does not scour a narrow chamber. By tolerance I do not mean an easy-going acceptance of everything that is "done." I mean a mind that is still open; a capacity to understand the point of view of others, and especially of the younger ones; a willingness to argue without acrimony, and yet with fire and spirit. By courtesy I mean the ability to put yourself in the place of other people. It is a rare and beautiful virtue, and it needs to be cherished continually.

The main practical thing to remember, however, is that you are now sixty-five and on the point of retirement. For heaven's sake retire and do not persuade yourself that you are a special case. If you have kept mind and body active, a world of new interests lies before you. If not, then you have no business to cling to office, or indeed to any voluntary or other service to which you are attached. Clear out. Do not rationalise by saying that you "want to see this thing through." That is just another barnacle argument; what you really want to do is to cling.

As we grow older, self-criticism tends to become blunted. I know of no better test than the one proposed by George Meredith:

> "You may estimate your capacity for comic perception by being able to detect the ridicule of them you love, without loving them less; and more by being able to see yourself somewhat ridiculous in dear eyes, and accepting the correction their image of you proposes."

Now remember.

Yours faithfully,
[Sgd] JAMES M. MACKINTOSH.

So he replied briefly to his earlier self:

20th February, 1956.

My dear MACKINTOSH,

Many thanks for your letter of twenty-three years ago. I opened it, as you directed, on my sixty-fifth birthday basal excretion on the previous day and the 0–12 hour excretion on the test day.

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[1] Lancet, 1947, i, 659.

Patients Studied

The present results were obtained in the first 98 people tested (excluding vitamin-D-resistant osteomalacia)—i.e., 21 patients in whom there was no reason to suspect metabolic bone disease, 12 patients with definite osteomalacia and steatorrhœa, 17 patients with steatorrhœa but no clear evidence of osteomalacia, 18 patients with osteoporosis, and 30 patients with miscellaneous conditions in which bone disease might be suspected. They were aged 14–67 and were either convalescent from an acute illness—e.g., cardiac infarction, peptic ulcer, acute nephritis, colitis, pneumonia, cerebral thrombosis—or had syringomyelia, early rheumatoid arthritis, hypertension, eczema, backache, or very early ankylosing spondylitis.

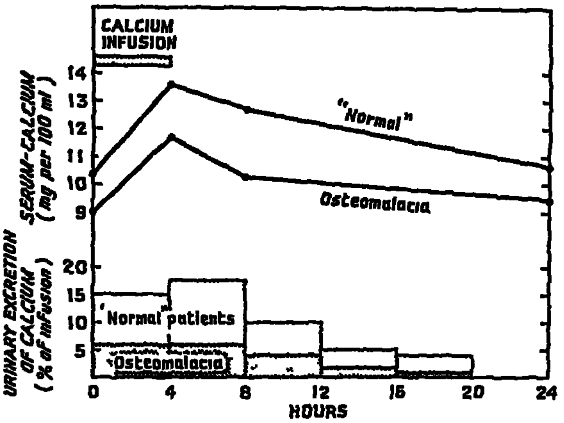

Fig. 1—Changes during test: upper diagram shows mean serum-calcium level during and after calcium infusion in 21 "normal" patients and 12 patients with osteomalacia; lower diagram shows mean urinary excretion of calcium expressed as net percentage of infused calcium (15 mg. per kg. of body-weight).

Patients were classified as having "definite osteomalacia" only if they provided evidence of a cause (all had steatorrhœa and fat absorption less than 90%), presented unequivocal skeletal rarefaction (usually with fractures) on radiography, and had a serum level of calcium × phosphate below 30 mg. per 100 ml. (table I). In almost every case the serum level of alkaline phosphatase was raised, the phosphate/creatinine clearance ratio was high in relation to their serum-phosphate level (Nordin and Fraser 1954, 1956), and biopsy revealed abnormal bone. Clearly some of the patients classed as having "steatorrhœa" may have had milder osteomalacia, but none of them fulfilled all the three criteria laid down above.

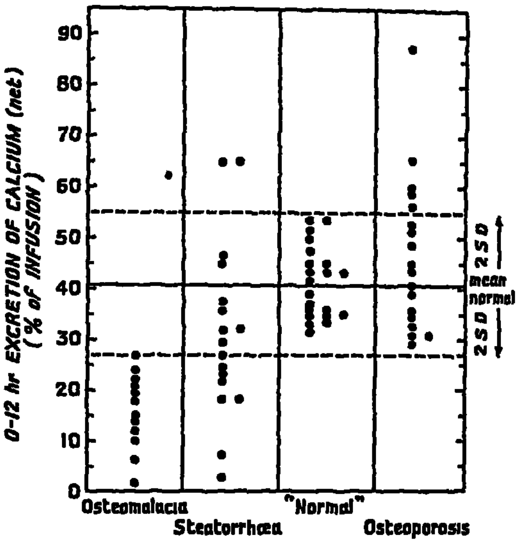

Fig. 2—Individual results obtained after calcium infusion in four main groups of patients.

Normal range, shown between broken lines (27–55%), embraces two standard deviations above and below mean normal excretion of 41% in 12 hr. Note subnormal results in all cases of osteomalacia and 8 of 17 cases of steatorrhœa. See table III for results in miscellaneous cases.

Patients were classified as having osteoporosis if they had definite rarefaction of the vertebral column (usually with "codfish" deformity and crush fractures) without other evident cause—i.e., with normal serum levels of calcium, phosphate, phosphatase, and protein and a normal blood picture.

Results

CHANGES OBSERVED DURING TEST

Fig. 1 shows the mean rise in serum-calcium level and the mean urinary calcium in 21 "normal" patients and

TABLE I—DETAILS OF CASES OF DEFINITE OSTEOMALACIA TESTED

Case no.	Diagnosis	Level in serum (mg. per 100 ml.)			Alkaline phosphatase	Cp/Ccr*	Radiological findings	Bone-biopsy findings	Ca test (0–12 hr excretion net %, of amount infused)
		Calcium	Phosphorus	Ca × P					
1	Cancer of pancreas	9.4	1.8	17	26°	0.5	Milkman fractures	Large osteoid seams	[illegible]
2	Obstructive jaundice	10.2	2.4	25		0.20	Thin bones	Possible osteoid seams	21.0
3	Obstructive jaundice	10.0	2.6	26		0.32	Vertebral collapse. Rib fractures	Possible osteoid seams	[illegible]
4	Idiopathic steatorrhœa	7.7	2.6	20	23	0.26	Multiple fractures ribs, long bones, pelvis	Large osteoid seams	[illegible]
5	Idiopathic steatorrhœa	8.1	2.2	18	11°	0.40	Vertebral collapse	Possible osteoid seams	20.8
6	Short circuit	9.3	2.6	24	20°		Very thin bones	Possible osteoid seams	[illegible]
7	Idiopathic steatorrhœa	8.9	1.9	17	16°	0.40	Multiple fractures. Milkman fractures	Large osteoid seams	[illegible]
8	Obstructive jaundice	9.1	2.3	21		0.20	Very thin bones	Probable osteoid seams	14.9
9	Obstructive jaundice	10.0	1.6	16		0.36	Thin bones	Large osteoid seams	13.2
10	Gastro-enterostomy	7.5	2.2	16	8.6°	0.25	Multiple fractures. Milkman fractures	Large osteoid seams	10.2
11	Fibrocystic disease of pancreas	9.2	2.9	27	39°	0.22	Very thin bones	Possible osteoid seams	[illegible]
12	Hepatic jaundice	7.9	3.4	27			Thin bones. Metatarsal fracture	Occasional large osteoid seams	[illegible]

* Ratio of clearance of creatinine to clearance of phosphate (see Nordin and Fraser 1954).

difficulties and problems Her own experiences of life and particular qualities of temperament gave her a special insight into such matters so that as a medical adviser she possessed a value quite unique and all her own

"She wrote with apparent facility What she had to say in popular language on all aspects of family life and planning, on sex difficulties and women's ailments deserved—and found—a wide public Indeed, some of her small books have rightly become best sellers The Family Planning Association has good reason to be grateful for all the time and hard work she devoted to its cause, for she was among the pioneers in this field

"But when all is said her most outstanding and endearing quality was a tenderness of heart that found expression in a desire both passionate and practical to help those in distress Though quite the reverse of a tough guy, she possessed a philosophy that enabled her to endure her own illnesses with equanimity and an obstinate courage that kept her in London throughout the war Her last journey—to New Zealand to do an exchange practice for six months—was just one more example of the valiant way in which she faced and grappled with disabilities and fears"

Dr Malleson was formerly the wife of Mr Miles Malleson, the actor Their two sons are both doctors

Diary of the Week

MAY 27 TO JUNE 2

Monday, 28th

MANCHESTER MEDICAL SOCIETY
9 P M (Medical Library Manchester University) *Section of General Practice* Dr H W Ashworth Dr N P Chamarette Psychosomatic Medicine

Tuesday, 29th

WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, St Mary's Hospital Medical School, W 2
5 P M Dr R E O Williams The Numbers and Significance of Bacteria in Air

ROYAL STATISTICAL SOCIETY
5 30 P M (Westminster Medical School Horseferry Road S W 1) *Medical Section* Dr A. C Dornhorst Dr J R Bignall Mr M P Curwen Should Research be Based on Routine Hospital Records ?

Wednesday, 30th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W 12
2 P M Prof A W Downie, F R S The Incubation Period in Infective Disease

ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P M Mr T N A Jeffcoate Forceps Delivery

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
11 A M (Queen Charlotte s Hospital Goldhawk Road, W 6) Miss Josephine Barnes Habitual Abortion

INSTITUTE OF DISEASES OF THE CHEST Brompton S W 3
5 P M Dr J G Scadding Trends in the Treatment of Pulmonary Tuberculosis

Thursday, 31st

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln s Inn Fields W C 2
5 P M Mr Eric Samuel The Anatomy of the Bile Ducts in Relation to the Post-cholecystectomy Syndrome (Hunterian lecture)

UNIVERSITY OF LONDON
5 P M (St Thomas s Hospital Medical School S E 1) Prof E Rothlin (Basle) The Pharmacological Basis of the Action of Lysergic Acid Diethylamide on Brain and Mind

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr C M Fletcher Morbid Effects of Atmospheric Pollution

GUY S HOSPITAL MEDICAL SCHOOL London Bridge S E 1
5 P M Prof Charles Rob The Place of Direct Surgery in the Treatment of Obliterative Vascular Disease (Carbutt Memorial lecture)

INSTITUTE OF NEUROLOGY, National Hospital Queen Square, W C 1
5 P M Dr Israel S Wechsler (New York) Some Clinical Hypothalamic Syndromes

HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place Edinburgh) Mr T McW Millar Some Problems in the Surgery of the Bile Ducts

UNIVERSITY OF ST ANDREWS
5 P.M (Queen s College Small's Wynd Dundee) Prof C de Duve (Louvain) Biochemical Properties of Isolated Cell Constituents

Friday, 1st

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
9 30 A.M *Neurology* Combined meeting with the Société Belge de Neurologie

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M Mr Arthur Jacobs Uretero colic Anastomosis Observations on Long term Survival and Wellbeing After Operation
4 P M Dr C L Cope The Adrenals and Stress

Notes and News

WORLD HEALTH ASSEMBLY

At the ninth World Health Assembly, which opened in Geneva on May 8,[1] the programme and budget committee has approved a budget of $10,700,000 for 1957 [2] The assembly elected the following six member States to serve on the Executive Board of W H O Syria, Mexico, India, Italy, United Kingdom, and Canada The board comprises eighteen members, of whom six retire each year By a vote of 51 in favour and none against, with 5 abstentions, the assembly adopted a resolution designed to facilitate the resumption by inactive members of their rights and obligations in W H O and the settlement of their arrears of contributions Notifications of withdrawal were received in 1949 from the U S S R , the Ukrainian S S R , the Byelorussian S S R , and Bulgaria, and in 1950 from Rumania, Albania, Czechoslovakia, Hungary, and Poland Official contacts between W H O and the U S S R and some of the other inactive members have been re established in the past year. At its meeting last January [3] the Executive Board welcomed U S S R representatives, who explained the position of their government, and expressed its satisfaction at the U S S R 's readiness again to participate actively in the Organisation's work

AN S.H.M O APPOINTMENT

Agreement has not yet been reached in Glasgow over the terms of the appointment of a physician at Bellefield Sanatorium, in Lanarkshire Hitherto the chest services of the area have been provided by consultants centred in Glasgow and by the physician-superintendent at Bellefield who was also a consultant Now that the latter has retired, the Western Regional Hospital Board propose to replace him by a senior hospital medical officer, in the position of superintendent, and to ask one of the Glasgow consultants to act in a supervisory capacity , the vacancy is announced in our advertisement columns this week The regional consultants and specialists committee has not so far been persuaded that the proposed arrangement is justified

NUTRITION RESEARCH AT COONOOR

The annual report for 1954–55 of the Nutrition Laboratories of the Indian Council of Medical Research at Coonoor is a record of steady activities The laboratories now have a research staff of 33, who are clearly maintaining the high standard of work at Coonoor

Studies of vitamins include the development of a fluorometric method for vitamin A assay and an examination of the effect of vitamin D on the metabolism of rachitic epiphyseal cartilages, in which it was shown that vitamin D caused a 100% increase in the citric acid content of the cartilage in twenty four hours Studies on proteins have been concerned with estimations of essential amino acids in common Indian food by microbiological techniques and with the combined effect of calorie and protein deficiencies on the enzyme contents of the organs of rats Human experiments on the maintenance requirements of protein in young Indian adults indicate that these are similar to those of Americans studied by Merlin Detailed quantitative analyses have been made of the octadecanedioic acids present in cow and buffalo fat and in vasaspati Clinical investigations have been carried out on kwashiorkor, with particular relation to the cause of the œdema Field investigations have shown that, whereas the skeletal age of well to do Indian children, determined radiologically, usually compares well with American standards, in half the poor children the appearance of ossification centres of bones of the wrist and hand was delayed by a year or more

THE FARMER AND THE TOWNSMAN

The increasing numbers of town dwellers in every country easily forget how dependent they are on the farmers for their food Farming may seem a dull and unexciting occupation in comparison with much of modern industry with its mechanical marvels , and, as an excellent F A O booklet clearly points out,[4] in every country the average income of the people on the farms is less than that of the people in industry and commerce For these reasons farming is failing to attract the without intervening therapy The results obtained in the two tests agreed closely as follows

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[1] See *Lancet* May 19, 1956, p 758
[2] *Times*, May 22, 1956
[3] See *Lancet* Feb 4, 1956, p 251
[4] Agriculture in the World Economy Rome, 1955 Pp [illegible] Obtainable from H M Stationery Office 5s

Case no	Diagnosis	0–12 hr net calcium excretion 1st test	0–12 hr net calcium excretion 2nd test
13	Osteoporosis	43% *	44% *
14	Rheumatoid	35%	34%
15	Pyelonephritis with renal failure	6%	6%
16	Renal stones	50%	46%
17	,, ,,	43%	41%
18	,, ,,	56%	53%
19	,,	31%	29%

*Gross calcium excretion given because basal excretion not measured

Value of Test

It may be suggested that measurement of the 24 hr urinary calcium on a low calcium diet could yield as much information as a calcium infusion We have not found this to be so Fig 3 shows the 24 hr urinary excretion of calcium on the third day of the low-calcium diet for comparison with fig 2 The separation of osteomalacia from the normal state by the calcium infusion was clearly not obtained by measurement of urinary calcium alone, nor did the separation improve when the figures were corrected for body weight It is possible that better separation could be achieved if the diet were continued for a considerably longer period, but the wide range of 24 hr urinary output of calcium on a low-calcium diet in our ' normal " patients (fig 3) is similar to that reported by Albright et al (1929)

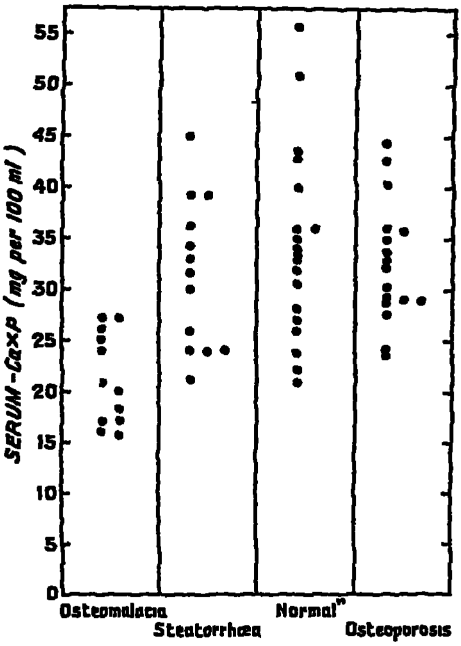

Fig 4—Serum calcium × phosphate levels (same groups as in fig 2)

Note less satisfactory separation of groups by these estimations compared with fig 2

Similarly, we have not found that the serum level of calcium × phosphate is a sufficiently sensitive guide to the state of the skeleton By definition, all our osteomalacia cases had a serum calcium × phosphate level below 30 mg per 100 ml, but fig 4 shows that some " normal ' patients also had a level below 30 mg per 100 ml These values were obtained from samples of blood taken at 10 A M on the day of the test

We do not suggest that this infusion test is infallible in the diagnosis of osteomalacia, nor that it will supplant other forms of investigation, but we believe that in doubtful cases it may provide additional evidence for or against a diagnosis of osteomalacia

Summary

A standard procedure is described for a calcium-infusion test and the results of the first 98 tests are reported

The calcium is administered as the gluconate over four hours in physiological saline solution The dose is 15 mg of calcium per kg of body weight

The net urinary excretion of calcium during the first twelve hours after the start of the infusion was 33–53% in 21 " normal " patients and 2–27% in 12 patients with definite osteomalacia due to steatorrhœa

Of 17 other patients with steatorrhœa 8 yielded results in the osteomalacia range Other evidence suggests that these probably had subclinical osteomalacia

In 18 cases of osteoporosis the excretion was invariably within or above the normal range

30 tests in various other conditions in which bone disease might be suspected yielded low excretion figures in 10 6 of these could be explained by the underlying metabolic disorder, the other 4 remain unexplained

We wish to acknowledge with gratitude the assistance of Dr A Jadresic, Miss Elaine Hunt, Miss Sheila Stewart, and the sisters and nurses of Hammersmith Hospital

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A CALCIUM-INFUSION TEST

II "FOUR-HR SKELETAL RETENTION" DATA FOR RECOGNITION OF OSTEOPOROSIS

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In a previous paper (Nordin and Fraser 1956) we reported the pattern of urinary excretion of calcium after a standard infusion in " normal " patients and in certain types of metabolic bone disease As predicted by earlier workers (Schilling and Laszlo 1951), we found that the urinary excretion of infused calcium was low in osteomalacia due to steatorrhœa, but in only a few cases of osteoporosis was this excretion abnormally high

Since this test therefore failed to differentiate between osteoporotic and ' normal " patients, we decided to elaborate the procedure further We have measured at the end of the infusion not only the net or excess urinary output of calcium, but also the excess calcium still circulating in the extracellular space We considered that this method would enable us to calculate the proportion of the infused calcium deposited in the skeleton—i e, that in neither of these two measured pools (urine and extracellular fluid)—and that this might be low in osteoporosis

We report here the results obtained with this calculation of ' skeletal retention "

Methods

Procedure

The calcium infusion procedure has been described elsewhere (Nordin and Fraser 1956) The estimations required for the ' skeletal retention " data are the basal

CHANGES IN MEDICAL EDUCATION*

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CHANGES in medical education are of two types. Either they are made deliberately to improve it, or they arise incidentally from changes in medicine and its basic sciences or in the conditions of medical practice. Such secondary changes, as we may call them, are frequent and inevitable but not always beneficial. Primary changes are necessary from time to time to incorporate new methods and techniques, but they are even more urgently needed to reorientate the educational processes to new objectives and to repair the damage done by secondary changes.

During the past half century medical teachers and official bodies have made careful and repeated assessments of these changes, and there has been no lack of recommendations on the reform of medical teaching. Some of these have been heeded and put into effect, but in recent years there has been increasing evidence that the process of adaptation has broken down. Whilst most are aware of what is wrong, few are agreed on how to put it right. To quote from a recent report of the Royal College of Physicians: "An American observer lately said that in the past ten years no country has produced so many wise reports on the improvement of medical education as Great Britain, and no country has done so little about it."[1]

My purpose here is to review the changes in medical education—particularly during the past decade—and to consider the further changes now required.

Evolution of British Medical Education

Until about the middle of the past century the training for medicine was entirely by personal apprenticeship. It was in the literal sense a "training," primarily technical and wholly vocational. The method was not appreciably altered even by the grouping of students in hospitals. The relationship of teacher and taught became less close, but the student continued to learn by imitation of his master and by practice for and under him. He continued to learn everything that was practised and very little that was not.

In the second half of the century scientific advance led to a fundamental alteration in medical education by necessitating the inclusion of theoretical study: the scope of medicine enlarged so much that fitness to practise could no longer be achieved by a purely technical and vocational training, but needed also the discipline of the basic sciences. This was a fundamental and primary change, but its implications have never been fully recognised by the profession as a whole. Hence we have been pursuing an educational policy whose very purpose has been neither clear to all nor accepted by all. Because of this basic defect in our educational strategy, there has been no concerted effort on an agreed plan, and such facilities as we possess have not been properly applied.

The 'Block System'

Whatever the reasons (and perhaps the English gift for compromise was not the least of them), we adopted a system of training divided into two parts, one largely theoretical and the other largely practical. This block system, very different from that which emerged on the Continent, continues to this day, the blocks being accurately described as preclinical and clinical. The objective during the preclinical period has been to lay the foundations for clinical practice. But with the progress of medical thought two weaknesses have been exposed. Firstly, the ancillary subjects added to the curriculum fifty years ago no longer provide a complete foundation; and secondly the idea of a foundation has been taken too literally—i.e., as something that is laid down and allowed to dry. A more satisfactory concept would be that of girders which rise vertically through the whole structure.

Fifty years ago the idea of medical education being built up layer by layer was entirely reasonable. Even thirty years ago it seemed adequate, and Flexner, in his comparative study of medical education throughout the world, described it in 1925 as the best that he had seen. But its deficiencies were beginning to be apparent, and he was critical of its application. He thought that the concept of normality gained by the student in the preclinical period suffered from the vocational character of the teaching. (It should be remembered that at this time the link between preclinical and clinical staff was very close: some of the heads of preclinical departments had themselves been engaged in medical practice, and most of the junior preclinical teachers were practising clinicians.) Similarly in clinical medicine he condemned the utilitarian approach. "Listening to a succession of bedside expositions," he wrote, "not infrequently quite chatty in substance and tone, one is struck by the positive note. . . . rarely is the unknown, the problematic, the profounder question, the historic background, attended to."[2] Yet he felt that the British student learned clinical medicine as an intelligent apprentice, one who "in virtue of previous training, is soon capable of orderly procedure in the analysis of symptoms, the arrangement of data, and the drawing of tentative conclusions." He recognised that the supreme strength of British medical education still lay in the careful inculcation of clinical method, and he saw too that this came less from teaching than from constant practise upon patients—freedom to practise clinical method, while having an obvious obligation to the patient as an incentive for doing so. The British student was then "indeed part of the functioning machine."

The Effects of the Growth of Medicine

In the thirty years since that time our educational system has altered very little—but our educational practice has been continuously subjected to *secondary* changes, so that it has altered almost out of recognition. Most of these changes have arisen from the growth of Medicine.

Preclinical teaching.—Scientific advance has added enormously to knowledge: the so-called basic sciences have swollen, reproduced as it were by binary fission, and swollen again. In anatomy a whole new field of living structure has been opened up in twenty years, and the dry bones of topographical anatomy have been agitated by the study of embryology. Physiology has spread so far and wide that it is not clear what is left at the centre. Like biochemistry, and indeed anatomy, it runs from the foundations upwards through the whole medical edifice. These are no longer subjects of which some elementary knowledge is useful for the comprehension of practical techniques—they are processes of thought which are indispensable if the mind is to be brought to bear efficiently upon any medical problem, whether that of an individual patient or of research.

But the student's experience of the preclinical subjects remains cramped between the old limits, not only of time but also of examinations. Confined and isolated between the first and second professional examinations,

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* The Goulstonian lectures for 1956 delivered before the Royal College of Physicians on Jan. 17 and 19.

[1] Royal College of Physicians. Second Interim Report of Medical Teaching Committee. *Lancet*, 1955, i, 133.

[2] Flexner, A. Medical Education. New York, 1925; pp. 58, 241.

(E) *Miscellaneous*

The "4-hr skeletal retention" in this group of patients was 31–59%. Thus none was above the normal range, but the following were below it:

(1) Malnutrition	17%
(2) Acromegaly	16%
(3) Polyostotic fibrous dysplasia	15%
(4) Vertebral compression fractures (unclassified)	41%
(5) Renal calculi	38%

COMPARISON OF "4 HR SKELETAL RETENTION" WITH 0–12 HR URINARY EXCRETION

The relationship between these two types of test result is shown in fig. 2, which shows that in 1 of the "normal" patients the 0–12 hr urinary excretion was less than the lower limit (27%) of the normal range which we have defined in our previous paper; this we cannot explain. The normal range of "4 hr skeletal retention" is slightly narrower than the range of 0–12 hr urinary excretion, and this suggests that the more complicated calculation is more precise.

Fig. 2 also shows that in most of the tests the "4-hr skeletal retention" and the 0–12 hr urinary excretion of calcium together usually accounted for 95% (85–105%) of the infused calcium. Thus, usually, the "4 hr skeletal retention" was about equal to the final total retention of calcium, since later urinary and fæcal losses were small; and so both the "4 hr skeletal retention" and (inversely) the 0–12-hr urinary excretion of calcium usually give a good index of the same function, presumably the final skeletal retention.

While in 11 of the 15 patients with *osteoporosis* the 0–12 hr urinary excretion was normal, in 7 of these 11 the "4 hr skeletal retention" was subnormal. It is these 7 cases in which the urinary excretion data were of no diagnostic value which fact provides the main justification for the rather elaborate procedure described here. 4 osteoporotic patients whose 0–12-hr urinary excretion of calcium was high also had a low "4 hr skeletal retention": 3 of these had Cushing's syndrome and the 4th was a case of post-pregnancy osteoporosis (Nordin and Roper 1955).

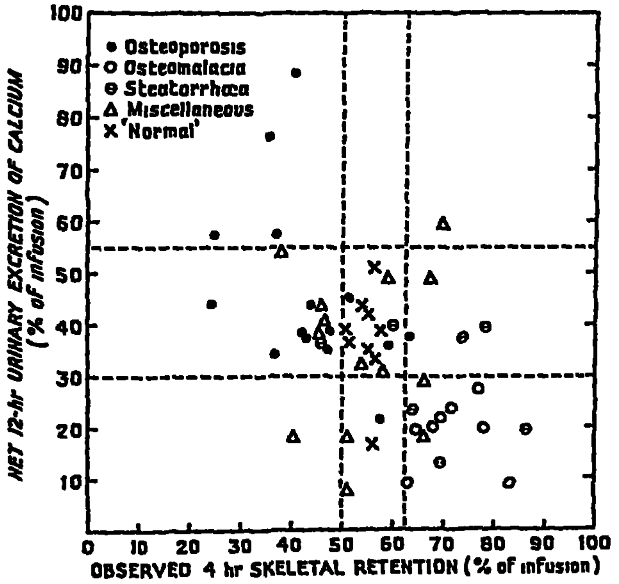

Fig. 2—Correlation between the "4-hr skeletal retention" and 0–12 hr net urinary excretion after calcium infusion.

Note: (1) most results lie within lines enclosing all results where these two figures total 85–105%, so that one figure is usually an inverse reflection of the other; (2) tendency of osteoporotic results to lie towards left of this area (i.e., for 0–12 hr urinary excretion to be more normal than "4 hr skeletal retention"); and (3) while only 4 of 15 osteoporosis cases show excessive urinary excretion, 7 of the other 11 osteoporotics show subnormal "4 hr skeletal retention."

All the patients with osteomalacia were found to have the combination of a high "4 hr skeletal retention" and a low 0–12 hr urinary excretion. 3 patients with steatorrhœa without obvious osteomalacia showed the same combination. 1 patient with steatorrhœa (who had been given intramuscular vitamin D some months previously) showed a combination of low "4 hr skeletal retention" with a normal 0–12 hr urinary excretion, resembling the results seen in osteoporosis.

In only 1 patient (a girl aged 16) with severe hyperthyroidism) was a high urinary excretion of calcium on the test combined with a high "4 hr skeletal retention." The patient with "vertebral compression fractures without evident cause" was unique in that her "4 hr skeletal retention" suggested osteoporosis, while her urinary excretion on the test suggested osteomalacia.

Discussion

We have assumed, for the purposes of the present work, that the infused calcium is ultimately either excreted in the urine or deposited in the skeleton, and that only an insignificant fraction will be lost in the fæces. Previous observations on healthy people (McCance and Widdowson 1939, Baylor et al. 1950) are in accord with these assumptions. Certainly at 4 hours, whatever may happen later, any infused calcium which may have reached the gut will be mostly in the small intestine whose electrolyte contents are normally in equilibrium with the extracellular fluid, and so included in our calculation of the latter's calcium content (Manery 1954).

We have shown that the urinary excretion of infused calcium fell within a fairly narrow range in "normal" patients, and that less was excreted in osteomalacia due to steatorrhœa. In our original series these two groups did not overlap, and we considered that an abnormally low excretion on this test is of diagnostic assistance when this disorder is suspected. The diagnosis of frank osteomalacia, of course, presents no difficulty; but the early diagnosis of incipient cases is impossible at present. Our data suggest that a calcium infusion may serve to distinguish between those cases of steatorrhœa in which osteomalacia is developing and those in which the bones are not so affected. We will be reporting elsewhere in more detail the fact that the urinary excretion in this test is normal in cases of vitamin-D-resistant osteomalacia.

Schilling and Laszlo's (1951) prediction that the excretion of infused calcium would be high in osteoporosis (owing to the failure of the matrix to accept calcium) was not fulfilled (Spencer et al. 1954), and for this there might have been at least two possible explanations: it was quite possible that the osteoporotic skeleton did not differ from the normal skeleton in its ability to accept calcium; but it was also possible that, while the skeleton was rejecting the calcium, the kidneys could not excrete this extra load at a sufficient rate to exceed that of the normals. This suggested that we were perhaps using too large a dose of calcium for our purpose, and that the calcium might be accumulating in the extracellular fluid in the osteoporotic cases. We were reluctant to use a smaller dose of calcium, because of the inevitable increase in the magnitude of the possible error arising from our deriving the excess or net excretion of calcium by deducting the previous day's basal excretion *from* the observed excretion.

Therefore we decided instead to estimate the amounts of calcium circulating in the extracellular space at the end of the infusion, and so to calculate from this and the urinary excretion the proportion of the dose deposited in the skeleton. This calculation showed that in 11 out of the 15 cases of osteoporosis less calcium had been deposited in the skeleton by the end of the infusion than in the "normal" patients. In 7 of these abnormal tests

As so much of the factual knowledge acquired in this manner and for examination purposes is rapidly forgotten, the committee concluded that "while it seems that the educational has been sacrificed to the vocational objective, in fact, neither has been gained." This indeed summarises the situation.

Similar observations were made by a committee of the British Medical Association, and at greater length in the far-reaching study by the Interdepartmental (Goodenough) Committee on Medical Schools. Before considering the changes they proposed and the action that has been taken, it is important to continue the story of changing conditions over the past ten years, for these have had if anything a more serious influence on medical education than all that went before.

The Effects of the National Health Service

The National Health Service has had an entirely unexpected effect on medical education. It is quite clear, both from the special position given to the teaching hospitals and from the Ministry of Health's memorandum in 1950 on the Development of Consultant Services,[4] that the intention was to give high priority to the training of doctors. The boards of governors of teaching hospitals are in fact required to provide special facilities for the clinical instruction of undergraduates, in accordance with the educational policy of the university or medical school concerned.

In the event, however, it has proved financially impossible to implement the plan for establishing consultant centres elsewhere, and the teaching hospitals have become the main regional consultant centres, providing specialist medical care. The effect on the medical schools has varied, being least in the provincial and Scottish teaching hospital groups and in the smaller London hospitals, and greatest in the bigger London hospitals in which specialisation was already advanced in 1948. Everywhere, however, it has become apparent that the educational requirements of the undergraduate teaching hospital are in many ways incompatible with the administrative requirements of a regional consultant centre.

In the first place, the establishment of large diagnostic and therapeutic departments within the teaching hospitals, rather than in associated regional hospitals, has enhanced the distortion of the student's clinical experience, which was already a matter of grave concern. Owing to limitations on new building the expansion of special departments has often been at the expense of general medical and surgical facilities. Segregation of clinical material has increased, and in many fields the clinical experience of the student has lost in breadth and variety, as it has gained in depth and detail. For the special departments have tended to collect rare and difficult cases as well as a disproportionate number of patients attracted by new techniques in surgical treatment. And so the range of cases suitable for undergraduate instruction has progressively contracted.

The changes in teaching-hospital staffs are no less important. Establishment of a special department almost always means the substitution of two specialists for one general physician or surgeon, and there has therefore been a rapid increase in the number of clinical teachers. This access of numerical strength, though obviously of advantage to patients, weakens the cohesion of the teaching team and further reduces the already tenuous contacts between students and staff. For a number of reasons many consultants spend more time at the teaching hospital than before. The development of operative techniques has made the specialist surgeon more dependent on his hospital team, and where private beds are available, private patients have followed the surgeon to the teaching hospital. There is thus a tendency to the geographically full-time status seen in American hospitals. Yet the terms of appointment under the National Health Service have hardly (if at all) allowed the consultant more time or energy for teaching activities, joint consultant rounds, clinical conferences, or tutorial functions. In fact, for most consultants teaching responsibilities are combined with ward rounds or outpatient sessions which are undertaken in contract with the Ministry of Health. Furthermore, the heavy burden of taxation and the shrinkage of private practice have led the young consultant in particular to seek additional sessions at regional hospitals. This has reduced still further his opportunities to meet his colleagues and to take part in those corporate activities of teaching and research which made such a vital contribution to medical education.

These changes have in turn influenced the character of clinical teaching. It is true that some of our wisest teachers have been specialists in some branch of medicine or surgery, and every physician and surgeon must nowadays be a specialist to some extent. A good teacher can teach general principles however narrow his clinical interests. Nevertheless, we cannot ignore the influence of excessive specialisation. Patients are increasingly selected and diagnosis increasingly uses instrumental techniques. The student finds it more and more difficult to gain a sense of proportion. Few clinicians in special departments have a clear conception of the curriculum as a whole, and if they are popular teachers they are all the more likely to contribute to the uneven distribution of emphasis for which the teaching hospitals are justly criticised.

Specialisation also damages the apprenticeship system, because the student is given less and less responsibility. Because of their complexity and importance, operative techniques, postoperative dressings and procedures, and special observation and investigation are carried out by registrars or trained nurses, and the student is reduced to the status of an observer with little sense of participation in the care of the patient or the activities of the medical team. Students tend to become passive listeners instead of active learners and to lose the habit of critical discussion and inquiry.

Many will think that this is an exaggerated picture or that these conditions apply in only a few badly regulated medical schools. I am well aware of the great differences in development and organisation of different teaching hospitals, in both London and the provinces, and I agree that what I have described is not a generally established state of affairs. But the trend is universal, and it has been much accelerated by the development of the National Health Service. The requirements of medical education demand that the teaching hospitals should remain in the forefront of medical progress. To do this they must encourage specialisation and provide the facilities for clinical and laboratory research. But a *balance* must be maintained. Some more authoritative organisation than exists at present must be given the responsibility for preventing or correcting the undesirable side effects on medical education which I have outlined.

Changes in Premedical Education

In the past ten years the field from which medical students have been selected has been considerably widened. Payment of fees and maintenance grants by education authorities has greatly reduced the hardships or stringencies previously imposed by finance. It is probable that these restrictions now operate, if at all, only on the children of those in higher income groups who may be ineligible for the payment of awards they have won. Although it is now easier for many parents, it is harder for those in the professional classes to send their sons or daughters into medicine.

An excess of applicants over places in medical schools has made selection possible. It is, however, very hard

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[4] Ministry of Health. The Development of Consultant Services. London, 1950.

Fig. 4 shows the results obtained with this calculation. The normal range becomes 44–56%. Again 9 of 15 osteoporotic cases retained less than the normal proportion of the dose.

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ROSEOLA INFANTUM

AN ISOLATED OUTBREAK

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A SMALL outbreak of roseola infantum in April and May, 1955, was confined to a single block of married quarters in Kensington Village, then the largest British Army families' cantonment in Fayid, Suez Canal Zone.

Epidemiology

The block of quarters involved in this isolated outbreak consisted of eight rooms forming a long bungalow. A separate stone-built ablutions block stood at the back of the main building, each family having its own bathroom and bucket latrine. The children associated with one another daily. This block was surrounded by other similar blocks at distances of 20–100 yards. Meals were eaten communally in a dining hall. The accompanying table shows the cases.

There was no case outside this block. The source of infection was not found. The only unaffected child living in this block was the eldest (9½ yr.) of three in rooms 6, 7, and 8. Five girls and two boys were affected. No adults were affected. Only one child (case 3) was of school age; he remained at school throughout, not having reported sick. In each family the younger child was affected first, suggesting that incubation may be lengthened by age. Cases 6 and 7 arrived in Fayid from the U.K. on May 1, 1955; they were the last two cases, and pyrexia developed on May 5 and May 8 respectively, a fact which sets a maximum of 4 and 7 days on their respective incubation periods. An incubation period of 2–5 days seems probable for this series as a whole.

Other infectious fevers in the village at the time were measles, scarlet fever, and chickenpox.

Clinical Manifestation

The clinical manifestations were very similar in all the cases. The onset took place with mild pyrexia lasting 2½–3 days, with temperatures of 101–102°F on the first 2 days and 99–100.6°F on the last day. At this stage no further clinical signs were noted except in case 4, who had nasal catarrh and mild conjunctival injection. None had noticeable faucial, palatal, or pharyngeal injection. The children were listless and fretful. On the 3rd day the pyrexia suddenly collapsed after the appearance of the rash. The exanthem was of rose maculopapules 2–10 mm. in diameter. The rash, always discrete and nowhere confluent, began on the face and spread rapidly to the upper limbs and neck and reached the back and abdomen in a few hours. Its maximal spread and intensity were reached within 24 hours. The final distribution was centripetal, the macules becoming very scanty towards the extremities and the hands and feet being free. The greatest concentration of macules was on the face, upper arms, and back. Within a few hours of the appearance of the rash the children all felt perfectly well again, and confinement to bed and house became difficult. Many of the maculopapules were surrounded by a striking zone of pallor giving them the appearance of being encircled by a white ring. This appearance is stated to be pathognomonic of roseola infantum (Zahorsky 1947). The rash faded away slowly in 3 or 4 days, leaving no stain or scaliness of the skin.

DATA ON CASES

Case no.	Room nos.	Age (yr.)	Sex	Date of rash
1	1 and 2	3	F	April 29, 1955
2	5	2	F	May 1
3	1 and 2	5	M	2
4	6, 7, and 8	1¾	M	4
5	6, 7, and 8	2¾	F	6
6	3 and 4	2¾	F	7
7	3 and 4	1	F	11

Discussion

The clinical picture and incubation period are those of roseola infantum, but enlargement of occipital lymph glands, catarrhal tympanitis, and palatal injection described by Clemens (1945), Windorfer (1954), and McQuitty (1955), were absent.

After seeing these few cases I am convinced that this infectious fever is a separate entity—a claim which is often denied. Some workers claim that it is atypical rubella. In this series too it was considered whether a common rubella contact could have caused the outbreak with small variations in the incubation periods; but cases 6 and 7, which were typical, prove that the incubation period of this group was far too short for rubella. The β-hæmolytic streptococcus is also sometimes cited as the cause, but clinically roseola infantum has no resemblance to scarlet fever.

The isolation of this outbreak in a single block is curious and unexplained. Among the young children of the block it was highly infectious; yet it did not spread through the school from case 3 or through the communal dining-hall from any of the cases during the incubation period. This suggests that droplet case-to-case spread is unlikely. Spread through intimate contact alone was a possible explanation. The isolation of the outbreak to the one block led to a search for a common source of infection there. Food or water borne infection was unlikely but could not be entirely excluded. Feeding was communal, and the water-supply came from the same mains as that of surrounding blocks. In these circumstances one would have expected other cases to arise. The block cleaner or one of the adults on the block may have been a carrier or, more likely, the bearer of fomites. The animals in this block consisted of some resident cats and several stray dogs, which spent most of the day there. These again were possible carriers. An alternative to the suggested case-to-case spread by intimate contact is therefore a common undiscovered source in the block.

Summary

A curious and isolated outbreak of 7 cases of roseola infantum is described.

Maximal incubation periods of 4 days and 7 days were found in two cases.

Certain commonly observed signs were absent and no complications were noted.

Roseola infantum is a striking separate entity.

I wish to thank Dr. J. Fleming, late captain R.A.M.C., my colleague at the time, Dr. H. W. S. Francis, late captain R.A.M.C., for suggesting the diagnosis; and Major-General F. J. O'Meara, Colonel M. J. H. Kelleher, and Colonel F. P. H. Lassen for encouragement and invaluable help.

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understand, but yet bearing an unpleasant similarity to those preclinical subjects which he found hard and dry.

So he spends little time methodically obtaining a basis of pathology, and in fact he learns very little for himself. Never having done so before, he hardly knows how to begin; and in any event he finds that he is given a large amount of teaching. Unfortunately the teachers, unlike those he has previously experienced, seem to teach at random—their subjects being in fact dependent on the ever-changing nature of the patients under their care—and, what is worse, teachers now conflict with each other. Medicine seems to be most confusing, and it would be pleasant indeed to escape by busying himself in doing something (however small) for the patients themselves.

Unhappily there is little he can do, and although he must learn about clinical investigations in the abstract he is but rarely considered competent to collect the specimens on which the tests are made, let alone make the tests. Thus he finds himself with almost no apparent responsibility to the patients still described as his; and, relegated to the rôle of observer, he wanders rather disconsolately from department to department, trying to remember as much as possible of the specialised knowledge poured out to him in each by his many teachers. And perhaps he takes the opportunity to see something of life, which he has been too busy to do since he was 16. Now at 21 he plays games again and does those things which many of his non-medical friends have already got tired of doing. Thus he continues, losing heart in medicine from which he drifts further away. A course of pathology may help, and then midwifery brings a most welcome change. At last he seems to be a part of the medical profession—at last he has something to do. He enjoys midwifery. Then quite suddenly he finds that his final examinations are now within measurable distance. His existence is threatened. His financial support may cease if his examinations are not passed. He remembers the very many learned discourses which have gone over his head since he began his clinical studies. Somehow he must now master this vast mass of knowledge, for that surely is medicine.

Appalled at his believed ignorance, and at the size of the task ahead, he cuts himself off from normal life, eschews all that remains of his curriculum which is not obviously or by repute directed towards the passing of his examinations, and struggles to learn what he now thinks is medicine—from books, and from those very "factual" teachers who are happy to give him lists of causes, lists of symptoms and signs, and descriptions of treatments which can be quickly memorised. Somehow or other he manages to pass, sooner or later, an examination which is primarily a test of knowledge but almost never a test of training.

Through this standardised curriculum the student often passes without guidance—one of a group, unknown as an individual. He is subjected to "group" training throughout, and his experience and learning are both affected by the "personality" that his particular group takes on. There are mature and immature, active and passive, interested and uninterested groups.

Fewer and fewer opportunities exist for him to choose some aspect of medicine for more particular study or to carry out some elementary scientific inquiry. As in a factory, he is placed on a belt, and this inexorably carries him through three years of production. He is mass produced, and the end-product is neither the practical doctor, capable of dealing with common problems, nor the young man who has learnt how to learn and has become capable of applying clear thought to clinical findings. Too often it is a somewhat immature young man, with a considerable knowledge of uncoordinated details and a weak understanding of principles; with an insecure foundation in clinical method and small ability for scientific appraisal; ill-prepared for the responsibilities to come, of which he has been made little aware.

This factory differs fundamentally from others in that at each stage of the process, in each department, what is done to the product matters much less than what the product does. Teaching is far less important than learning.

The dean's office keeps the production line moving; the teachers teach (year in year out, without pause for respite, reflection, or assessment of results); but the incentive to learning comes mainly from fear of examinations, and the learning is directed to the accumulation of factual data with which to pass them. This fear is greater than it has ever been before, and so is the body of factual knowledge.

Again, many may think that I have exaggerated. Obviously the picture varies from school to school, but I submit that the trend is in the same direction everywhere—and the direction leads away from the patient. It is only too easy to be unaware of this; for as teachers our period of observation of the individual student is limited, and it gets smaller as the number of teachers increases. Our assessment of the results of education is made, for the most part, on house officers usually selected because they were regarded as the best students. Moreover, it is made during a period of rapid maturation, when enthusiasm is replacing boredom, and the mental infarction of five years is being recanalised.

Attempts at Reform

Having reviewed the major environmental changes which in recent years have reacted, usually unfavourably, on the practice of medical teaching, I turn now to the remedial aspects. What has been done to correct these secondary deviations? Many excellent recommendations were made in the various reports. The most far reaching were those of the 1944 committee of the Royal College of Physicians and of the Goodenough Committee, and some of these found expression in the Recommendations of the General Medical Council in 1947 and in the Medical Act of 1950 on preliminary-registration house-appointments. The General Medical Council was mainly concerned with correcting a number of deficiencies in the clinical curriculum. Thus it recommended that certain special subjects such as social medicine, pædiatrics, and psychological medicine should be given greater emphasis and teaching time. But it was also concerned at the intellectual gap between preclinical and clinical studies and recommended the addition of a three month introductory course transitional between these two phases of training. The majority of medical schools have tried to fulfil most of these demands, and the increase in number and strength of the whole time clinical units, advocated in the college report, has been an undoubted factor in doing so.

The introductory course has, I believe, done much to secure smoother transition between the systematic disciplines of anatomy and physiology and the unsystematic teaching of clinical medicine. It has been the more effective where preclinical and clinical teachers have previously joined forces in clinical demonstrations to illustrate the applications of anatomy and physiology. Nor can one be critical of the greater emphasis which has been placed on social and psychological medicine, for the doctor is increasingly faced with practical problems in these fields. Yet the regrettable outcome of these changes has undoubtedly been to increase the already unreasonable load of instruction with which the student is faced during his clinical years. What is more, the burden has in some schools been increased by special examinations in pædiatrics and psychological medicine.

pressin Other experiments (Falbriard et al 1955) indicated that the secretion of aldosterone was possibly stimulated by corticotrophin

Conclusion

Our experiment demonstrates a homœostatic mechanism affecting the secretion of aldosterone as a consequence of changes in the volume of body fluid This regulation seems to be independent of the pituitary adrenal system Liddle et al (1955) note a diminution of the sodium-retaining factor in the urine of dogs and man after the administration of vasopressin, and they suspect that it is not the serum sodium level but the volume of the body-fluid that influences the secretion of aldosterone Apart from this homœostatic regulation of the production of aldosterone by some volume of body fluid, the production of aldosterone probably also depends on corticotrophin Studies are now in process to establish which fluid compartment may be involved in this homœostatic regulation of aldosterone

Summary

Evidence is presented that the urinary excretion of aldosterone is controlled by some volume of the body fluid

This homœostatic regulation of the secretion of aldosterone is independent of the secretion of corticotrophin, but corticotrophin nevertheless can also influence the secretion of aldosterone independently

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INGUINAL ENDOMETRIOSIS

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In 3 patients seen within five months in the surgical outpatient department of the Hackney General Hospital a fairly confident clinical diagnosis of inguinal endometriosis was confirmed

This rare condition was first reported by Cullen in 1896 Thirty years later Polster, in a collective review of over 1000 cases of endometriosis, found 34 inguinal lesions, including intraperitoneal and the apparently less common extraperitoneal deposits

There was no inguinal localisation in a number of later series (Pumphrey 1937, Moss 1939 Dreyfuss 1940 Colcock and Lamphier 1950), but a very unusual case was included in Sanders's survey (1943) a patient who bled from a sinus opening in the groin during her periods Masson (1945) reviewing 2686 recorded cases of endometriosis affecting 4307 sites found no example of inguinal endometrioma though he noted 2 cases with deposits in femoral hernial sacs Fallon et al (1950) found 1 in 400 cases of external endometriosis and Scott and Te Linde (1950) 1 in 514 cases

In 1954 Daro et al wrote

> In a survey of the 3250 cases of external endometriosis reported during the past 17 years there were only 26 (0 8%) in which the condition was localised in the round ligament and only 13 (0 4%) in which it was definitely demonstrated to be in the extraperitoneal part

This bears out Counsellor's statement (1948) that contrary to what the close anatomical relationship between pelvic organs and inguinal canal would lead one to expect, the latter is one of the rarest sites of endometriosis

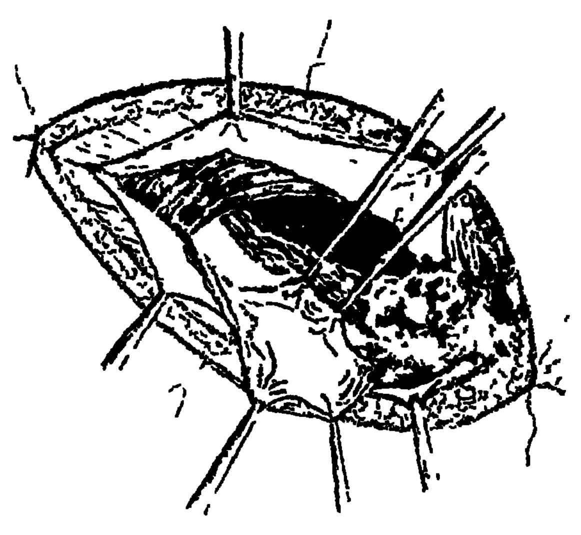

Fig 1—Operative exposure of the inguinal endometrioma in case 1 The canal of Nück has been opened

Among individual cases described in clinical detail are those of Cullen (1920) Sampson (1925) Dickinson (1939) Lyall (1943) Mazza (1949), Rubinstein and Kurzon (1952), Daro et al (1954), and Labry and de Mourgues (1954)

Case-reports

THE FIRST CASE

Mrs A, aged 38 was referred to the outpatient department with "recurrent inguinal lymphadenitis" She gave a fifteen years' history of a painful lump in her right groin which regularly increased in size two or three days before her period At the same time the pain and tenderness became more intense She had already had two courses of injections—one from her own doctor, and one in the casualty department at another hospital—but neither had benefited her more than temporarily

During her most recent menstrual period the pain in her groin had kept her confined to bed for seven days and had reduced her to exhaustion

Apart from the inguinal pain she had never suffered from any form of menstrual discomfort, intermenstrual bleeding, vaginal discharge, backache, or dyspareunia During the past ten months she had noticed a lengthening of the intermenstrual period and a diminishing loss Her general health was excellent

She had one son, aged 17, whose delivery had been normal Three years after his birth she was operated on for a right tubal pregnancy Three years after this she had a miscarriage

Examination

A lower right paramedian abdominal incision was soundly healed and not tender There was moderate tenderness and diffuse induration over the right external inguinal ring but no redness, subcutaneous œdema, or enlarged lymph nodes A faint but definite cough impulse was present in both groins Rectal and vaginal examination were negative The diagnosis of endometriosis of the canal of Nück was made

Operation

Through an inguinal skin-crease incision a grey mass of fibrous consistence the size of a cherry was displayed It overlapped the external ring and was densely adherent to the external oblique aponeurosis the emerging round ligament and the fat of the abdominal fascia The inguinal canal contained an empty indirect hernial sac which reached the fibrous mass and was inseparable from it On opening the sac the glistening peritoneal surface appeared intact (fig 1) The sac was divided and its proximal end closed In separating and removing the distal part together with the fibrous nodule and round ligament small cysts were entered and dark fluid escaped The internal ring was obliterated the inguinal canal reinforced with floss nylon darn the external oblique aponeurosis sutured and the skin closed with drainage

Follow up

The patient made an uneventful recovery Since her discharge she has had several menstrual periods without recurrence of symptoms

TABLE I—SEX DISTRIBUTION AMONG GENERAL POPULATION

Age (yr)	No of men in group	Preponderance of women in general population	Expected no of women
45–49	34	0	34
50–59	95	10%	104
60–69	78	31%	102
70 or more	44	49%	66
Total	251		306

the effect of parity and of weight on the incidence of diabetes The study comprised 1134 patients, of whom 181 were excluded because of inadequate data regarding height or weight at the time of diagnosis Many of the excluded patients had originally attended other clinics, and it was impossible to obtain the necessary information about them Of the remaining 953 patients 583 were women and 370 were men Their ages at diagnosis are shown in fig 1 A preponderance of women is seen among those in whom diabetes is diagnosed in middle and late life

TABLE II—PARITY OF NORMAL WOMEN (MARRIED AND UNMARRIED) AGED 45–49 (1% SAMPLE OF 1951 CENSUS)

Parity	Percentage	Parity	Percentage
0	32 6	4	5 9
1	21 8	5	3 0
2	20 6	6	2 0
3	11 2	7 or more	2 9

If a division is made at the age of 45, there are 106 women and 119 men under this age but 477 women and 251 men over this age An attempt has been made to account for the preponderance of women among the older patients

Sex-distribution among the General Population

Part of the difference is due to the fact that there are more middle aged and elderly women than men in the general population In the age-group 40–49 the sexes are equally numerous, in that of 50–59 there are 10% more women, in that of 60–69 31% more women, and over the age of 70 there are 49% more women These figures indicate that some excess of women would be expected apart from any factor operating selectively (table I) Part of the sex difference in older diabetics is due to the excess of women in the general population at this age

TABLE III—EXPECTED NUMBER OF WOMEN IN EACH PARITY GROUP

Parity	No of women expected	Parity	No of women expected
0	100	4	18
1	67	5	9
2	63	6	6
3	34	7 or more	9
		Total	306

Parity

Figures for the parity of normal women aged 45–49 in England and Wales may be obtained from the 1% sample of the 1951 Census * and are shown in table II

If the 306 women, who would be expected to correspond to the 251 men aged more than 45 among the present group of diabetics, are divided in these proportions, the figures shown in table III are obtained

The numbers in each parity group among the diabetic women are given in table IV

If the observed figures are compared with those theoretically expected (table V), it is found that the excess of diabetic women is confined to those who have borne children, the number of nulliparæ (91) being about that expected (100) The relative excess of women increases with each degree of parity A woman with five children has about three times as much chance of developing diabetes as a woman with none This is represented in fig 2

TABLE IV—PARITY OF 477 WOMEN IN WHOM DIABETES WAS DIAGNOSED OVER THE AGE OF 45 (ONLY LIVE BIRTHS ARE INCLUDED)

Parity	No of women	Percentage
0	91	19 6
1	69	15
2	89	19 3
3	58	12 5
4	44	9 5
5	27	5 8
6	25	5 4
7 or more	60	12 9
Not recorded	14	
Total	477	

It thus appears that parity and the normal difference in sex-distribution among the general population together account for all the excess of women observed in diabetics

TABLE V—COMPARISON OF OBSERVED AND EXPECTED NUMBER OF WOMEN IN EACH PARITY GROUP

Parity	Theoretical no expected	Observed number	Observed/ expected (%)
0	100	91	91
1	67	69	103
2	63	89	141*
3	34	58	171†
4	18	44	244†
5	9	27	300†
6	6	25	417†
7 or more	9	60	667†
Total	306	463	

*P (χ^2) < 0 01 n = 1 †P (χ^2) < 0 001 n = 1

Parity and Age at Diagnosis

Parity does not lead to the appearance of diabetes earlier in life Table VI shows the average age at diagnosis for women aged more than 45 The age at diagnosis is similar for all degrees of parity

TABLE VI—AGE AT DIAGNOSIS OF WOMEN OVER 45 IN RELATION TO PARITY

Parity	No of women	Average age at diagnosis (yr)
0	91	60 4
1	69	59 0
2	89	60 4
3	58	60 6
4	44	60 7
5	27	59 0
6	25	63 7
7 or more	60	63 3

Weight

That the effect of parity on the incidence of diabetes is not merely a reflection of a greater incidence of obesity among multiparæ is suggested by table VII, which shows that about 31% of the nulliparæ are overweight † inch and a half in diameter, spreading over the insertions of the inguinal ligament, the conjoint tendon, and the anterior rectus sheath and densely adherent to the subfascial fat and pubic periosteum. It was of an almost cartilaginous consistence but enclosed three cystic areas which contained pale green fluid; it was associated with an empty indirect hernial sac and a dilated and tortuous pampiniform plexus.

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* Figures are not given for the parity of women aged more than 49 It must therefore be assumed that the parity of women aged more than 49 in 1951 was not significantly different from that of those then aged 45–49

† Overweight is here defined as 10% or more above, and underweight as 10% or more below, the average weight for height and age given by the Association of Life Insurance Directors and Actuarial Society of America in 1912 and cited by Duncan (1952)

The mass, the round ligament, the plexus, and the fundus of the sac were excised, and the posterior wall of the inguinal canal was repaired.

Histological Examination

Endometriosis was seen in an atrophic phase (fig. 3): the glandular clefts were in part denuded of their lining layer; scanty muscle tissue was interspersed with hyalinised patches of fibrosis; and there was but one central area, surrounding a small blood-filled space, which contained macrophages in any number.

Follow-up

Since her operation the patient had two menstrual periods without discomfort. She is completely relieved of her nagging pain.

Discussion

Though endometriosis is increasingly diagnosed in gynæcological departments I could find no mention of the inguinal variety in six standard general surgical textbooks (four British and two American) and two books on diagnosis.

Diagnosis

Despite the characteristic history a preoperative diagnosis is but rarely made.

Hernia.—Hernia was diagnosed in the majority of reported cases.

The patient of Daro et al. (1954) was not only forewarned of impending menstruation by the appearance of the inguinal pain, but she could foretell whether the loss would be slight or heavy by its intensity. Despite this history, and the swelling which appeared with the onset of the period, the condition was thought to be a strangulated omentocele. "As a general rule," reflects Daro, "the symptoms of inguinal endometriosis are rather uniform. . . . However, this condition is so rare that endometriosis is seldom considered as the exciting factor in the train of events."

In Labry and de Mourgues's patient (1954) the "hernia" appeared suddenly after unaccustomed exercise. It was at first easily reducible and freely transmitted the cough impulse.

In all our three patients a patent canal of Nück was present and in two a cough impulse could be elicited. It is also possible, if the endometrioma is small and mobile, to perform a *reduction en masse* into the inguinal canal. Not only may this lead to the wrong preoperative diagnosis, but even at operation the familiar sight of a peritoneal sac may divert attention from a comparatively inconspicuous endometrial nodule.

Inguinal Lymphadenitis.—Novak (1947) pointed out the pitfall of enlarged inguinal lymph-nodes. As the painful endometrial swelling tends to disappear at the end of each period, spurious cure follows any treatment; and when an antibiotic has been used, this is regarded as proof of its infective origin. Only the first of our patients mentioned spontaneously that her attacks coincided with her periods; the other two had not connected the two events in their own mind.

Unlike inguinal lymphadenitis with its multiple nodules, inguinal endometrioma usually presents as a solitary lump, or, in the quiescent state, as diffuse induration rather than as a well-defined mass.

Varicocele of the round ligament.—I recently operated on a patient who gave a history of a painful lump in the groin which had appeared three times with the approach of menstrual periods and had disappeared each time shortly after the bleeding had stopped. In the groin she had an ill-defined, partially reducible, tender swelling which transmitted the cough impulse. Exploration for yet another case of endometriosis revealed a tortuous and partially thrombosed pampiniform plexus.

Though uncommonly diagnosed, this condition is not rare, and it shares with endometrioma a periodicity of symptoms which is governed by the menstrual cycle. Varicoceles may become painful and prominent in the premenstrual phase, as they do during the first few months of pregnancy; and thrombosis in the dilated veins results in a firm, tender, irreducible swelling (Tomkinson and Winterton 1955).

Pathology

Three forms of inguinal endometriosis have been described.

1. Sampson (1927) in a classical paper advanced endometriosis of hernial sacs as one of his arguments in favour of his "spill" hypothesis. This intraperitoneal variety—which includes endometriomata arising from cysts of the canal of Nuck—could also be derived from endometrial islands in the peritoneal serosa (Ivanoff 1898, Meyer and Kitai 1924).

2. Less commonly, endometriomata are found extraperitoneally. In our 3 cases, though hernial sacs were present, careful naked-eye and microscopic examination revealed no continuity between the intact peritoneum and the endometrioma. For this group "endometriosis of the round ligament" is a description *faute de mieux*: in our sections this structure was clearly defined, but in none did it contain ectopic uterine tissue.

3. Endometriomata may also appear in the form of lymph-node deposits, supporting in MacLeod's view (1950) the hypothesis of lymphatic spread. Such deposits can be histologically distinguished from the foregoing types by the absence of all muscle tissue.

In our 3 cases one could judge from the microscopic section the approximate phase of the menstrual cycle at which the operation was performed. The inguinal endometrioma removed from a pregnant patient by Rubinstein and Kurzon (1952) showed advanced decidual change.

In these 3 patients—as in 9 out of 12 cases individually reported in the literature—the endometrioma was on the right side.

Treatment

All symptoms were relieved by excision of the endometrioma in our patients, and in view of their age recurrence is unlikely.

Summary

3 patients with inguinal endometriosis were seen within five months in a surgical outpatient department. All 3 complained of a painful lump in the groin which recurred with each menstrual period.

Unless this history is elicited there may be difficulty in distinguishing this condition from hernia, enlarged inguinal lymph-nodes, or a thrombosed varicocele. Any of these may coexist, and distract attention from the endometrioma at operation.

The literature of inguinal endometriosis is reviewed and three pathological types are recognised: an intraperitoneal and an extraperitoneal variety, and the purely endometrial lymph-node deposit.

Like congenital hernias and undescended testicles the condition appears to be commoner on the right side than on the left.

Treatment by excision brought complete relief in all cases.

I should like to thank Mr. J. R. Stead for permission to publish these cases, for guidance and encouragement, and Miss Gladys H. Dodds for helpful criticism and advice.

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BED REST IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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IN 1926 Stocks and Karn claimed to show statistically that patients with pulmonary tuberculosis who were treated in sanatoria fared no better than those who were not, and the controversy arising from this work has continued spasmodically with no clear cut result Most workers in pulmonary tuberculosis know of patients who have overcome their disease without entering a sanatorium This raises the question whether their disease would have been more quickly or more certainly arrested if they had followed the conventional path In other words Is rest in bed really necessary for most patients with pulmonary tuberculosis ? I describe here the preliminary results of an attempt to answer this question

Material and Method

In May, 1954, it was possible to admit to sanatoria only some of the patients with pulmonary tuberculosis in Glasgow, and the remainder were of necessity treated as outpatients From a public health viewpoint this situation was clearly unfortunate, but it did offer an opportunity of assessing the therapeutic value of bed rest It was accordingly decided to admit to hospital every alternate new patient in the Northern area of the city and to treat the others as ambulant outpatients The criteria for acceptance into the trial were that the patient (1) had active pulmonary tuberculosis, (2) was aged 14–54, (3) was not living in lodgings, and (4) was ambulant when first seen Those allocated to inpatient treatment were admitted to the sanatorium within two weeks of diagnosis and were kept on strict rest in bed

TABLE I—AGE DISTRIBUTION OF INPATIENTS AND OUTPATIENTS, BY SEX

Group	Age (yr)				Av age (yr)
	14–24	25–34	35–44	45–54	
Males					
Inpatients	14	11	5	4	29 5
Outpatients	12	11	7	3	30
Females					
Inpatients	24	8	4	2	24 6
Outpatients	17	13	7	1	27 5

The outpatients in the trial were encouraged to remain up and about, and all except 5, who were treated similarly by their own doctors, reported to the hospital for injections of streptomycin Apart from the amount of exercise allowed, the inpatient and outpatient groups had identical investigation and treatment

Altogether 141 patients have completed three months' treatment, and 94 of these have completed six months' treatment In these 94 cases the chemotherapy consisted of streptomycin 1 g and isoniazid 400 mg on the same day twice weekly, and the remaining 47 patients, who have so far completed only three months' treatment, received the same chemotherapy on five days each week 1 male outpatient and 1 male inpatient had to be withdrawn from the trial before three months' treatment was completed because of drug sensitivity and tuberculous empyema respectively, 3 females in the six-month treatment group left hospital between the three and six month periods

Table I shows that the inpatient and the outpatient groups were closely matched in age distribution

Results

Erythrocyte sedimentation Rate

Table II shows the number of patients in each group who had an erythrocyte-sedimentation rate (E S R) greater than 10 mm in the first hour (Westergren) at the three periods of assessment

TABLE II—E S R LEVELS

Group	No completed 3 months' treatment			No completed 6 months treatment		
	Total	E S R >10 mm		Total	E S R >10 mm	
		At start	At 3 mos		At start	At 6 mos
Males						
Inpatients	34	23	10	23	17	3
Outpatients	33	27	8	22	20	4
Females						
Inpatients	37	27	15 −2 preg	22	15	6 −1 preg
Outpatients	37	28	14	24	21	8 −2 preg

Of the 25 female inpatients in the six month treatment group (including 1 who was pregnant), 3 left hospital irregularly between three and six months, so the numbers of patients who actually completed six months' treatment in the various groups are

Males inpatients 23 outpatients 22
Females inpatients 22 outpatients 24

Table II shows that 2 of the inpatients at the three-month stage and 1 at the six month stage were pregnant, and 2 of the outpatients were pregnant at the six-month stage All 5 had an E S R greater than 10 mm, but are not included in the main figures as their pregnancies may have been the cause of the raised E S R Table II shows no significant difference between the groups in regard to E S R response to treatment That the two groups were well matched in initial severity of illness is also shown by the fact that 35 of the inpatients and 31 of the outpatients had an E S R of 30 mm or more at the outset

Body weight

At the start of treatment, both the male and female inpatients were on the average slightly lighter than the outpatients (table III) At three months the male inpatients and outpatients had gained approximately the same weight, whereas the female inpatients showed an appreciably greater gain than the female outpatients At six months both male and female inpatients had gained a further appreciable amount of weight, whereas on the average the male and female outpatients had lost

TABLE III—AVERAGE BODY-WEIGHTS

Group	Average weight (lb) at start	Average gain (lb)	
		At 3 mos	At 6 mos
Males			
Inpatients	127	9	15 5
Outpatients	132 5	8	5 9
Females			
Inpatients	109 2	14 5	21 1
Outpatients	113 4	6 6	5 2

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inch and a half in diameter, spreading over the insertions of the inguinal ligament, the conjoint tendon, and the anterior rectus sheath and densely adherent to the subfascial fat and pubic periosteum. It was of an almost cartilaginous consistence but enclosed three cystic areas which contained pale green fluid; it was associated with an empty indirect hernial sac and a dilated and tortuous pampiniform plexus.

The mass, the round ligament, the plexus, and the fundus of the sac were excised and the posterior wall of the inguinal canal was repaired.

Histological Examination

Endometriosis was seen in an atrophic phase (fig. 3): the glandular clefts were in part denuded of their lining layer; scanty muscle tissue was interspersed with hyalinised patches of fibrosis; and there was but one central area, surrounding a small blood-filled space, which contained macrophages in any number.

Follow-up

Since her operation the patient had two menstrual periods without discomfort. She is completely relieved of her nagging pain.

Discussion

Though endometriosis is increasingly diagnosed in gynæcological departments I could find no mention of the inguinal variety in six standard general surgical textbooks (four British and two American) and two books on diagnosis.

Diagnosis

Despite the characteristic history a preoperative diagnosis is but rarely made.

Hernia.—Hernia was diagnosed in the majority of reported cases.

The patient of Daro et al. (1954) was not only forewarned of impending menstruation by the appearance of the inguinal pain, but she could foretell whether the loss would be slight or heavy by its intensity. Despite this history, and the swelling which appeared with the onset of the period, the condition was thought to be a strangulated omentocele. ‘ As a general rule ’ reflects Daro, ‘ the symptoms of inguinal endometriosis are rather uniform. . . . However, this condition is so rare that endometriosis is seldom considered as the exciting factor in the train of events.’

In Labry and de Mourgues’s patient (1954) the ‘ hernia ’ appeared suddenly after unaccustomed exercise. It was at first easily reducible and freely transmitted the cough impulse.

In all our three patients a patent canal of Nück was present and in two a cough impulse could be elicited. It is also possible, if the endometrioma is small and mobile, to perform a *reduction en masse* into the inguinal canal. Not only may this lead to the wrong preoperative diagnosis, but even at operation the familiar sight of a peritoneal sac may divert attention from a comparatively inconspicuous endometrial nodule.

Inguinal Lymphadenitis.—Novak (1947) pointed out the pitfall of enlarged inguinal lymph-nodes. As the painful endometrial swelling tends to disappear at the end of each period, spurious cure follows any treatment; and when an antibiotic has been used, this is regarded as proof of its infective origin. Only the first of our patients mentioned spontaneously that her attacks coincided with her periods; the other two had not connected the two events in their own mind.

Unlike inguinal lymphadenitis with its multiple nodules, inguinal endometrioma usually presents as a solitary lump, or in the quiescent state as diffuse induration rather than as a well-defined mass.

Varicocele of the round ligament.—I recently operated on a patient who gave a history of a painful lump in the groin which had appeared three times with the approach of menstrual periods and had disappeared each time shortly after the bleeding had stopped. In the groin she had an ill-defined, partially reducible, tender swelling which transmitted the cough impulse. Exploration for yet another case of endometriosis revealed a tortuous and partially thrombosed pampiniform plexus.

Though uncommonly diagnosed, this condition is not rare, and it shares with endometrioma a periodicity of symptoms which is governed by the menstrual cycle. Varicoceles may become painful and prominent in the premenstrual phase, as they do during the first few months of pregnancy; and thrombosis in the dilated veins results in a firm, tender, irreducible swelling (Tomkinson and Winterton 1955).

Pathology

Three forms of inguinal endometriosis have been described:

1. Sampson (1927) in a classical paper advanced endometriosis of hernial sacs as one of his arguments in favour of his “ spill ” hypothesis. This intraperitoneal variety—which includes endometriomata arising from cysts of the canal of Nuck—could also be derived from endometrial islands in the peritoneal serosa (Ivanoff 1898, Meyer and Kitai 1924).

2. Less commonly, endometriomata are found extraperitoneally. In our 3 cases, though hernial sacs were present, careful naked-eye and microscopic examination revealed no continuity between the intact peritoneum and the endometrioma. For this group “ endometriosis of the round ligament ” is a description *faute de mieux*: in our sections this structure was clearly defined, but in none did it contain ectopic uterine tissue.

3. Endometriomata may also appear in the form of lymph-node deposits, supporting, in MacLeod’s view (1950), the hypothesis of lymphatic spread. Such deposits can be histologically distinguished from the foregoing types by the absence of all muscle tissue.

In our 3 cases one could judge from the microscopic section the approximate phase of the menstrual cycle at which the operation was performed. The inguinal endometrioma removed from a pregnant patient by Rubinstein and Kurzon (1952) showed advanced decidual changes.

In these 3 patients—as in 9 out of 12 cases individually reported in the literature—the endometrioma was on the right side.

Treatment

All symptoms were relieved by excision of the endometrioma in our patients, and in view of their age recurrence is unlikely.

Summary

3 patients with inguinal endometriosis were seen within five months in a surgical outpatient department. All 3 complained of a painful lump in the groin which recurred with each menstrual period.

Unless this history is elicited there may be difficulty in distinguishing this condition from hernia, enlarged inguinal lymph-nodes, or a thrombosed varicocele. Any of these may coexist, and distract attention from the endometrioma at operation.

The literature of inguinal endometriosis is reviewed and three pathological types are recognised: an intraperitoneal and an extraperitoneal variety, and the purely endometrial lymph-node deposit.

Like congenital hernias and undescended testicles this condition appears to be commoner on the right side than on the left.

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tion, (*b*) no significant change, or (*c*) improvement (slight, moderate, or excellent), the films taken at six months were compared with those taken at three months The results are shown in table x, which reveals no essential difference between response of the two groups to treatment

Discussion

In this investigation the same chemotherapy was applied to a group of patients on strict bed rest in hospital and to a similar group of ambulant outpatients The principal aspect under consideration was the effect of exercise, but some of the outpatients had domestic conditions of a type which have always been regarded as adverse in the treatment of tuberculosis—including bad housing conditions, domestic disharmony, and financial difficulties—and most of this group were treated under circumstances far from ideal Since outpatient treatment is being employed on a large scale in this country, it is important to determine whether it increases propagation of the disease The household contacts of both groups of patients are, therefore, being closely supervised, to ascertain the subsequent incidence of infection

Despite the adverse environmental factors in the outpatient group, examination of the position after three months' treatment showed no significant difference between the response of the two groups assessed by fall in E S R, sputum conversion, extent of clearance of lung disease, and cavity closure It is true that the inpatients as a group gained more weight than the outpatients, but this must surely be regarded as reflecting physical inactivity rather than regression of disease, because, as is generally agreed, weight gained by patients in a sanatorium is usually rapidly lost when they resume outside activities

A few patients in both groups have been assessed after completion of six months' treatment Here again there is little difference in the general response, but cavity closure was commoner in the inpatients It would, of course, be unwise to reach any firm conclusion before greater numbers are compared, but it would not be surprising if further experience confirmed this trend Apart from any question of toxæmia or activity of the disease process, there is possibly a mechanical factor in cavity closure which is exploited in many centres by, for example, reversed postural drainage

It is highly probable that enough hospital beds for all newly diagnosed cases of pulmonary tuberculosis will soon be available, and then immediate admission to hospital in the first instance should be the standard procedure Before abandoning bed rest in the treatment of pulmonary tuberculosis it would be necessary to study the long term results in a larger number of patients, but it would seem that, if the results in this preliminary study are confirmed, patients who have ceased to excrete tubercle bacilli might be allowed to resume their everyday occupations much earlier than is now generally thought desirable In addition, patients with pulmonary tuberculosis might be allowed much greater physical freedom than at present with resultant lessening of the burden on nursing staff and diminished tedium for the patients Where domestic conditions are suitable, home treatment could confidently be carried out on an even larger scale than at present, and this form of treatment would undoubtedly be preferred by many patients

Summary

The value of rest in the treatment of pulmonary tuberculosis has been assessed in 141 newly diagnosed cases Alternate patients were admitted to hospital within two weeks of diagnosis, and treated as ambulant outpatients Both groups received the same chemotherapy and were assessed in a standard way

After three months' treatment progress, assessed by reduction of E S R, sputum conversion, cavity closure, and over all radiographic improvement, was as good in 70 ambulant outpatients as in 71 patients on strict bed rest in hospital

After six months' treatment no difference was found between 45 patients on strict bed rest in hospital and 46 ambulant outpatients as regards reduction of E S R, sputum conversion, and over-all radiographic improvement, but cavity closure was commoner in the patients on strict bed rest than in the ambulant outpatients

I should like to thank Dr A W Lees, consultant chest physician, Ruchill Hospital, for his constant interest in this investigation and Dr Agnes Macgregor for her painstaking assessment of the radiographs

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A CALCIUM-INFUSION TEST

I URINARY EXCRETION DATA FOR RECOGNITION OF OSTEOMALACIA

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THE use of calcium infusions in the diagnosis of metabolic bone disease was first suggested by Schilling and Laszlo (1951), who argued that the amount of calcium appearing in the urine after a standard infusion should be inversely related to the "avidity" of the skeleton for calcium, and that this urinary excretion should consequently be slight in osteomalacia (where the skeleton is inadequately calcified) and copious in osteoporosis (where the protein matrix is deficient) They gave some preliminary results obtained with four hour infusions of calcium 450 mg which appeared to support their thesis

Numerous workers have published data on various aspects of calcium infusions (McCance and Widdowson 1939, Baylor et al 1950, Howard et al 1953, Goldman and Bassett 1954, Kyle et al 1954, Schaaf and Kyle 1954, Spencer et al 1954,) but no satisfactory procedure has yet been evolved for the diagnosis of metabolic bone disease We report here a standard procedure which we have applied to patients in whom there was no reason to suspect bone disease and in more than 100 cases of known or suspected bone disorder, we believe it to be of diagnostic value in suspected osteomalacia

Procedure

All the subjects of the experiments reported here were given a low-calcium diet (100–150 mg of calcium and 500–700 mg of phosphorus daily) for three days before and throughout the test Their urine was collected from 6 A M on the third day to 6 A M on the fourth day, and then four-hourly until 6 A M on the fifth day An infusion of calcium gluconate (15 mg of calcium per kg of body-weight) was given in 500 ml of physiological saline solution from 10 A M to 2 P M on the fourth day Samples of blood were taken at the beginning and end of the infusion and at 6 P M and 10 A M next day

The methods used for the estimation of calcium, phosphate, and creatinine have been reported elsewhere (Nordin and Fraser 1954) The net output of calcium after the infusion is expressed as a percentage of the administered dose after deduction of a basal excretion figure calculated from the previous twenty-four hours' urinary output of calcium For the interpretation of the urinary excretion of calcium it suffices to measure the tions were adequate without carbon dioxide and oxygen did however, increase from 3–5 minutes to 18–20 minutes by the twelfth hour after admission Thereafter the depth of coma remained constant while supportive measures were continued for a further fourteen hours Twenty eight hours after admission bemegride 50 mg and amiphenazole 15 mg were administered intravenously, these doses being repeated four times at intervals of five minutes After the fourth injection the patient began to moan and responded to painful stimuli A plantar withdrawal reflex indicating lightening coma (Shulman et al 1955) and tendon reflexes could be elicited for the first time since admission During the next two hours unconsciousness deepened The same dosage of the bemegride and amiphenazole was therefore repeated A plantar withdrawal reflex returned, together with muscle tone and involuntary movements, after the second injection, and a state of light anæsthesia was attained when the total amount had been given An hour later consciousness returned, and within two hours the patient could answer questions although she was confused, and she complained of being unable to see She had been unconscious for about forty eight hours That night she remained awake, no sedative being given Next night she did not sleep despite having gr 1½ each of sodium quinalbarbitone and sodium amylobarbitone Quinalbarbitone gr 6 on each of the two succeeding nights produced only a state of drowsiness, and it was not until the fifth night after regaining consciousness that she actually slept She became rational eighteen hours after consciousness returned, her sight improved rapidly

Seven hours after admission her right thumb and the radial side of her right hand became swollen, and shortly afterwards blisters formed Three days later the skin peeled off and some sensory loss was demonstrated A retrospective diagnosis of frostbite was made Full movement and sensation gradually returned over two weeks Her further progress was uneventful and she made a good recovery

Comments

This case illustrates the dramatic effect which bemegride and amiphenazole can have on barbiturate coma Cerebral stimulants and supportive measures had lightened the level of coma slightly for twenty eight hours—a rate of progress which was in contrast to that produced by bemegride and amiphenazole

Both oxygen and carbon dioxide were essential before treatment with bemegride and amiphenazole The effectiveness of carbon dioxide in maintaining the depth and rate of respiration was rather surprising in view of the fact that the respiratory centre's response to stimulation by carbon dioxide is depressed in barbiturate poisoning (Goodman and Gilman 1955)

It is considered that the hypothermia consequent on prolonged exposure (shown by the frostbite) contributed to the patient's survival by lowering cellular metabolism The small amount of oxygen supplied by the depressed respiratory and circulatory systems was thus able to meet the diminished oxygen requirements of the tissues

Summary

A case of barbiturate coma complicated by hypothermia is reported

The effects of cerebral stimulants of purely supportive measures, and of bemegride and amiphenazole successively in the same patient are described

Hypothermia is thought to have contributed to this patient's survival

Our thanks are due to Prof I G W Hill for permission to publish and for his helpful criticism and to Dr W T Strauss for guidance in the management of this case

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PHENOBARBITONE POISONING TREATED WITH BEMEGRIDE

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BEMEGRIDE (β-ethyl β methylglutarimide, 'Megimide') is said to be of value in the treatment of poisoning by barbiturates (Shaw et al 1954, Harris 1955, Montuschi and Wickenden 1955, Shulman et al 1955, Bingle and Whitwam 1955, Webb 1955, Buckman 1955, Holten 1955, Perinpanayagam 1955, Perinpanayagam et al 1955)

We report here the recovery of a baby from a very large dose of phenobarbitone and comment on the use of bemegride

Case-report

A boy, aged 14 months, was admitted to hospital on Dec 18, 1955, in coma Two days previously his family doctor had prescribed succinylsulphathiazole for a mild gastro intestinal upset Shortly after the first dose the child became drowsy, but administration of the medicine was continued, and he received either five or six doses in thirty six hours During the two days before admission his drowsiness deepened into coma

On admission he weighed 26 lb, his temperature was 100°F, pulse rate 140, and respirations 30 a minute He was well nourished and rather fat He was deeply comatose and responded with only a very slight withdrawal movement to painful stimuli, but was breathing quietly and was not cyanosed His pupils reacted to light and were equal in size The corneal, gag, swallowing, tendon, and abdominal reflexes were all unobtainable The plantar responses were flexor Lumbar puncture showed normal cerebrospinal fluid under a pressure of 240 mm of water

Diagnosis—Phenobarbitone poisoning was diagnosed when analysis by isolation, melting point, elementary analysis, and ultraviolet spectra of the remainder of the medicine showed it to contain phenobarbitone and no sulphonamide By this time the child had been in coma for about thirty six hours At no time was there evidence of respiratory or circulatory failure No rash appeared

Treatment and Progress—It was decided to treat the child with bemegride because of the long continued coma and the large amount of phenobarbitone taken (later estimated at gr 65) A scalp vein infusion was set up and 25 mg bemegride injected into the infusion tubing The child at once stirred and moaned, and his face flushed Two further injections were given at intervals of five minutes After the last of these the face again flushed and the pulse rate quickened from 95 to 120 During one injection the fluid was noticed to be running into the subcutaneous tissues This caused no apparent local reaction During the subsequent one hour and forty minutes nine injections of 25 mg of bemegride were given into the infusion tubing at intervals of five to thirty four minutes Three of these were preceded by amiphenazole (2 4 diamino-5 phenylthiazole hydrochloride, 'Daptazole') 7 5 mg At the end of this period the child was crying had a strong grasp reflex, was moving all limbs and objected to having his eyelids opened Depressing his tongue caused "gagging" The later injections caused spasm of the vein next to the needle, making transfusion difficult, so bemegride was mixed with the transfusion fluid in the bottle The first such bottle contained 500 mg of bemegride and 100 ml of 0 18% sodium chloride with 4 3% dextrose After two hours the child became more deeply comatose, so bemegride 25 mg preceded by amiphenazole 7 5 mg was injected into the tubing The child at once cried and moved his hands The next transfusion bottle contained 620 ml of 5% dextrose and 1000 mg of bemegride No more amiphenazole was given The child's condition gradually improved, and on Dec 20 although he was not fully conscious, his eyes were open and he was reacting vigorously to painful stimuli The transfusion was stopped A few hours later he was sitting up and taking notice of his surroundings He had received 2827 mg of bemegride in eighty hours Throughout treatment the pulse rate was 95–120 and the respirations were 20–25 a minute Two Penicillin and streptomycin were given prophylactically

12 cases of osteomalacia In the "normal" patients the mean serum-calcium level rose from 10·4 to 13·5 mg per 100 ml and in osteomalacia from 9·0 to 11·5 mg per 100 ml, but in none of the patients were there any signs of calcium intoxication, and twenty hours after the end of this infusion the serum calcium level had almost invariably returned to its original value Most of the excess urinary calcium due to the infusion was excreted in the first twelve hours, and we have therefore used the 0–12-hr net total as our index of calcium excretion to express the result of the test

NET URINARY CALCIUM EXCRETION 0–12 HOURS

"Normal"

Fig 2 shows the individual results in the four main groups studied In the "normal" patients the net 0–12 hr excretion was 33–53%, with a mean of 41% and a standard deviation of 7·0 The normal range shown in the charts embraces two standard deviations above and below the mean—i e, 27–55%

Definite Osteomalacia

In proved osteomalacia all the results were below the normal range (see table I) the highest being 26·8% and the lowest 1·5% Within the group there did not appear to be any correlation between the amount of calcium excreted and the severity of the disease, the patient with the highest excretion had multiple Milkman fractures and a short history It should be remembered that the results in vitamin-D resistant osteomalacia have been excluded

TABLE II—CASES OF APPARENTLY SIMPLE STEATORRHŒA SUB DIVIDED BY INFUSION TEST INTO THOSE WITH SUBNORMAL CALCIUM EXCRETION (GROUP A) AND OTHERS (GROUP B)

—	Group A	Group B
12 hr excretion	0–27%	> 27%
No of cases	8	9
No with steatorrhœa for more than 2 yr	6	3
No with bone density definitely normal	1	7
Serum calcium (mean) (mg per 100 ml)	8·2	9·9
Serum phosphorus (mean) (mg per 100 ml)	3·6	3·4
Urinary output of calcium in 24 hr (mean) (mg)	49	94

Group A with low calcium excretion had a longer history of steatorrhœa more suspicious bone radiographs lower serum calcium levels and lower urinary output of calcium on low calcium diet (P > 0·01)

Steatorrhœa without proved Osteomalacia

In 8 of these patients the 0–12 hr net excretion was 27% or less, in 7 it was normal, and in 2 it was increased The reliability of the infusion test depends on whether the 8 patients with low excretion really had a minor degree of osteomalacia and the others not This is suggested by the additional data shown in table II

(1) Most of the patients with a low 0–12 hr excretion (group A) appeared to have had steatorrhœa for a longer time than had group B,

(2) The radiographic density of the bones was questioned by the clinician or the radiologist in all but 1 of group A, but was normal in 7 of 9 in group B,

(3) The mean serum calcium and the 24-hour urinary calcium levels were significantly lower in group A than in group B (P<0·01)

It therefore seems probable that these 8 patients had early osteomalacia, although it could not have been definitely diagnosed in any of them by the conventional procedures, since none of them had definitely abnormal bones on radiography combined with a low Ca × P level in the serum

It is also worth noting that none of them had a raised serum-alkaline phosphatase level (except those with jaundice), a low serum phosphate level, or a raised phosphate/creatinine clearance ratio, in contrast to the definite osteomalacia group

Osteoporosis

All the results were in or above the normal range

TABLE III—EXCRETION OF CALCIUM AFTER INFUSION IN MISCELLANEOUS CASES NOT INCLUDED IN FIG 2

(Vitamin-D resistant osteomalacia excluded)

Diagnosis	Urinary excretion of calcium in 12 hr from start of infusion (% of amount infused)	
Prostatic carcinoma with osteoblastic metastasis	4	
Pyelonephritis with renal failure	6	
Diabetes with thin bones	8	
Hypoparathyroidism	11	
Temporary hypoparathyroidism	14	
Hypoparathyroidism	15	
Acromegaly	16	
Parathyroid tumour with renal failure	17	
Rheumatoid arthritis	19	
Adult cœliac disease	24	
Acromegaly	28	Normal range
Cœliac disease follow up	30	
Osteogenesis imperfecta	30	
Myelosclerosis	31	
Chronic bronchitis	31	
Paget's disease	31	
Hæmochromatosis	33	
Hysterical immobilisation	35	
Chromophobe adenoma	36	
Cœliac disease follow up	36	
Paget's disease	39	
Polyostotic fibrous dysplasia	43	
Osteogenesis imperfecta	43	
Renal stones	48	
Parathyroid tumour with renal failure	49	
Cœliac disease follow up	51	
Intestinal tuberculosis	53	
Hypercalcuria	53	
Cœliac disease follow up	57	
Cœliac disease follow up	65	

Miscellaneous Cases

In most of these cases the net excretion of calcium was normal, but it was less than 27% in 10 (table III) This is hardly surprising in renal failure (2 cases), untreated hypoparathyroidism (3), and prostatic carcinoma with osteoblastic metastases (1) The other 4 "false positives" whose diagnoses are given in table III are at present unexplained

REPRODUCIBILITY

7 patients have received more than one calcium infusion (usually after an interval of at least a year)

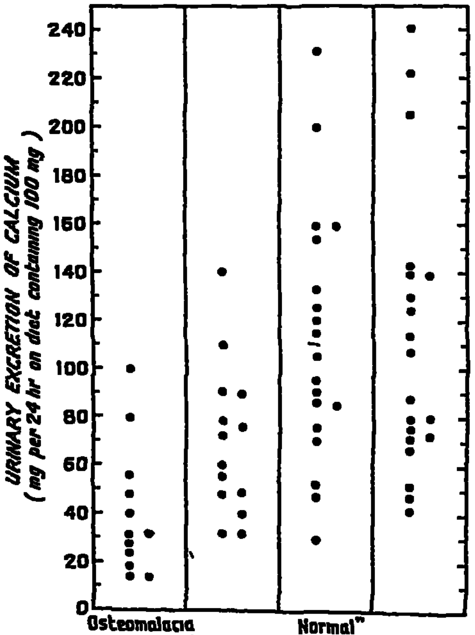

Fig 3—24-hr urinary excretion of calcium on third day of diet containing not more than 100 mg of calcium (same groups as in fig 2)

tions were adequate without carbon dioxide and oxygen did, however, increase from 3–5 minutes to 18–20 minutes by the twelfth hour after admission. Thereafter the depth of coma remained constant while supportive measures were continued for a further fourteen hours. Twenty-eight hours after admission bemegride 50 mg. and amiphenazole 15 mg. were administered intravenously, these doses being repeated four times at intervals of five minutes. After the fourth injection the patient began to moan and responded to painful stimuli. A plantar withdrawal reflex indicating lightening coma (Shulman et al. 1955) and tendon reflexes could be elicited for the first time since admission. During the next two hours unconsciousness deepened. The same dosage of the bemegride and amiphenazole was therefore repeated. A plantar withdrawal reflex returned, together with muscle tone and involuntary movements, after the second injection, and a state of light anæsthesia was attained when the total amount had been given. An hour later consciousness returned, and within two hours the patient could answer questions although she was confused, and she complained of being unable to see. She had been unconscious for about forty-eight hours. That night she remained awake, no sedative being given. Next night she did not sleep despite having gr. $1^1/_2$ each of sodium quinalbarbitone and sodium amylobarbitone. Quinalbarbitone gr. 6 on each of the two succeeding nights produced only a state of drowsiness and it was not until the fifth night after regaining consciousness that she actually slept. She became rational eighteen hours after consciousness returned; her sight improved rapidly.

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Comments

This case illustrates the dramatic effect which bemegride and amiphenazole can have on barbiturate coma. Cerebral stimulants and supportive measures had lightened the level of coma slightly for twenty-eight hours—a rate of progress which was in contrast to that produced by bemegride and amiphenazole.

Both oxygen and carbon dioxide were essential before treatment with bemegride and amiphenazole. The effectiveness of carbon dioxide in maintaining the depth and rate of respiration was rather surprising in view of the fact that the respiratory centre's response to stimulation by carbon dioxide is depressed in barbiturate poisoning (Goodman and Gilman 1955).

It is considered that the hypothermia consequent on prolonged exposure (shown by the frostbite) contributed to the patient's survival by lowering cellular metabolism. The small amount of oxygen supplied by the depressed respiratory and circulatory systems was thus able to meet the diminished oxygen requirements of the tissues.

Summary

A case of barbiturate coma complicated by hypothermia is reported.

The effects of cerebral stimulants, of purely supportive measures, and of bemegride and amiphenazole successively in the same patient are described.

Hypothermia is thought to have contributed to this patient's survival.

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REFERENCES

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PHENOBARBITONE POISONING TREATED WITH BEMEGRIDE

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BEMEGRIDE (β-ethyl-β-methylglutarimide; 'Megimide') is said to be of value in the treatment of poisoning by barbiturates (Shaw et al. 1954, Harris 1955, Montuschi and Wickenden 1955, Shulman et al. 1955, Bingle and Whitwam 1955, Webb 1955, Buckman 1955, Holten 1955, Perinpanayagam 1955, Perinpanayagam et al. 1955).

We report here the recovery of a baby from a very large dose of phenobarbitone and comment on the use of bemegride.

Case-report

A boy, aged 14 months, was admitted to hospital on Dec. 18, 1955, in coma. Two days previously his family doctor had prescribed succinylsulphathiazole for a mild gastro-intestinal upset. Shortly after the first dose the child became drowsy, but administration of the medicine was continued, and he received either five or six doses in thirty-six hours. During the two days before admission his drowsiness deepened into coma.

On admission he weighed 26 lb., his temperature was 100°F, pulse-rate 140, and respirations 30 a minute. He was well nourished and rather fat. He was deeply comatose and responded with only a very slight withdrawal movement to painful stimuli, but was breathing quietly and was not cyanosed. His pupils reacted to light and were equal in size. The corneal, gag, swallowing, tendon, and abdominal reflexes were all unobtainable. The plantar responses were flexor. Lumbar puncture showed normal cerebrospinal fluid under a pressure of 240 mm. of water.

Diagnosis.—Phenobarbitone poisoning was diagnosed when analysis by isolation, melting-point, elementary analysis, and ultraviolet spectra of the remainder of the medicine showed it to contain phenobarbitone and no sulphonamide. By this time the child had been in coma for about thirty-six hours. At no time was there evidence of respiratory or circulatory failure. No rash appeared.

Treatment and Progress.—It was decided to treat the child with bemegride because of the long-continued coma and the large amount of phenobarbitone taken (later estimated at gr. 55). A scalp-vein infusion was set up and 25 mg. bemegride injected into the infusion tubing. The child at once stirred and moaned, and his face flushed. Two further injections were given at intervals of five minutes. After the last of these the face again flushed and the pulse-rate quickened from 95 to 120. During one injection the fluid was noticed to be running into the subcutaneous tissues. This caused no apparent local reaction. During the subsequent one hour and forty minutes nine injections of 25 mg. of bemegride were given into the infusion tubing at intervals of five to thirty-four minutes. Three of these were preceded by amiphenazole (2 : 4-diamino-5-phenylthiazole hydrochloride, 'Daptazole') 7.5 mg. At the end of this period the child was crying, had a strong grasp reflex, was moving all limbs, and objected to having his eyelids opened. Depressing his tongue caused "gagging." The later injections caused spasm of the vein next to the needle, making transfusion difficult, so bemegride was mixed with the transfusion fluid in the bottle. The first such bottle contained 300 mg. of bemegride and 400 ml. of 0.18% sodium chloride with 4.3% dextrose. After two hours the child became more deeply comatose, so bemegride 25 mg. preceded by amiphenazole 7.5 mg. was injected into the tubing. The child at once cried and moved his hands. The next transfusion bottle contained 620 ml. of 5% dextrose and 1000 mg. of bemegride. No more amiphenazole was given. The child's condition gradually improved, and on Dec. 20, although he was not fully conscious, his eyes were open and he was reacting vigorously to painful stimuli. The transfusion was stopped. A few hours later he was sitting up and taking notice of his surroundings. He had received 2827 mg. of bemegride in eighty hours. Throughout treatment the pulse-rate was 95–120 and the respirations were 20–25 a minute. Tw

Penicillin and streptomycin were given prophylactically.

urinary excretion of calcium on the previous day, the 0–4-hr urinary excretion of calcium on the test day, the plasma calcium at 0 and 4 hr after the start of the infusion, and, on one of the last samples, the level of ultrafiltrable calcium

Biochemical Methods

Serum and ultrafiltrable calcium were measured either by a modification of Lehmann's ethylene diamine-tetra acetic acid (E D T A) titration procedure * (Lehmann 1953) or more recently by flame photometry * (McIntyre 1956) Urinary calcium was measured by the standard Kramer Tiddall procedure described by King (1951) or, more recently, by flame photometry

Ultrafiltration of serum was done by a method which will be described elsewhere (Nordin et al 1956) The pre-infusion serum was used for this purpose, and it was assumed that the proportion of ultrafiltrable to total calcium remained unaffected by the infusion This assumption has been tested and found valid (Nordin et al 1956)

Calculation

The "4 hr skeletal retention" of infused calcium is estimated at the end of the 4 hr infusion To derive this we deduct from the administered dose the amount of infused calcium which can be accounted for in the extracellular fluid (E C F) at 4 hr and in the 0–4 hr urine, and express the result as a percentage of the infused dose (which is proportional to body-weight)

For the purpose of this calculation the extravascular fluid is assumed to be 15% and the intravascular fluid 5% of the body-weight (Manery 1954) The level of calcium in the extracellular fluid is assumed to be the same as in serum ultrafiltrate (Manery 1954) The amount of infused calcium appearing in the urine over 0–4 hr is estimated by deducting $^1/_6$ of the previous 24-hr urinary output of calcium from the total amount excreted during the infusion—i e , the net or excess excretion of calcium The figure obtained when the sum of these three estimations is deducted from the administered dose is expressed as a percentage of the dose and termed "the 4 hr skeletal retention"

The steps in the calculation are as follows

Increase in extravascular E C F calcium = Rise in ultrafiltrable serum calcium × 15% of body weight (a)

Increase in plasma-calcium = Rise in serum calcium × 5% of body weight (b)

Net urine excretion = Total 0–4 hr calcium less $^1/_6$ previous 24 hours urinary excretion of calcium (c)

Calcium not accounted for in E C F or urine or "4 hr skeletal retention" } = Administered dose −([a] + [b] − [c]) (d) (expressed as percentage of the administered dose)

Alternative procedures for this calculation, when ultrafiltrable calcium has not been measured, are given in the appendix to this article

Patients Studied

We have sufficient data to calculate 4 hr skeletal retention in 54 patients † They fell into the following diagnostic categories

(A) *Normal* this group consisted of 10 patients with no bone disease or disturbance in calcium metabolism The diagnoses were as follows peptic ulcer (3), hypertension, cerebral thrombosis (2), pleural effusion spontaneous pneumothorax, simple obesity, and narcolepsy

(B) *Proved osteomalacia* (8) in 7 patients with steatorrhœa the radiographic and biochemical findings were typical of osteomalacia (as defined in Nordin and Fraser 1956), and in 6 the diagnosis was confirmed by biopsy of the iliac crest 1 patient with osteomalacia immediately following removal of a parathyroid adenoma is included in this group

(C) *Steatorrhœa without proved osteomalacia* 6 cases

(D) *Osteoporosis* this group consisted of 15 patients (13 females and 2 males), of whom 10 had vertebral compression fractures ("definite osteoporosis") The remaining 5 were classified as "probable osteoporosis" and consisted of 3 cases of Cushing s syndrome 1 case of rheumatoid arthritis treated with cortisone for two years, and 1 of postmenopausal backache and radiographically "thin bones"

(E) *Miscellaneous* this group consisted of 15 patients with diseases which might involve bone metabolism and 1 elderly patient with vertebral crush fractures without evident cause whom we have been unable to clarify (see below)

Some of the patients received a low calcium diet before the infusion but others did not No distinction has been made between the two groups

Results

"4 HR SKELETAL RETENTION" (INDIVIDUAL RESULTS BY DIAGNOSTIC CATEGORIES) (FIG 1)

(A) "*Normal*" *Patients*

The "4 hr skeletal retention" in the 10 "normal" patients was 50–62% of the dose (mean 55 2%) The standard deviation is 3 3%, and two standard deviations above and below the mean embrace the range 48 6–61 8% Since the normal group consists of only 10 patients, we have shown the absolute normal range on our graphs until we have collected further data

(B) *Osteomalacia*

In all the 8 patients with osteomalacia the 4 hr retention of calcium was above the normal range The highest retention (88%) occurred in the patient who had just undergone parathyroidectomy

(C) *Steatorrhœa*

Of 7 patients with steatorrhœa without obvious osteomalacia, 5 retained more than 62% of the dose, 1 patient retained 60%, and 1 46%

(D) *Osteoporosis*

11 patients with osteoporosis retained less than 50% of the dose of calcium at 4 hr The retention in 4 patients was within the normal range 1 of these was a "possible" osteoporosis, and the 3 others had been treated with hormones for from 4 months to 5 years Only 1 of the patients with a low skeletal retention had received any treatment at the time of the infusion

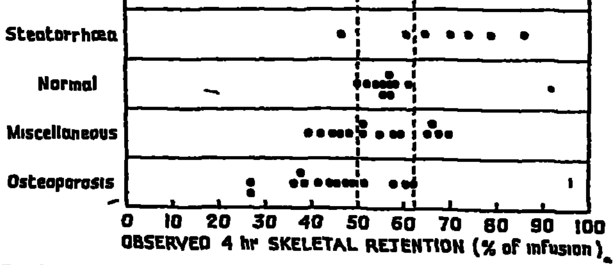

Fig 1—"4-hr skeletal retention" of calcium infusion in 5 main groups of patients studied

Note (1) normal range of 50–62%, (2) high skeletal retention in each of 8 cases of definite osteomalacia due to steatorrhœa and in 5 of 7 cases of steatorrhœa without obvious osteomalacia, and (3) subnormal skeletal retention in 11 of 15 cases of osteoporosis (contrast 0–12 hr excretion on same tests in fig 2 of Nordin and Fraser [1954], abnormal in only 4 of 15) tions were adequate without carbon dioxide and oxygen did, however increase from 3–5 minutes to 18–20 minutes by the twelfth hour after admission Thereafter the depth of coma remained constant while supportive measures were continued for a further fourteen hours Twenty-eight hours after admission bemegride 50 mg and amphenazole 15 mg were administered intravenously, these doses being repeated four times at intervals of five minutes After the fourth injection the patient began to moan and responded to painful stimuli A plantar withdrawal reflex indicating lightening coma (Shulman et al 1955) and tendon reflexes could be elicited for the first time since admission During the next two hours unconsciousness deepened The same dosage of the bemegride and amphenazole was therefore repeated A plantar withdrawal reflex returned, together with muscle tone and involuntary movements, after the second injection, and a state of light anæsthesia was attained when the total amount had been given An hour later consciousness returned, and within two hours the patient could answer questions although she was confused, and she complained of being unable to see She had been unconscious for about forty eight hours That night she remained awake, no sedative being given Next night she did not sleep despite having gr $1^1/_2$ each of sodium quinalbarbitone and sodium amylobarbitone Quinalbarbitone gr 6 on each of the two succeeding nights produced only a state of drowsiness, and it was not until the fifth night after regaining consciousness that she actually slept She became rational eighteen hours after consciousness returned, her sight improved rapidly

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* Compared estimations were about equivalent on these methods (McIntyre 1956)

† All those patients tested by July, 1955, for whom were available in addition to urinary data, the required data of ultrafiltrable calcium and the necessary two serum samples, measured by E D T A or flame photometry In 1 osteoporotic patient the ultrafiltration measurement was not available, and so the value obtained by the appendix methods has been used

Seven hours after admission her right thumb and the radial side of her right hand became swollen, and shortly afterwards blisters formed Three days later the skin peeled off, and some sensory loss was demonstrated A retrospective diagnosis of frostbite was made Full movement and sensation gradually returned over two weeks Her further progress was uneventful and she made a good recovery

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The findings in the other patients suggest that the '4 hr skeletal retention" is a reliable index of the skeleton's avidity for calcium The normal range is slightly narrower than that of the 0–12-hr urinary excretion, and it still reveals the excessive skeletal avidity of all the osteomalacia patients tested Indeed, as noted, it is striking how closely the '4 hr skeletal retention" reflects the final retention of calcium, or that not excreted in the 0–12-hr urinary excretion except in osteoporosis and in defective skeletal avidity For the recognition of osteomalacia due to steatorrhœa, however, this complication of the test by the estimation of serum levels is unnecessary, and the 0–12-hr urinary excretion of calcium reliably reveals the excessive avidity for calcium

The low '4-hr skeletal retention' which we found in osteoporosis does not necessarily imply any abnormality of the protein matrix in these cases, as suggested by Albright and Reifenstein (1948) The only definite statement that can be made about the osteoporotic skeleton is that it contains less bone than does a healthy one (Follis 1954) This reduction in mass, with its associated reduction in surface area, may explain the reduced rate of deposition of calcium in the skeleton during the test

The practical value of the calcium infusion test in osteoporosis remains to be seen but the possession of even one biochemical criterion of osteoporosis should be valuable to workers in this field particularly those interested in studying the effects of therapy, and it is just possible that the procedure we have described may meet this need

Summary

The results of the calcium infusion test, described in the previous paper, have been analysed to show, in 54 patients the '4 hr skeletal retention" of calcium—the proportion of the infused calcium neither in the urine nor in the extracellular fluid at 4 hr

In 10 "normal" patients this '4 hr skeletal retention" was 50–62% (mean value 55%) In all of 8 patients with osteomalacia due to steatorrhœa, and in 5 of 7 patients with steatorrhœa without obvious osteomalacia, this "4 hr skeletal retention" was above the normal

In 11 of 15 patients with osteoporosis the "4-hr skeletal retention" was below the normal, although the 0–12 hr urinary excretion of calcium was abnormal in only 4 of them We suggest that this "4-hr skeletal retention' may offer a biochemical criterion for osteoporosis

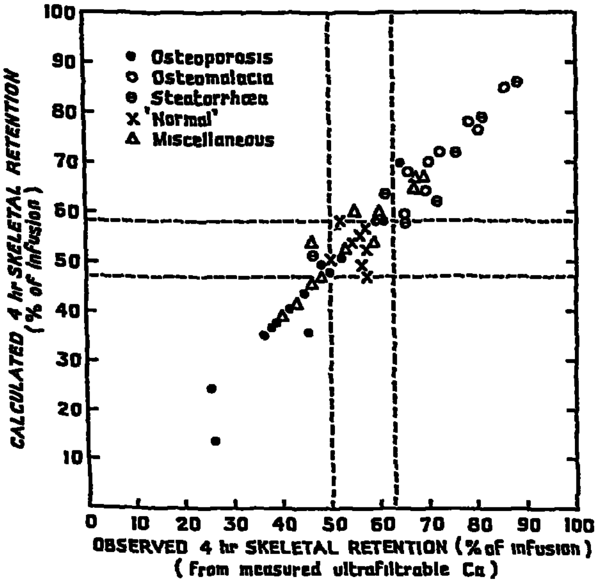

Fig 3—Correlation between observed 4-hr skeletal retention and that calculated by formula correcting for serum protein levels See appendix

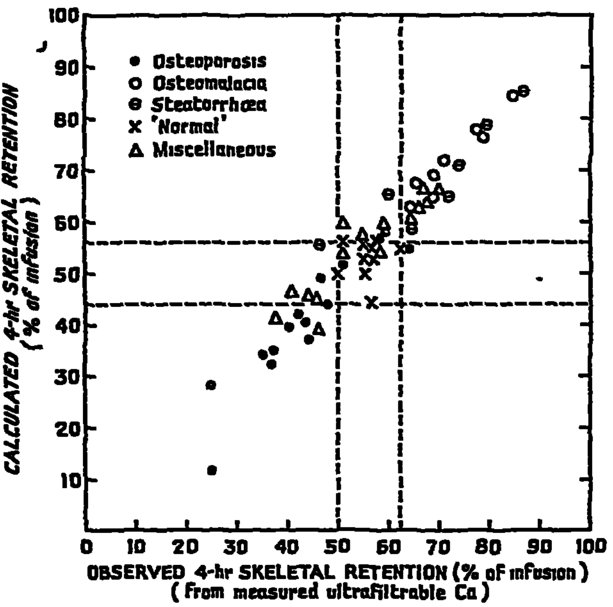

Fig 4—Correlation between observed '4-hr skeletal retention' and that calculated assuming normal serum levels See appendix

We wish to acknowledge with gratitude the assistance of Miss Sheila Stewart, B SC, and of the sisters and nurses of Hammersmith Hospital, and to thank Mr C R Brecknall and Mr F Saunders of the illustration department of the Postgraduate Medical School of London for the illustrations, and several colleagues for referring patients

Appendix

The procedure described above involves the ultrafiltration of serum We have however, recalculated all our data in two ways which eliminates this necessity

(a) *Correcting for plasma protein levels* (fig 3)

We may calculate the percentage of calcium which is ultrafiltrable from the albumin and globulin concentrations according to a formula which we are publishing elsewhere (Nordin et al 1956) (Protein bound Ca % = −3 1 + 7 6 × albumin (g per 100 ml) + 2 9 × globulin (g per 100 ml.))

In fig 3 the results obtained by this calculation are compared with those obtained in the same cases by measurement of the ultrafiltrable calcium It will be seen that there is very little difference in the results although the absolute normal range by this calculation becomes 47–58 instead of 50–62% The number of osteoporotic patients with subnormal retention becomes 9 or 10 instead of 11 out of 16

(b) *Assuming normal plasma proteins* (fig 4)

We have assumed that, with normal plasma proteins, the ultrafiltrable calcium is always 67% of the total serum calcium (Nordin et al 1956)

The total circulating extracellular calcium thus becomes the sum of

(i) Rise in serum calcium level × 5% of body weight and

(ii) Rise in serum calcium level $\times \frac{67}{100} \times$ 15% of body weight

This solves to rise in serum calcium level × 15% of body weight tions were adequate without carbon dioxide and oxygen did, however increase from 3–5 minutes to 18–20 minutes by the twelfth hour after admission Thereafter the depth of coma remained constant while supportive measures were continued for a further fourteen hours Twenty eight hours after admission bemegride 50 mg and amphenazole 15 mg were administered intravenously, these doses being repeated four times at intervals of five minutes After the fourth injection the patient began to moan and responded to painful stimuli A plantar withdrawal reflex indicating lightening coma (Shulman et al 1955) and tendon reflexes could be elicited for the first time since admission During the next two hours unconsciousness deepened The same dosage of the bemegride and amphenazole was therefore repeated A plantar withdrawal reflex returned, together with muscle tone and involuntary movements, after the second injection, and a state of light anæsthesia was attained when the total amount had been given An hour later consciousness returned, and within two hours the patient could answer questions although she was confused, and she complained of being unable to see She had been unconscious for about forty eight hours That night she remained awake, no sedative being given Next night she did not sleep despite having gr 1½ each of sodium quinal barbitone and sodium amylobarbitone Quinalbarbitone gr 6 on each of the two succeeding nights produced only a state of drowsiness, and it was not until the fifth night after regaining consciousness that she actually slept She became rational eighteen hours after consciousness returned, her sight improved rapidly

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On admission he weighed 26 lb his temperature w 100°F, pulse rate 140, and respirations 30 a minute He w well nourished and rather fat He was deeply comatose an responded with only a very slight withdrawal movement painful stimuli, but was breathing quietly and was n cyanosed His pupils reacted to light and were equal in siz The corneal, gag, swallowing, tendon, and abdominal reflex were all unobtainable The plantar responses were flex Lumbar puncture showed normal cerebrospinal fluid under pressure of 240 mm of water

Diagnosis —Phenobarbitone poisoning was diagnosed wh analysis by isolation, melting point elementary analysis a ultraviolet spectra of the remainder of the medicine show it to contain phenobarbitone and no sulphonamide By th time the child had been in coma for about thirty six hour At no time was there evidence of respiratory or circulator failure No rash appeared

Treatment and Progress —It was decided to treat the chil with bemegride because of the long continued coma and th large amount of phenobarbitone taken (later estimated a gr 35) A scalp vein infusion was set up and 25 mg bemegrid injected into the infusion tubing The child at once stirre and moaned, and his face flushed Two further injection were given at intervals of five minutes After the last o these the face again flushed and the pulse rate quicken from 95 to 120 During one injection the fluid was notic to be running into the subcutaneous tissues This caused apparent local reaction During the subsequent one hou and forty minutes nine injections of 25 mg of bemegride wer given into the infusion tubing at intervals of five to thirty fou minutes Three of these were preceded by amphenazol (2 4 diamino 5 phenylthiazole hydrochloride, 'Daptazole 7 5 mg At the end of this period the child was crying, h a strong grasp reflex, was moving all limbs and objected t having his eyelids opened Depressing his tongue caus "gagging" The later injections caused spasm of the vein next to the needle, making transfusion difficult, so bemegrid was mixed with the transfusion fluid in the bottle The fir such bottle contained 500 mg of bemegride and 400 ml o 0 18% sodium chloride with 4 3% dextrose After two hour the child became more deeply comatose, so bemegride 25 mg preceded by amphenazole 7 5 mg was injected into th tubing The child at once cried and moved his hands Th next transfusion bottle contained 620 ml of 5% dextrose an 1000 mg of bemegride No more amphenazole was given The child's condition gradually improved and on Dec 2 although he was not fully conscious, his eyes were open an he was reacting vigorously to painful stimuli The tran fu was stopped A few hours later he was sitting up and takin notice of his surroundings He had received 2827 mg of bemegride in eighty hours Throughout treatment the pul rate was 95–120 and the respirations were 20–25 a minute Penicillin and streptomycin were given prophylactically Tw

CONTROL OF ALDOSTERONE EXCRETION BY CHANGES IN VOLUME OF BODY-FLUID

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VASOPRESSIN, a long-acting extract of the posterior lobe of the pituitary gland administered to normally hydrated people for three days produces acute retention of water and the resulting abnormal increase of the body-fluid evokes by homœostasis renal loss of sodium and chloride (Leaf et al 1953) The urinary excretion of sodium has also been increased by acutely overloading healthy people with water (Stewart and Rourke 1942) and by giving an infusion of hypotonic saline solution (Strauss et al 1952)

According to Leaf et al (1953) this loss of electrolyte can be prevented by administering either corticotrophin or a low-sodium diet Since the latter stimulates the urinary excretion of aldosterone, it seems reasonable to assume that the increased renal excretion of sodium which follows the increase of body-fluid may be due to diminished production of aldosterone, and that the striking retention of sodium after vasopressin has been withheld might be secondary to increased secretion of aldosterone by the suprarenal cortex

Methods

The subject studied was a healthy man, aged 32, maintained on a constant low sodium diet and a fluid intake of 2000–2500 ml a day After an initial control period posterior pituitary extract was administered intramuscularly as vasopressin tannate in oil every twelve hours

Urine was collected every twelve or twenty four hours from 7 A.M and analysed for sodium in a flame photometer The urinary 17 hydroxycorticoids were determined according to a modification of Reddy's method (Hertoghe et al 1955) Aldosterone was analysed chromatographically after acidification of the urine at pH 1 for twenty four hours (method *d* of Neher and Wettstein [1955]) *

Results

The accompanying figure shows the typical response of a healthy person to vasopressin tannate over two and a half days, as described by Leaf et al (1953) The retention of water as the antidiuretic effect of vasopressin is seen in the abrupt decrease in volume of the urine and the corresponding increase in body-weight As expected on the second and, especially the third days of administration of vasopressin the urinary sodium increased Though the appearance of increased excretion of electrolytes was delayed making a direct action of vasopressin on sodium very unlikely, there was an immediate decrease in the urinary excretion of aldosterone following the retention of water and the abnormal increase of body fluid It is therefore highly probable that this decreased urinary excretion of aldosterone as a direct consequence of increase of body-fluid, caused secondarily the delayed renal loss of sodium

The withholding of vasopressin was followed by a large water diuresis and a loss of body weight This significant diminution of body-fluid took place pari passu with an increased urinary excretion of aldosterone The latter was the immediate cause of the pronounced retention of sodium three days after vasopressin had been withheld The fact that the urinary excretion of aldosterone remained high for several days can be explained by the body-fluid volume expressed as body-weight being below the level found at the beginning of the study

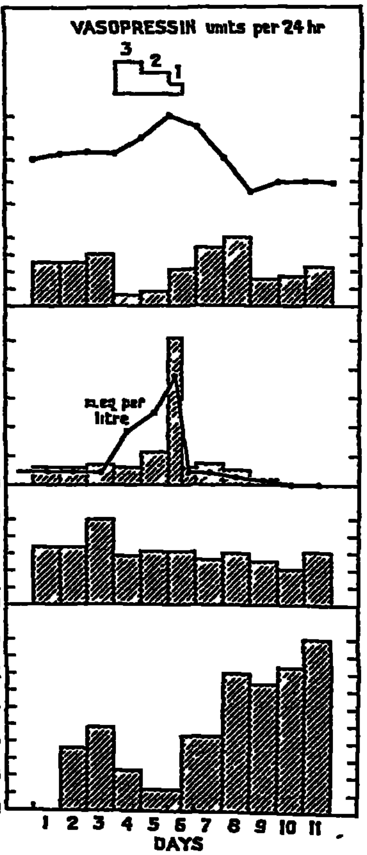
During the whole of this investigation the amount of urinary 17-hydroxycorticoids did not show any significant change

Discussion

Leaf et al (1953) interpreted the renal loss of sodium resulting from retention of water as a homœostatic response to abnormal increase of body-fluid That this increased urinary excretion of electrolytes in man is a direct effect of decreased production of aldosterone is suggested by the results of the present study The sequence of events after the administration of vasopressin is as follows (1) retention of water, (2) decrease of secretion of aldosterone as a homœostatic response to increase of body-fluid, and (3) increase in urinary excretion of sodium as a direct consequence of the diminution of aldosterone

Withholding the vasopressin reverses the process (1) a large water diuresis causes a loss of weight, (2) the diminution of body-fluid stimulates the production of aldosterone, and (3) pronounced renal retention of sodium

The significant variations in the amount of aldosterone excreted, in spite of a constant amount of 17-hydroxycorticoids excreted throughout the whole study, strongly suggest an adaptive mechanism which independent of any effect of corticotrophin and acting through some volume of body-fluid, regulates the secretion of aldosterone in favour of homœostasis In a recent similar experiment (A F Muller and A M Riondel, unpublished), however, exogenous corticotrophin was found to influence the excretion of aldosterone The 'rebound' production of aldosterone after vasopressin has been withheld was much increased and hastened by an injection of corticotrophin twelve hours after the last dose of vaso-



Effect of vasopressin on body weight, volume of urine and urinary excretion of sodium, 17 hydroxycorticoids and aldosterone The relatively high values of aldosterone are due to the constant low-sodium diet with its effect on the volume of the body fluid use of the frame was an essential part of their regime, the head of the femur could always be brought down but was commonly left standing out from the acetabulum 75 operations had been performed and only once had they failed to find an inverted limbus, which might be very large, the limbus could not be everted The position of subsequent plaster immobilisation depended on the degree of internal rotation required to reduce the head fully, in 1 case posterior capsulotomy had been needed to permit this Three weeks later a rotation osteotomy was done, leaving the upper fragment unmoved and rotating the shaft to the neutral position Five weeks later the patients were left free from splintage and early weight bearing was permitted The total duration of treatment had now been reduced to fourteen weeks Further dislocation had taken place in 3 cases, either because the limbus had not been excised or because derotation had been insufficient and further operation was required All cases had a range of movement 90% or more of normal

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* We wish to thank Dr A Wettstein and Dr R Neher for their valuable help in setting up this method in our laboratory

Slipping of Upper Femoral Epiphysis

Mr P H Newman reported the results of surgical treatment of slipping of the upper femoral epiphysis in 30 cases The results were excellent in 23, good in 8 fair in none, and poor in 8 If there was less than one third diameter posterior and less than one quarter diameter medial displacement the femoral head was pinned in situ Because of the difficulty of insertion into the epiphysis, the danger of damaging its blood supply, and the possibility of a subtrochanteric fracture at the point of insertion, he had abandoned the use of a Smith Petersen nail and used a modification of Moore's pins In this first group only 1 out of 19 had a poor result If the position was unacceptable an attempt to improve it by very gentle manipulation was made and pins were inserted if adequate reposition was obtained There were 7 cases in this group, perfect reduction was rarely obtained, but in the single poor result the patient had had a stiff hip before operation Where closed reduction failed open reduction through an anterior approach, with excision of a wedge of bone where necessary was performed A pin inserted up the neck ready before the open correction was done could be driven on immediately the head was reduced, and this prevented loss of position during the later stages of the operation The results had been poor in 3 out of 9 Treatment of the fourth group was by subtrochanteric osteotomy, which he had now abandoned Treatment in these cases was urgent Poor results followed avascular necrosis and operations on hips already stiff from delayed diagnosis or prolonged traction In such cases two months' physiotherapy to mobilise the hip and improve the local blood supply was indicated before operation could be considered

Mr A M Rennie (Aberdeen) reported his results in 15 cases Avascular necrosis had developed in 3, and he agreed that operations on stiff hips, which had resulted in 2 poor results in his own series must be avoided

Dr E Thomasen (Aarhus) had tried to stimulate fusion by drilling across the epiphysial plate keeping the patient eight weeks in bed on traction without plaster fixation Occasionally he had left a Kirschner wire across the plate for a few months as additional fixation A subcapital wedge osteotomy with drilling and fixation by Kirschner wires was reserved for later cases Avascular necrosis had developed in 3 out of 14 cases

Fractured Neck of Femur Treated by Compression

Mr John Charnley (Manchester) described the treatment of fractures of the neck of the femur by compression With present methods a third failed to unite within the first year He had been using a coarse threaded screw in the femoral head the smooth shaft of this screw passed through a socket inserted into the femoral neck and fixed by a plate to the femoral shaft A nut and spring allowed compression to 25 lb The angle was fixed at 120 Special tools were required and while all other movements were prevented the spring maintained compression between head and neck should absorption of the latter occur The apparatus permitted measurement of the degree of shortening taking place in the neck Cases fell into two groups one in which extrusion of the bolt was seen to cease after three months and another in which it continued to progress for a year or more Of 33 cases available for study 82% united satisfactorily

Arthrodesis of Hip

Mr McKee reported the results in 50 cases of arthrodesis of the hip by a lag screw reviewed at least two years after operation The operation was done through a lateral approach Afte removal of the articular cartilage the hip was fixed by a lag screw inserted up the femoral neck and into the ilium The neck was drilled out to allow the smooth shaft of th screw free passage when final compression was applied an it was important to ensure that all the threaded part was i the ilium The greater trochanter was removed and used a an iliofemoral graft In 76% of cases no additional plast fixation was used The screw broke in 16%, but in only ha of these did it need to be removed this complication ha not occurred in the last 38 cases There had been 2 death 1 from delayed shock and the other from coronary thrombo In only 1 case had union failed to take place owing to a ischaemic necrosis in the femoral head Final results show 34% excellent, 32% good, and 28% fair

Knock-knee in Children

Mrs M Morley reported an investigation into knock kne in children In general knock knee became increasingl common and severe up to the age of 3½ years, after whic it diminished steadily Sex made no difference to th incidence, but the more severe the knock knee the great was the weight of the children No correlation with heigh was found, and valgus ankles and flat feet (the latter almo universal in the very young) diminished with age and wer unrelated to knock knee She had failed to find any association between knock knee and the age of first walking th duration of breast feeding, additional vitamins, or the lengt of time spent in bed because of illness

Paralytic Scoliosis

Mr J I P James had attempted to correlate the distribution of paralysis with the curve patterns in paralytic scolios Of 193 cases, divided into high thoracic, thoracic thoracolumbar, lumbar, combined thoracic and lumbar, and "telescopic" spine he had chosen the high thoracic, thoracolumbar, and lumbar for special study When the onset was before the age of 5 the curvature usually exceeded 100° but if delayed till after the age of 10 it was usually less than 70 The high thoracic curve usually started at T1 In contradistinction to Colonna he had failed to find any correlation between paralysis of the shoulder girdle or proximal segment of the upper limb in this type of curvature The erector spinae was usually normal and there was no significant relationship to abdominal paralyses He had however, found almost constant paralysis of the intercostal muscles on the convex side, and in contradistinction to idiopathic curves the ribs were not spread on this side but were crowded and hung almost vertically so that they were obscured by the spine on the anteroposterior radiograph A cine radiographic film showed the ribs on the concave side moving well on respiration in contrast to those on the convex side In thoracolumbar curves with the apex at D11 or D12, and in lumbar curves weakness of the lateral flexors on the convex side was constant Weakness of the erector spinae, anterior abdominal muscles psoas, glutei, or lower limbs was apparently unrelated The only other factor that he believed to be significant was gravity On the M R C scale adequate muscle charting of the trunk muscles was extremely difficult and of the intercostal obviously impossible by clinical methods

Fractures and Dislocations of Cervical Spine

Mr F C Durbin (Exeter) discussed 75 cases of fracture and dislocations of the cervical spine seen in a ten year period 12 of these involved atlas and axis and were excluded from consideration The rest were chiefly in young active males road accidents being the commonest cause Where paraly was absent and there were other serious injuries, the lesion was easily missed A fractured spinous process always implied damage to the interspinous ligament In the injuries if no dislocation was present he advised that radiographs in flexion carefully controlled by the surgeon should be taken to test the stability of the spine In over half the cases with dislocation the cord or nerve roots were injured In 26 the cord was injured, in 15 there was complete quadriplegia and 14 of these patients had died He recommended gradual reduction by skull traction with Crutchfield ice tong callipers which were safe and effective if tightened daily The 4 failures of reduction by this method were due to locked facets which needed operative reduction Simpl immobilisation after reduction was not sufficient, recurrence of displacement as shown by radiographs in flexion [illegible] occurred in 8 cases 3 of them even after six months in plaster and 2 associated with fractures of a spinous process [illegible]

Histology

The excised nodule contained uterine glandular and muscular elements interspersed with blood filled spaces (fig 2) Red blood cells also appeared in the lumen and stroma of the glands which were lined by darkly staining columnar cells In several sections the round ligament could be seen traversing the central part of the endometrioma The endothelial layer of the hernial sac was separated from both by dense fibrous tissue

THE SECOND CASE

About Mrs B, a clerk aged 49 her family doctor wrote there is a cystic, tense swelling in the right groin At first I thought it was a hernia but I am now inclined to think that it might be a hydrocele of the canal of Nuck If it is then it is the first I have seen in twenty years

The swelling had appeared abruptly three months previously it had rapidly increased in size and had become agonisingly painful On direct questioning the patient readily confirmed that the onset had coincided with the first day of a menstrual period and that after menstruation the symptoms had disappeared as quickly as they had come

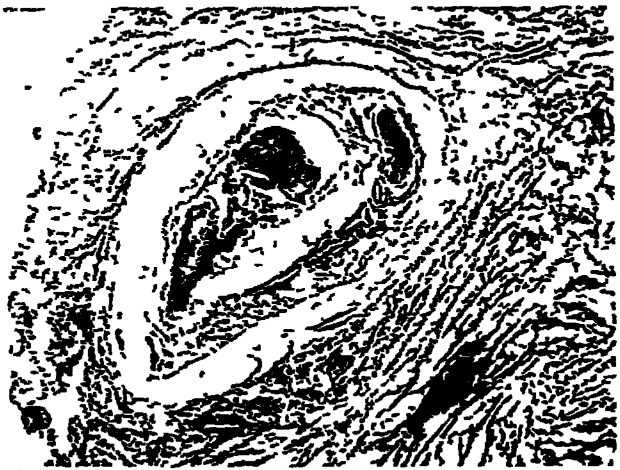

Fig 2—Microphotograph of the round ligament and inguinal endometrioma in case 1 (Low magnification Hæmatoxylin and eosin.)

The next ' acute attack had occurred during the following period, four weeks later and the latest episode had ended three weeks before admission

Over the past twenty years she had noticed from time to time tenderness and mild discomfort in her right groin but this was not associated with menstruation Her cycles had been regular and there were no gynæcological symptoms She had been married for twenty one years and though both she and her husband had been anxious to have a family, their union had remained childless

Examination

In the right groin a firm non tender swelling the size of a walnut was palpable One observer in addition to the patient's doctor who had seen her in the acute phase, recorded a cystic sensation imparted by the lump but there was no suspicion of a cough impulse and the mass was not only irreducible but firmly anchored to underlying structures The skin was freely moveable over it and of normal appearance Rectal examination was negative

Operation

Operation was preceded by a pelvic examination under anæsthetic The uterus was slightly and somewhat irregularly enlarged but no abnormality of the external genitalia or uterine adnexa was found

Exploration through an inguinal skin crease incision revealed a mass issuing from the external ring and obscuring the round ligament and its companion structures It had the colour and consistence of scar tissue but cystic spaces, varying in size from a pin head to a lentil were visible as dark patches through the transparent fibrous covering Unlike the mass in our first patient this one showed no tendency to infiltrate, indeed a clear plane of cleavage made it appear encapsulated The inguinal canal sheltered an empty indirect sac whose distal extremity was lightly tethered to it The hernial sac was transected its proximal end was sutured, and the contents of the inguinal canal were excised

Pathology

The excised mass had an almost honeycomb appearance the content of the cysts, reminiscent of that of ovarian ' chocolate cysts ' stained their lining dark brown On everting the fundus of the hernial sac there was no evidence of endometrial tissue arising directly from the peritoneal lining

Tubular glands surrounded by abundant musculature, were seen under the microscope They showed the characteristic tortuosity and scalloping of premenstrual endometrium A number of macrophages with deeply staining mottled cytoplasm were congregating in the subendometrial layer

Follow up

Menstruation started three days after operation and passed without discomfort or reappearance of the lump The next two menses were similarly uneventful

THE THIRD CASE

Mrs C aged 40 complained of a nagging pain ' in the right groin of three or four years duration which not only limited her outdoor activities but had lately started to interfere with her regular household duties In reply to leading questions she said that though the discomfort was present most of the time, it was worse during menstruation. She had also noticed on occasion a small swelling in the groin but this, she maintained had been present on and off since childhood

She had been married for twenty four years but there had been no pregnancies

Examination

In the right groin faith rather than touch demonstrated an irreguler thickening overlying and adherent to the body of the pubis This area was moderately tender and the patient complained of aching after palpation There was no cough impulse and she had no palpable lymph nodes Routine investigations and pelvic examination under anæsthetic again revealed nothing abnormal

Operation

Operation was performed two days after the end of a menstrual period The principal finding was a mass about an

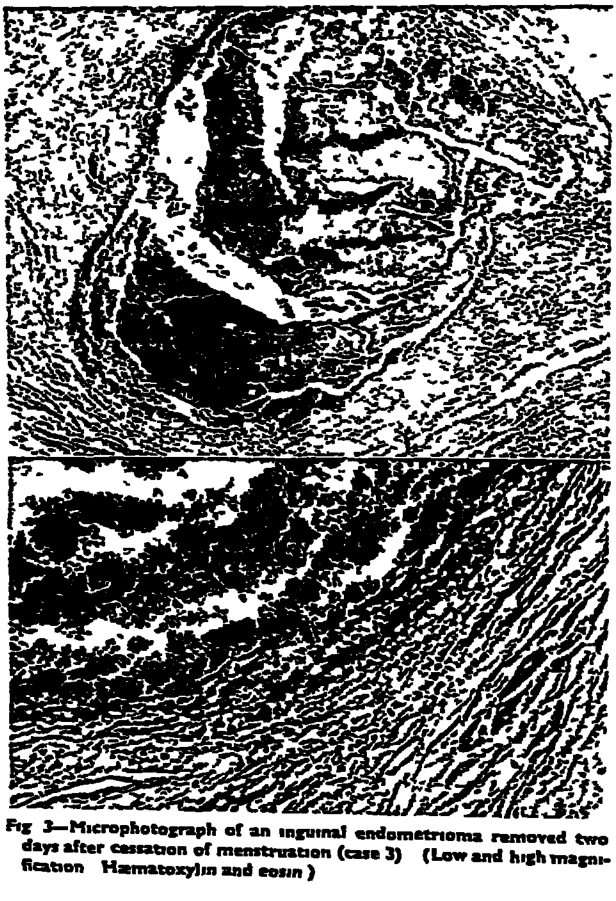

Fig 3—Microphotograph of an inguinal endometrioma removed two days after cessation of menstruation (case 3) (Low and high magnification Hæmatoxylin and eosin)

year to soft tissue, from an atmosphere with a radon content of 3×10^{-13} curie per litre of radon This figure would of course be very much higher, and may be of considerable significance, under higher radioactive atmospheric conditions

Estimates of total gonad dose rates vary from 90 m rad per year for outdoor workers in Leeds to 146 m rad per year for Swedes living in concrete houses

Estimates of the total lung dose-rate from background sources have also been made In addition to soft tissue radiation from "external" background sources and "internal" radiation by ^{40}K, further irradiation will occur as a result of inhaling particulate matter carrying radon and thoron daughter products The resultant lung dosage from this source will depend upon many variable factors, the chief of which are the solubility of the inhaled material, the size of the inhaled particles, the conditions of inhalation, and the ventilation rate High lung ventilation rates reduce radon and thoron doses by a factor of about 4 In view of the variables involved, a number of assumptions have been made The total dose rate to superficial bronchial tissues is about 300 m rem per year—three times that calculated for general soft tissue elsewhere in the body

Lastly, Professor Spiers presented the results of calculations on the quantities of two fission products—cæsium and strontium—which would be required to produce tissue dose rates equal to those already being received by body-tissues from natural sources Both cæsium and strontium, which are long-lived, are capable of being taken into the body structure, and at the present time accidental ingestion of radioactive materials must be regarded as at least a possible accompaniment of nuclear-energy development

Radioactive cæsium (^{137}Cs) may be expected to follow potassium in behaviour and distribution, and it is calculated that a body content or burden of 0 6 microcuries is required to give a soft tissue dose rate equal to the background rate of 100 m rem per year Radioactive strontium (^{90}Sr) and its daughter yttrium (90) are known to be taken up in bone, and are estimated to require a body burden of 45×10^{-9} curie to give an average dose rate to osteocytes equal to that from the natural background The International Commission on Radiological Protection recommend the introduction of a factor of 5 to allow for the fact that strontium concentrations in bone may be five times higher than those observed for radium, if this is the case, a body burden of 9×10^{-9} curie would be the equivalent strontium burden to give a dose rate to bone equal to the natural background

Professor Spiers reiterated that the radiation dose rate from natural sources has been an inevitable accompaniment of Man's life and evolution, and that it must therefore be at least a reasonably tolerable factor in his environment It follows that in the assessment of "permissible" doses and dose rates for present and future use the background dose rate must be considered and compared with radiation dose-rates known to be harmful

The background dose is small compared with doses known to produce acute radiation effects, and it is likely that genetic and long-term carcinogenic effects are the main considerations In this context, the background dose rate to gonads of 0 1 rad per year or 3 rad in a generation of 30 years should be compared with the radiation dose-rate required to double the spontaneous human mutation rate This dose is uncertain, because the radiosensitivity of human genes is unknown and variable but the most recent estimate that can be quoted is that of Muller which suggests that the 'doubling dose' is unlikely to be more than 10 times this background dose

The soft tissue background dose-rate in bone is estimated at 0 12 rad per year or about 6 rad in 50 years This should be compared with the dose rate in people with small accidentally acquired radium burdens who show detectable radiographic bone changes, and where the dose rate is about 2000 times the background dose rate

A similar comparison, assuming a normal atmospheric radon content of 3×10^{-13} curie per litre, of the background dose to lungs with the radiation doses causally associated with cancer in soft tissue gives a value 100–1000 times lower for background dose This background dose of 15 rad in 50 years (i e, three times the gonad dose) is probably 10,000 times less than the lung dosages of the Joachimstal uranium miners, in whom the incidence of lung cancer was so high

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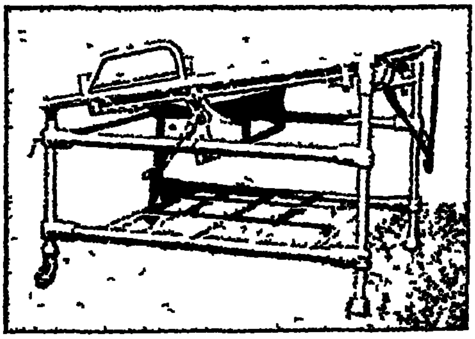
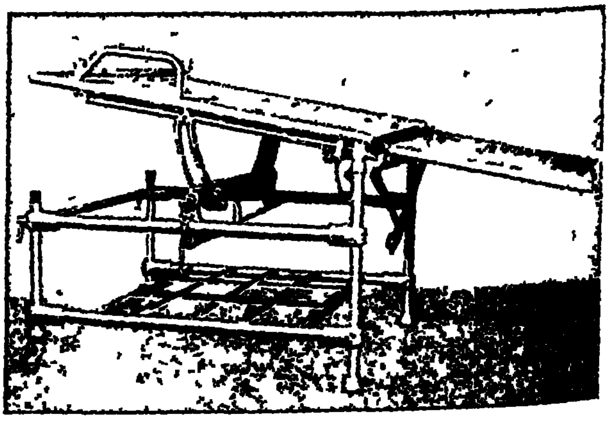
New Inventions

MODIFIED "OXFORD" LABOUR-WARD BED

SAFETY in unprepared cases needing a general anæsthetic depends somewhat on the ability of the anæsthetist to posture the patient quickly Either a head-down or a foot-down position may be desirable A head-down position will help to prevent aspiration into the lungs should vomiting occur, while a foot-down position may prevent reflux from the œsophagus (or stomach in certain circumstances) before intubation with a cuffed endotracheal tube during application of a muscle relaxant technique





In hospital obstetrical practice there are no reasons why special anæsthetic techniques for emergency general surgery should not be used in the labour ward, if they are to the patient's advantage[1] With this in mind the well-known "Oxford" labour-ward bed has been modified so that it can be quickly tilted into either a head-down or a foot-down position (see figures) The bed can be tilted 20° in either direction in three seconds This bed has now been in use at St Thomas's Hospital for just over a year and has proved equally satisfactory to midwives obstetricians, anæsthetists, and patients It is made by Hoskins & Sewell Ltd, Bordesley Birmingham, 12

W D WYLIE
M A, M B Camb
M R C P, F F A R C S

St Thomas's Hospital
London

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[1] See Proc R Soc Med 195[illegible] 48 10[illegible]

BARBITURATE COMA WITH HYPOTHERMIA

D W Eason
M B St And

F I Macnaughton
M B Edin

LATE HOUSE OFFICERS ARBROATH INFIRMARY

Various methods have been used in the past for treating barbiturate coma Cerebral stimulants in the form of amphetamine derivatives and picrotoxin appear to have little effect when coma is deep, and purely supportive measures have recently tended to take the place of these drugs (Locket and Angus 1952) More recently two new drugs, bemegride and amiphenazole, the latter a respiratory stimulant and both barbiturate antagonists, have been introduced

An opportunity for comparing the effectiveness of these methods of treatment arose when a case presented in a small country hospital where the new drugs were not immediately available and treatment in the first instance was with picrotoxin, methedrine, and supportive measures Later, with persistent coma, treatment with bemegride and amiphenazole was given Further interest is added to the case by the complicating factors of exposure and hypothermia

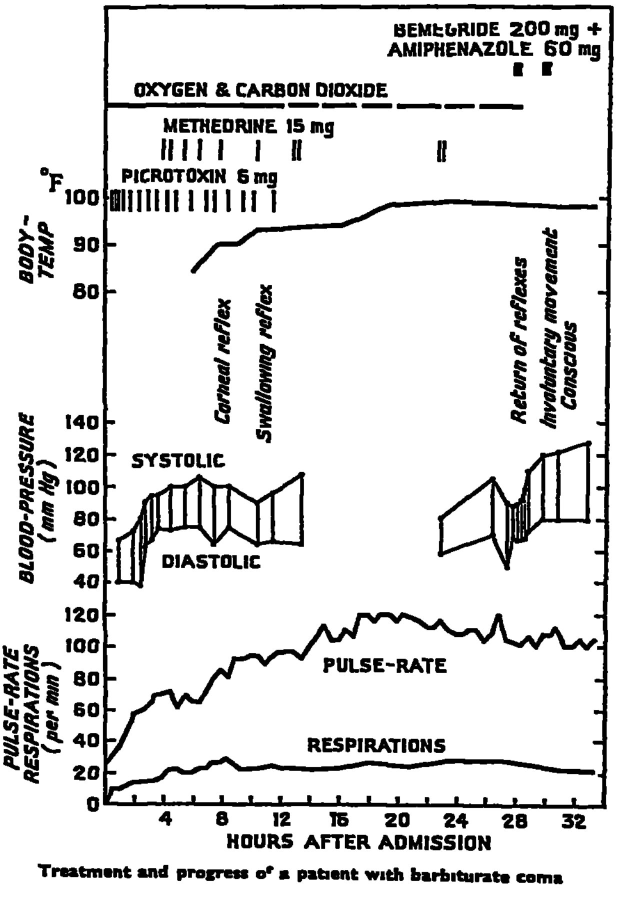
Case-report

A married woman, aged 35 and weighing 105 lb , disappeared from her home on the morning of Oct 15, 1955, and twenty six hours later was found lying below the cliffs on the sea shore, apparently moribund She was dry but lightly clad (light coat, cotton house coat, cotton underwear, shoes, and stockings) The maximal and minimal environmental temperatures during the night of her exposure were 58°F and 45°F respectively Investigations showed that she had taken at least 21 ' Carbrital ' capsules, representing at least gr 31½ of soluble pentobarbitone and gr 84 of carbromal In addition she had probably taken phenobarbitone and aspirin

On admission to hospital at 10 45 A M on Oct 16 she was an ashen grey colour, and her whole body was cold She was pulseless, and her blood pressure was not recordable Faint heart sounds were present at the rate of 25 a minute with much prolonged systole showing by the spacing of the heart sounds Her respirations were shallow and irregular, from 1 to 3 a minute All her reflexes were absent and her pupils dilated A small amount of salicylate was detected in her urine There was no evidence of trauma

Treatment —An endotracheal tube was passed, through which oxygen with 10% carbon dioxide was administered mechanically with a Boyle s apparatus After fifteen minutes, respiration having become regular, the concentration of carbon dioxide was reduced to 5% Warmth was applied and later, a heat cage at its lowest setting was used intermittently The stomach was washed out, with a negative result Picrotoxin was given intravenously in 6 mg doses until 102 mg had been given It was then discontinued because little progress had been made (see figure) Methedrine was given intravenously in 15 mg doses to maintain the systolic blood pressure at 100 mm Hg Later, 30 mg was added to 1 pint of intravenous fluid on two occasions Continuous intravenous infusions were given, alternately of physiological saline solution and of dextrose , the solutions were warmed to approximately the patient's body temperature Her trachea and bronchi were cleared by suction every thirty minutes , on each occasion 5–15 ml of brown offensive secretions was aspirated Intramuscular penicillin 1,000,000 units was given, followed by 500 000 units eight hourly A catheter was passed six-hourly during coma, with little result initially Intramuscular mersalyl 2 ml was given to increase the excretion of barbiturate

Progress —After fifteen minutes' administration of 10% carbon dioxide in oxygen respiration became regular at a rate of 10 a minute Forty five minutes after admission a faint radial pulse was detectable and the heart rate had increased to 35 a minute The circulation improved over the next forty-five minutes, the pulse rate rising to 50 and the blood-pressure, which was very labile, to 70/40 mm Hg Pulse and blood pressure showed further improvement over the next two hours Six hours after admission, warmth having been applied throughout this period a thermometer graduated to a sufficiently low temperature became available Oral and axillary temperatures of 84 2°F were recorded Thereafter the axillary temperature rose steadily by about 2°F an hour for the next five hours, and then more slowly until it became normal eighteen hours after admission With restoration and maintenance of peripheral circulation and respiration the patient's colour and general condition improved but all her reflexes were still absent four hours after admission Her pupils did however, gradually decrease in size and eight hours after admission, reacted to light, and a corneal reflex was elicited Three hours later a feeble swallowing reflex was present When carbon dioxide and oxygen were temporarily withheld, the respirations diminished in depth and then in frequency , and the pupils dilated, with suppression of reaction to light and of the corneal reflex These changes also took place when 100% oxygen was administered for more than five minutes The interval during which the patient s respira-



Treatment and progress of a patient with barbiturate coma

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commode is still a practical possibility—" the worst enemy of patient morale is the bedpan "

This is a useful, short, practical book It must be one of the few medical textbooks to be enlivened by drawings from the pen of as great an artist as the late Raoul Dufty

Éléments d'immunologie générale

P GASTINEL, professeur a la Faculte de Medecine de Paris,
R FASQUELLE, agrege de bacteriologie a la Faculte,
P BARBIER, chef de travaux de bacteriologie a la Faculte
Paris Masson 1955 Pp 335 Fr 2000

THE authors' aim is to cover the syllabus of French diplomas in immunoserology and to give an introduction to research-workers The treatment is rather uneven and it is not clear what knowledge is assumed in the reader For example, a few lines are devoted to the elementary chemistry and physics of amino-acids and proteins This is superfluous for those who have reached 2nd M B standard and inadequate for those who have not The development of ideas of immunity does not seem suitable for those unfamiliar with the subject, and the information about special aspects of immunology is at the same time too detailed for elementary students requiring a general survey, yet too fragmentary for the advanced worker

The Lacrimal System

Clinical Application EVERETT R VEIRS, M D, professor of ophthalmology, University of Texas Postgraduate School of Medicine New York and London Grune & Stratton 1955 Pp 156 $7 50

As Dr Veirs points out in a preface, many papers have been published on various aspects of the lacrimal apparatus, but none has so far covered the entire field He has made this interesting and well-arranged monograph as comprehensive as possible and he has written at length and in detail about the clinical features, methods of investigation, and conservative and surgical treatments of disorders of the lacrimal system

The work is admirably illustrated by photographs and clear pen and wash drawings There is a useful bibliography at the end of each of the twelve chapters Dr J V Cassady contributed the chapter on developmental anatomy Several techniques of performing dacryocystorhinostomy by the intranasal route are excellently described

Perhaps after the description of Summerskill's polythene intubation of a dacryocystorhinostomy and of permanent intubation of the naso lacrimal duct, some comment should have been made about the failures and serious complications of these techniques In the full description of the dacryocystorhinostomy operation the author has omitted to mention that the bony fenestration in the lacrimal fossa may be achieved very well, and without damage, either to the nasal mucosa or the lacrimal sac, by using Traquair's elevator, Citelli's punch, and then Ferris Smith's nibblers There is also no reference to the value of Stryker's electric saw trephine

The book is well produced and will appeal not only to the eye surgeon but to the rhinologist and pædiatrician

The Pediatric Years

LOUIS SPEKTER, M D, director, bureau of maternal and child hygiene, Connecticut State Department of Health Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 734 90s

THE aim of this book is to provide an understanding of the child in health and sickness for those working with doctors in a pædiatric service It is written for the American worker and much of it reflects the views of that continent both in practice and education Comprehensive and up to date, it achieves the rare feat of making the pathology of children's diseases understandable to those without basic medical training

The British medical auxiliary will value highly the digest of children's diseases and the chapters on development hospital care and pædiatric procedures The chapters on the range and scope of the social services will appeal to those interested ls of solving social and medical problems in the non welfare State More might usefully have been said about parents, whose attitudes exert such a profound influence for good or ill, and to whom much of the advice in this book will be passed on

Few teachers of students, nurses, almoners, and other medical workers would not be glad of the help this book can give

Laboratory Control of Dairy Plant

J G DAVIS, D SC PH D, F R I C London Dairy Industries Ltd 1956 Pp 395

THE dairy industry is exceptional in the use which it makes of chemistry and bacteriology in its daily practice No other branch of the food trade is so " laboratory-minded " or offers so much responsibility to those with a scientific training Among these, few are better qualified to write this book than Dr Davis It is a working manual for manager and technician which covers all the details of day-to-day control without losing sight of the principles upon which these are based Nowadays the technicalities of the milk trade seldom trouble the medical officer of health but, when they do, it would be difficult to recommend a source of information so lucid so succinct, and so well indexed

Functional Otology

The Practice of Audiology MORRIS F HELLER, M D chief, audiology clinic, Mount Sinai Hospital, New York New York Springer London Interscience Publishers 1955 Pp 209 40s

IT is immediately clear to the reader that Dr Heller's experience in audiology is unusually broad He goes into considerable detail about the staff, equipment, and administration of an audiology centre and deals quite fully with all those important borderline aspects of his subject that are so often lacking or inadequate in a textbook of otolaryngology There is a useful chapter on " non organic deafness " and a helpful and timely description of the transistor hearing-aid Some discussion of the medical and surgical aspects of deafness would have been welcome, but nevertheless the book provides valuable supplementary reading to the otologist who has a particular interest in the problems of deafness

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The Chemical Constitution of Natural Fats (3rd ed London Chapman & Hall 1956 Pp 664 95s)—With the present great interest in the physiology of fats and their possible roles in disease, the new edition of this standard work by Prof T P Hilditch, F R S, comes opportunely It gives the details of the chemical constitution of both animal and vegetable fats from a great variety of species set out clearly but with encyclopædic thoroughness A feature of the book is the separate indexes for individual fats and waxes, individual fatty acids, individual glycerides and of plant families There is also a valuable chapter on analytical methods The only criticism is that Professor Hilditch has confined himself strictly to the letter of his title and so there is no reference to margarines and other processed fats which feature in human diet The information collected in this book is nowhere else so readily available and will continue to be of great value to biologists and medical research workers

The Back and its Disk Syndromes (2nd ed Philadelphia Lea & Febiger London Henry Kimpton 1955 Pp 942 £6 15s)—The foundation of this book is the close personal experience with over 40 000 'back cases' This seems a prodigious experience, and if Prof Philip Lewin has applied to each patient all the clinical tests he describes it is hard to understand how he has managed to find time to write similar books on the foot and on the knee Hardly anything has been left out, and the effort to include everything has made an indigestible book The familiar is intermingled with the erudite, and the inexperienced reader will find difficulty in gleaning an orderly scheme of treatment for any individual case The diagrams are clear and helpful and the general production of high quality Many of the author's pithy remarks are admirably suited to stick in the student's memory The book is a further monument to Dr Lewin's industry and learning

BARBITURATE COMA WITH HYPOTHERMIA

D W Eason
M B St And

F I Macnaughton
M B Edin

LATE HOUSE OFFICERS ARBROATH INFIRMARY

Various methods have been used in the past for treating barbiturate coma Cerebral stimulants in the form of amphetamine derivatives and picrotoxin appear to have little effect when coma is deep, and purely supportive measures have recently tended to take the place of these drugs (Locket and Angus 1952) More recently two new drugs, bemegride and amiphenazole, the latter a respiratory stimulant and both barbiturate antagonists, have been introduced

An opportunity for comparing the effectiveness of these methods of treatment arose when a case presented in a small country hospital where the new drugs were not immediately available and treatment in the first instance was with picrotoxin, methedrine, and supportive measures Later, with persistent coma, treatment with bemegride and amiphenazole was given Further interest is added to the case by the complicating factors of exposure and hypothermia

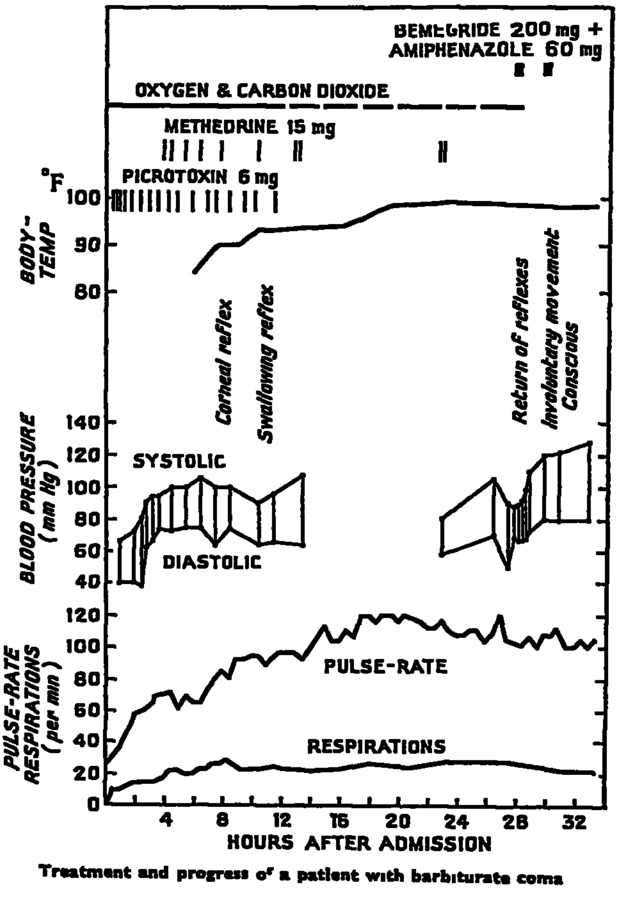
Case-report

A married woman, aged 35 and weighing 105 lb disappeared from her home on the morning of Oct 15, 1955, and twenty six hours later was found lying below the cliffs on the sea shore, apparently moribund She was dry but lightly clad (light coat, cotton house coat, cotton underwear shoes, and stockings) The maximal and minimal environmental temperatures during the night of her exposure were 58°F and 45°F respectively Investigations showed that she had taken at least 21 'Carbrital' capsules, representing at least gr $31^1/_2$ of soluble pentobarbitone and gr 84 of carbromal In addition she had probably taken phenobarbitone and aspirin

On admission to hospital at 10 45 A M on Oct 16 she was an ashen grey colour, and her whole body was cold She was pulseless, and her blood pressure was not recordable Faint heart sounds were present at the rate of 25 a minute with much prolonged systole showing by the spacing of the heart sounds Her respirations were shallow and irregular, from 1 to 3 a minute All her reflexes were absent and her pupils dilated A small amount of salicylate was detected in her urine There was no evidence of trauma

Treatment —An endotracheal tube was passed, through which oxygen with 10% carbon dioxide was administered mechanically with a Boyle's apparatus After fifteen minutes, respiration having become regular, the concentration of carbon dioxide was reduced to 5% Warmth was applied and, later, a heat cage at its lowest setting was used intermittently The stomach was washed out, with a negative result Picrotoxin was given intravenously in 6 mg doses until 102 mg had been given It was then discontinued because little progress had been made (see figure) Methedrine was given intravenously in 15 mg doses to maintain the systolic blood pressure at 100 mm Hg Later, 30 mg was added to 1 pint of intravenous fluid on two occasions Continuous intravenous infusions were given, alternately of physiological saline solution and of dextrose, the solutions were warmed to approximately the patient's body temperature Her trachea and bronchi were cleared by suction every thirty minutes, on each occasion 5–15 ml of brown offensive secretions was aspirated Intramuscular penicillin 1,000,000 units was given, followed by 500,000 units eight hourly A catheter was passed six-hourly during coma, with little result initially Intramuscular mersalyl 2 ml was given to increase the excretion of barbiturate

Progress —After fifteen minutes' administration of 10% carbon dioxide in oxygen respiration became regular at a rate of 10 a minute Forty five minutes after admission a faint radial pulse was detectable, and the heart rate had increased to 35 a minute The circulation improved over the next forty five minutes, the pulse rate rising to 50 and the blood-pressure, which was very labile, to 70/40 mm Hg Pulse and blood pressure showed further improvement over the next two hours Six hours after admission, warmth having been applied throughout this period a thermometer graduated to a sufficiently low temperature became available Oral and axillary temperatures of 84 2°F were recorded Thereafter the axillary temperature rose steadily by about 2°F an hour for the next five hours, and then more slowly until it became normal eighteen hours after admission With restoration and maintenance of peripheral circulation and respiration the patient's colour and general condition improved, but all her reflexes were still absent four hours after admission Her pupils did, however, gradually decrease in size and, eight hours after admission reacted to light, and a corneal reflex was elicited Three hours later a feeble swallowing reflex was present When carbon dioxide and oxygen were temporarily withheld the respirations diminished in depth and then in frequency, and the pupils dilated, with suppression of reaction to light and of the corneal reflex These changes also took place when 100% oxygen was administered for more than five minutes The interval during which the patient's respira



Treatment and progress of a patient with barbiturate coma

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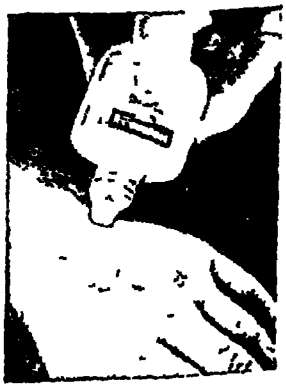

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ALSO FROM THE GLAXO CORTISONE RANGE EF-CORTELAN SKIN OINTMENT NO 1 (1% and 2½% hydrocortisone acetate in *non-greasy* base), EF-CORTELAN SKIN OINTMENT NO 2 (1% and 2½% hydrocortisone acetate in *greasy* base) Both in 5 g and 15 g tubes, 30 g jars

GLAXO LABORATORIES LTD , GREENFORD, MIDDLESEX BYRon 3434 days later, on Dec. 22, the child was discharged home still slightly ataxic but reacting normally to his parents and feeding well.

All the urine was collected from the time of diagnosis—i.e., thirty-six hours after the onset of coma—for seventy-two hours. In the first twenty-four hour specimen 56 mg. of phenobarbitone was found; in the second 13 mg.; and in the third 10 mg. Metabolites of the drug were not detected.

Follow-up.—Seen on Jan. 2, 1956, the child was well; in fact his parents complained that he was sleeping badly.

Discussion

This child received a large dose of phenobarbitone (about gr. 55 in divided doses in thirty-six hours) and was in coma for at least thirty-six hours before treatment was begun. Since his respiration did not become depressed, he might well have recovered without active treatment.

The fact that he was fat may have been to his advantage. It is known that some of the short-acting barbiturates—e.g., thiopentone—are absorbed from the blood-stream by fatty tissue (Goodman and Gilman 1955). The fact that respiration was not affected in this case suggests that a similar mechanism may apply to phenobarbitone.

The small amounts of phenobarbitone found in the urine can be explained by the lapse of time before collection was begun and the amount which must have been metabolised (Goodman and Gilman 1955).

Unless respiration is depressed, the use of amiphenazole as well as bemegride seems unnecessary, although it has been recommended (Shulman et al. 1955).

Bemegride does not appear to be toxic. The chief danger in its use seems to lie in failing to realise that it may have to be given for a long time. The patient's condition is liable to regress if the dose is reduced prematurely. This was well shown in the present case, where bemegride had to be given for eighty hours. For this reason it seems more sensible to mix it with the intravenous transfusion fluid in the bottle rather than to inject it intermittently.

Summary

A case of phenobarbitone poisoning in a child aged 14 months is reported. Phenobarbitone had been administered for thirty-six hours by mistake for succinylsulphathiazole.

On admission the child was deeply comatose, but his respiration and circulation were not depressed.

He was treated successfully with 2827 mg. of bemegride mixed with a convenient intravenous transfusion fluid, given continuously for eighty hours.

We wish to thank Dr. T. Stapleton, who was in charge of the case, for advice and encouragement; Prof. A. Neuberger for help in the diagnosis and for the chemical analyses; and Dr. Keith Mant, Dr. T. A. B. Harris, and Dr. T. E. Oppé for advice.

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Medical Societies

BRITISH ORTHOPÆDIC ASSOCIATION

The association's spring meeting was held at Gleneagles on May 3–5, under the presidency of Mr. Philip Wiles.

Conservative Treatment of Spinal Tuberculosis

Mr. J. P. Jackson (Harlow Wood) discussed 89 cases of spinal tuberculosis, reviewed not less than two years after treatment, which had consisted of immobilisation on a frame or plaster bed and streptomycin 1 g. and *p*-aminosalicylic acid 18 g. daily for ninety days. 3 patients had died, all from meningeal or genito-urinary infection. Amyloid disease and sepsis were no longer problems, and sinuses closed more readily, although five had persisted and one new sinus had developed under treatment. Posterior fusion by tibial grafts was usually undertaken when the lesion was quiescent, and of these 36% proceeded to anterior fusion also; anterior fusion had occurred in 46% of cases which had not been operated on but gave no certain guard against relapse, which ensued in 11% of such cases. The relapse rate after surgery was, however, only half that where no operative fusion had been performed. Abscesses were not opened routinely, but it was found that only 24% of those with persistent abscesses proceeded to bony fusion. Mr. Jackson concluded that general treatment was still necessary; conservative treatment with three months' chemotherapy gave 21% unsatisfactory results, but total duration of treatment was shorter and mortality was reduced. Posterior grafting was well worth while.

Mr. Robert Roaf (Liverpool) remarked that chemotherapy is now given usually for nine to twelve months, and that we have learnt how fallacious the interpretation of radiographs can be in assessing quiescence.

V-nail Fixation for Fractured Neck of Femur

Mr. A. W. Fowler (Bridgend) recommended V-nail fixation for trochanteric and basal fractures of the neck of the femur. This was a modification of the "low nail" operation described by Brittain in 1942. A V-nail (actually a clover-leaf Küntscher nail with half of the lateral leaves shaved down) provided fixation based on three solid points—the dense bone of the head, the upper end of the medial cortex of the shaft, and the outer cortex at the point of penetration. He permitted weight-bearing after eight weeks, and earlier in stable fractures. This admittedly experimental method was mechanically sound and cheaper and more efficient than pin or bladeplate, and it permitted telescoping when necessary, but not coxa vara.

Mr. G. K. McKee (Norwich) had had similar favourable experience of the procedure, but remarked that some apparently pertrochanteric fractures were really subtrochanteric posteriorly, so a nail might split the cortex in this region. He therefore preferred to add to a vertical nail a slotted plate which would allow some telescoping.

Mr. Roland Barnes (Glasgow) did not think that this method was adequate for the unstable type of fracture because the comminution of the inner cortex would preclude stability and permit varus deformity with danger of the nail breaking through the head as in other methods.

Internal Fixation for Bennett's Fractures

Mr. F. C. Badger (Birmingham) described his method of treating Bennett's fractures, whereby through a dorsal incision the fragment was reduced and fixed by a small screw passed through the base of the shaft. No plaster was necessary. The patients were off work on average for three weeks. In 13 out of 17 cases the results had been good, the failures resulting either from the use of too short a screw with later redisplacement of the fragment, or from a badly placed screw.

Mr. O. J. Vaughan-Jackson said that he used a small pin and a mid-lateral approach; in 2 cases the small fragment had been found turned over so that the articular cartilage was apposed to cancellous bone on the major fragment.

Congenital Dislocation of Hip

Mr. J. C. Scott (Oxford) reported the interim results of 75 cases of congenital dislocation of the hip treated at Oxford since 1949, under the régime devised by Mr. E. W. Somerville and himself. The cases were treated within what he called the "critical period"—from the beginning of weight-bearing to the age of 4. The method consisted in (1) gradual reduction by traction on a special frame, (2) operative removal of the limbus where this was shown by the arthrogram to be inturned, and (3) rotation osteotomy to correct anteversion when required. He believed that the dislocation was first anterior and later became superior and then posterior for the head to lie on the dorsum ilii. He thought that it was usually the lesser trochanter that pushed in the limbus; the secondary reduction in circulation was responsible for the smallness of the epiphysial head and cases of later osteochondritis. The a satisfactory rise in hæmoglobin. It is for this reason that we wonder whether it would not be better to have the second blood examination earlier—say, between the 28th and 32nd weeks. If patients with anæmia of pregnancy fail to respond properly to parenteral iron, they have almost certainly a megaloblastic anæmia. Israëls and Da Cunha[7] stated that the only certain method of establishing the diagnosis was by examination of the bone-marrow, and they pointed out that the investigator must look for transitional megaloblasts and giant metamyelocytes, and not rely on finding classically developed megaloblasts. These findings have been confirmed by Lowenstein et al.,[8] working in Canada, and by many others. The Canadian group found that there is nearly always an iron-deficiency anæmia as well, and that the response to therapy is often slower than that in addisonian pernicious anæmia. They found that 4 of their 18 patients responded to treatment with vitamin B_{12}, but most reports from temperate climates state that patients are resistant to B_{12} and the proper treatment is folic acid (15–20 mg. daily, orally or parenterally).

The more controversial part of Edgar and Rice's recommendations is that iron should be given to all pregnant women, so that all of them go through pregnancy with a hæmoglobin level of 90% or so. Fisher and Biggs[9] gave iron supplements to 104 mothers and all but 12 had hæmoglobin levels of 90% at term, and there is little doubt, as Jennison and Ellis[10] pointed out, that by using parenteral iron most of the non-responders could have their hæmoglobin levels similarly raised at term. What is not clear is whether it is really beneficial for the mother to have a higher hæmoglobin at term than in the normal course of events. We have seen that the red-cell mass is not decreased in a normal pregnancy; presumably (though we have no data) if the hæmoglobin level at term is 90% instead of 75% of normal, the red-cell mass will be notably increased. Is this helpful? Fisher and Biggs promised their patients that they would be "fighting fit" for labour and for the duties of the puerperium, but all they tell us is that they "gathered the impression" that the patients were more energetic. There is now no doubt that anæmia of pregnancy can be prevented if the patients will attend their antenatal clinics or see their own doctors in time, and if anæmia develops it can be efficiently treated. But we should not lose sight of the other factors in nutrition: iron is only one factor and the ideal of "a quart of milk, 4 oz. of meat, and one egg" daily, in addition to any iron supplement, should still be aimed at.

Upper Respiratory Virus Infections

Virus infections of the upper respiratory tract probably form the largest group of illnesses encountered in general medical practice. When the common colds and virus influenzas are subtracted from the total there remain a large number of infections which are variously diagnosed as pharyngitis, laryngitis, tracheitis, bronchitis, &c.—that is, names which describe the site at which symptoms and signs are most prominent. It is well known, however,[1] that different viruses can produce illnesses which are clinically indistinguishable, and conversely that a single agent, the influenza virus, may produce a very variable clinical picture in different individuals. Laboratory research on this subject is therefore very welcome, and an excellent review[2] of recent papers has come from Dingle and Feller.

We are learning rapidly about the part played by a new group of viruses in infections of the upper respiratory tract, but, surprisingly, one of the difficulties that plagues everyone who writes or talks about these viruses is what to call them. Rowe et al.[3] described the first isolation of the new viruses—from adenoidal tissue removed at operation from children. Since these viruses caused degeneration of adenoidal cells in tissue culture they were called adenoidal degeneration (AD) viruses. Shortly afterwards Hilleman and Werner[4] recovered a serologically related agent from an outbreak of upper respiratory disease in a military camp, and called their virus RI-67. Huebner and his co-workers[5] have now isolated as many as 11 distinct immunological types of virus from man, of which type 3 has been related to outbreaks of non-bacterial pharyngitis,[6] types 4 (i.e., RI-67 virus) and 7 have been related to outbreaks of acute respiratory disease in recruits,[2] and type 8 may be implicated in the ætiology of epidemic keratoconjunctivitis.[5 7] Huebner et al.[6] proposed to call the group of viruses the adenoidal-pharyngeal-conjunctival (A.P.C.) viruses, but Dingle and Feller[2] prefer to call them the viruses of acute respiratory disease (A.R.D. viruses), and Hilleman et al. describe them as the RI group of viruses. At a recent meeting one virologist suggested that to commemorate the work of Huebner, Dingle, and Hilleman, the group should be called the Hudihi or Hidihu viruses—a suggestion which could hardly increase the present state of confusion. Since we have earlier used the name A.P.C.,[8] we shall retain it for the time being.

Types 4 and 7 of the A.P.C. viruses have now been clearly associated with what Stuart-Harris et al.[1] called "febrile catarrh" and what was subsequently called acute respiratory disease (A.R.D.).[9] This is an acute respiratory infection which characteristically occurs in epidemics among military recruits but not in seasoned men. Andrews et al.[9a] found little evidence of A.P.C. infection in 10 R.A.F. stations which did not receive recruits. The illness is an acute, febrile, influenza-like infection in which constitutional upset is usually less prominent and sore throat, hoarseness, and cough are more noticeable than in influenza. Among the physical signs injection of the pharynx and slight enlargement of the cervical lymph glands are common. There are a number of mysteries in the epidemiology of this infection. Its association with recruits suggests that it produces much more immunity than does virus influenza, which attacks recruits and seasoned men

days later, on Dec 22, the child was discharged home still slightly ataxic but reacting normally to his parents and feeding well

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[2] Dingle, J. H., Feller, A. E. *New Engl. J. Med.* 1956, 254, 46

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In the same year DALTON [18] and MADDER [19] gave the method a trial with equally gratifying results, and BLAND SUTTON followed WEBB-JOHNSON immediately.

Whatever the reason for the leaps and jumps by which surgery advances (surgical fashion being no more suited to reasoned analysis than the changing fashion in hats and politics), they prove at least the need for periodical re-examination of the practices on which we rely. The no-dressing technique merits re-examination, not only because some of the arguments in its favour may be even more valid today than they were in the past, but because the success recorded by WEBB-JOHNSON and others casts unexpected light on the uncommonness of wound infection in clean surgical incisions forty-four years ago. Though no comparable figures are available, its prevalence is almost certainly much higher today.

FRANK MELENEY [20] says that "if we were to ask the average surgeon how often his clean wounds become infected, he would probably answer, 'Very *seldom, not* once in a hundred times,' or 'I haven't had an infection for years.' In actual fact, the number will vary from 5 to 20 per cent, or more, of all clean cases. Of those 1 to 5 per cent will be serious, resulting in pain, fever, suppuration, weakness of the wound, disruption or hernia, prolonged hospitalisation and occasionally death." (One must include here fatal complications of antibiotic treatment.) "The others may be called trivial, but they are annoying to the patient and usually delay his departure from the hospital. In the average case of infection the patient must remain in hospital just twice as long as the patient in whom infection does not occur."

If indeed more operation wounds become infected today than forty years ago, the explanation is not far to seek. In 1912 wound infection meant a major disaster: at best it delayed the patient's convalescence by weeks or months, at worst it killed him. Today, on the other hand, if sterile technique falls short of the highest standard, there is a strong temptation to say "What does it matter? A few pricks—or the latest fashionable 'mycin'—will take care of that." It all sounds very simple, yet LOWBURY [21] was right when he remarked that the "dilemma of hospital infection has been complicated rather than solved by chemotherapy."

In their investigation in a thoracic surgical unit in the North of England, BLOWERS et al.[22] were impressed by the fact that, far from diminishing the incidence of wound-infection, the routine use of "penicillin-cover" merely increased the number of resistant organisms, and thus made the management of cases more difficult. Furthermore, they found that most of the wound-infections originated in the theatre at the time of the operation—the chief reasons for infection being inefficient ventilation, the use of blankets in the theatre, and excessive movement by the staff.

It should be unnecessary in 1956 to point to the advantages of asepsis over antisepsis. All the minutiæ of its technique have been worked out over the past fifty years—the autoclaving of instruments, the scrubbing of hands, the masking of noses, the preparation of operation fields, the avoidance of contamination by air currents, the use of silk a
nylon, the gentle handling of tissues, the car
hæmostasis. Nevertheless, at a time when all th
precautions should bring the incidence of wou
infection in clean surgical fields to less than 1-2
antisepsis—euphemistically labelled "prophylac
antibiotic cover"—is creeping back into our practi
Antibiotics have become heirs of the carbolic spra
and as they multiply in number and broaden th
spectra, the scrubbing-up time shortens, the ther
door slams, the anæsthetist rattles his newspap
student nurses wander about in aimless bewild
ment, and sister absentmindedly adjusts her ma
on her nose. Unless we recognise that the defen
of this revived antisepsis are already breaking down
and COLEBROOK [23] can see no sign that we do—a ti
may come when we run out of comparatively harml
drugs to counter sepsis, but have forgotten the routi
that prevents it. We shall then need all too plain
a new VON BRUNN to inaugurate a "*new*" *era* wi
the contemporary version of the Teutonic thund
Fort mit dem Spray!

Annotations

PROGNOSIS OF CARDIOVASCULAR SYPHILIS

IT has never been conclusively proved that speci
treatment prolongs life in cardiovascular syphilis. Twent
years ago Padget and Moore [24] claimed that the mortali
of syphilitic aneurysm and aortic incompetence w
halved by arsenical treatment, but they also foun
that the average duration of life in those who died w
not significantly prolonged. Grant's figures [25] from th
country, when re-examined by Moore [26] in 1949, reveal
the same phenomenon. There are several reasons wh
different expressions of the same result may lead t
conflicting conclusions. In the first place, it is only fu
to compare the duration of life when all the patient
are dead. This may mean waiting fifteen or twenty yea
to complete a follow-up study, and few have sufficien
patience for this; yet if the average duration of lif
is calculated before all the patients are dead the figur
will be weighted by those who die early. Another reaso
lies in the exceptional difficulty of arranging a properl
controlled investigation in an increasingly rare disease
which exhibits wide variations of age-incidence, dura
tion, and severity. Moreover, it is a disease which i
subject to complications, such as neurosyphilis, where
specific treatment is undoubtedly effective and cannot
be withheld; this prevents the random allocation of
patients into treated and control groups which is the
essence of a sound therapeutic trial.

An interesting commentary on these problems ha
been provided in the past year by two notable studies
of arsenical treatment in cardiovascular syphilis. In
Chicago, O'Brien and his colleagues [27] found no difference
in mortality between those who received "adequate
treatment (more than 20 arsenical injections) and those
who did not. On the other hand, Grimble,[28] in a careful
study of fatal cases treated at Guy's Hospital between
1923 and 1944, reached the opposite conclusion. He
claimed that the average duration of life in aneurysm
and aortic incompetence was approximately doubled
by arsenical treatment, increasing *from two to four*
and a half years.

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[18] Dalton, J. J. A. *Ibid*, 1912, ii, 76.

[19] Madder, E. C. *Ibid*, p. 76[illegible].

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[23] Colebrook, L. *Ibid*, p. 88.

[24] Padget, P., Moore, J. E. *Amer. Heart J.* 19[illegible], 10, 1017.

[25] Grant, R. T. *Heart*, 19[illegible], 16, 27[illegible].

[26] Moore, J. E. *Amer. J. Syph.* 1949, 33, [illegible].

[27] O'Brien, J. F., Smith, C. A., [illegible], M. A. *Brit. J. ven. Dis.* 19[illegible], 31, 71.

[28] Grimble, A. *Guy's Hosp. Rep.* 19[illegible], 104, 23[illegible].

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Discussion

This child received a large dose of phenobarbitone (about gr 55 in divided doses in thirty-six hours) and was in coma for at least thirty-six hours before treatment was begun Since his respiration did not become depressed, he might well have recovered without active treatment

The fact that he was fat may have been to his advantage It is known that some of the short acting barbiturates—e g, thiopentone—are absorbed from the blood stream by fatty tissue (Goodman and Gilman 1955) The fact that respiration was not affected in this case suggests that a similar mechanism may apply to phenobarbitone

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A case of phenobarbitone poisoning in a child aged 14 months is reported Phenobarbitone had been administered for thirty-six hours by mistake for succinylsulphathiazole

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He was treated successfully with 2827 mg of bemegride, mixed with a convenient intravenous transfusion fluid, given continuously for eighty hours

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FUNGUS INFECTIONS OF BONE

THE relative importance of diseases caused by pathogenic fungi has increased as the power of chemotherapy has subdued the bacteria. Lesions of bone are by no means rare in many fungus infections, and they are sometimes responsible for the first signs and symptoms of illness. A recent paper by Toone and Kelly[5] notes, for example, 8 instances of bone involvement among 25 cases of systemic fungal infection seen over a period of five years at two general hospitals in Richmond, Virginia. 5 of the 8 cases were examples of blastomycosis and 1 coccidioidomycosis—two conditions rarely if ever seen outside the American continent. The 2 remaining infections were cryptococcosis (torulosis)—a condition well recognised all over the world and occasionally reported in this country.

There have been many American reports of bone lesions in these infections. Potter,[6] in 1910, and Stober,[7] in 1914, were among the earliest to describe bone changes. In systemic blastomycosis multiple granulomatous lesions are associated with local bone destruction and definite periosteal reaction. The bones are said to be involved in as many as 60% of fatal cases,[8] and the lesions are often connected with discharging sinuses. Carter[9] later described rather similar disseminated bony lesions in coccidioidomycosis, and Collins[10] has noted 17 examples of the same type of bony involvement in 200 published cases of torulosis. Bony involvement as the first sign has even been recorded in histoplasmosis,[11] which is occasionally seen in this country and is usually marked by fever, emaciation, anæmia, and widely disseminated lesions.

Actinomycosis is, of course, the commonest systemic fungal infection in this country,[12] and bones are often involved. Bones are usually infected by local extension from soft-tissue lesions: thus the mandible may be attacked in cervicofacial actinomycosis and the spine in the abdominal form of the disease. This mode of spread is in contrast to the blood-stream dissemination which is responsible for bone lesions in the other fungus infections. Infection can also spread directly to bone in maduromycosis (Madura foot) in which a variety of different fungi may be present.

In all these conditions, diagnosis depends ultimately on recovering organisms from pus or other material. Special bacteriological techniques are often needed, and they should be used in the investigation of material from all cases of obscure infection, whether or not fungal cells have been identified on direct microscopic examination. In some, but not all of these infections, fungal elements can be identified in histological sections, and in recent years the periodic-acid Schiff staining technique has been found effective.[13-15] Complement-fixing antibodies or hypersensitivity to fungal vaccine are sometimes a help in diagnosis at certain stages of infection.

It is clear that we should be more aware of fungal infections even in a part of the world where relatively few are endemic. One of the best introductions to the subject for the general reader is the brief monograph[16] by Conant and his colleagues, of Duke University, North Carolina. Added importance has recently been given to prompt and accurate diagnosis by encouraging therapeutic results[17-19] with the aromatic diamidines, particularly 2-hydroxystilbamidine, in blastomycosis, actinomycosis, and cryptococcosis, but no effective treatment has yet been found for coccidioidomycosis and histoplasmosis or for cryptococcosis involving the central nervous system.

CHILD MENTAL WELFARE

MUCH mental illness can be attributed, in part at least, to disturbances in parent-child relations in the earliest years of childhood. In the past, child-guidance clinics have been regarded as preventive services, but they have never in fact been this, since few children come to these clinics until several years after their troubles begin. The foundations of the parent-child relationship are laid in the antenatal period and during the first few months of the child's life. At this time the parents are facing new anxieties, and their emotional attitudes are often changing. They are then most accessible to help, and quite simple measures may tip the balance in the right direction. Early action necessarily depends upon early recognition, and here the staffs of antenatal and child-welfare clinics have a unique opportunity. But this help can succeed only if the clinic staffs are encouraged to take an interest in mental-health problems and concern themselves actively with preventive mental-health work. There have lately been cheering signs that more is being done in this direction.[20]

The recent report of the committee on maladjusted children[21] recommended that the staffs of child-guidance clinics should cooperate more closely with those of the welfare centres. This is not a new idea: several child-guidance clinics in London have been established in child-welfare centres for eight or nine years, and in 1952 the first comprehensive health centre was opened by the London County Council at Woodberry Down. It is encouraging, however, to read of further developments. Mackenzie[22] has lately discussed a scheme for "voluntary training" of welfare-centre staff, who are interested in this work. Since 1953 weekly case conferences have been held at a child-welfare centre. At first they were attended by a welfare-centre doctor and health visitor and by a psychiatrist and a psychiatric social worker. The team was later expanded to include 3 welfare-centre doctors and 2 health visitors. Patients did not attend the conferences. No rigid scheme was followed, but the discussion was generally directed towards clinical problems, the initiative being left with the welfare team. Mackenzie attaches great importance to the presence at the discussion of the welfare-centre doctor and the health visitor concerned with a particular patient, and much of the success of the scheme has sprung from the different approaches of the various members of the team. New

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Mr G K MCKEE (Norwich) had had similar favourable experience of the procedure, but remarked that some apparently pertrochanteric fractures were really subtrochanteric posteriorly, so a nail might split the cortex in this region He therefore preferred to add to a vertical nail a slotted plate which would allow some telescoping

Mr ROLAND BARNES (Glasgow) did not think that this method was adequate for the unstable type of fracture because the comminution of the inner cortex would preclude stability and permit varus deformity with danger of the nail breaking through the head as in other methods

Internal Fixation for Bennett's Fractures

Mr F C BADGER (Birmingham) described his method of treating Bennett's fractures, whereby through a dorsal incision the fragment was reduced and fixed by a small screw passed through the base of the shaft No plaster was necessary The patients were off work on average for three weeks In 13 out of 17 cases the results had been good, the failures resulting either from the use of too short a screw with later redisplacement of the fragment, or from a badly placed screw

Mr O J VAUGHAN JACKSON said that he used a small pin and a mid-lateral approach in 2 cases the small fragment had been found turned over so that the articular cartilage was apposed to cancellous bone on the major fragment

Congenital Dislocation of Hip

Mr J C SCOTT (Oxford) reported the interim results of 75 cases of congenital dislocation of the hip treated at Oxford since 1949, under the régime devised by Mr E W Somerville and himself The cases were treated within what he called the " critical period "—from the beginning of weight bearing to the age of 4 The method consisted in (1) gradual reduction by traction on a special frame, (2) operative removal of the limbus where this was shown by the arthrogram to be in turned, and (3) rotation osteotomy to correct anteversion when required He believed that the dislocation was first anterior and later became superior and then posterior for the head to lie on the dorsum ilii He thought that it was usually the lesser trochanter that pushed in the limbus, the secondary reduction in circulation was responsible for the smallness of the epiphysial head and cases of later osteochondritis The

Special Articles

BEDWETTING

PREVALENCE AMONG CHILDREN AGED 4-7 YEARS

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THE importance of bedwetting as a public health problem is emphasised by Bransby, Blomfield, and Douglas (1955). We describe here more fully its prevalence in different groups of the population and discuss the extent to which it might be prevented or reduced by changes in environment or in upbringing.

Our data are derived from 5386 children born during the first week of March, 1946. These children were followed up by health visitors during the pre-school years, and on reaching school age were kept under observation both by school nurses and by school doctors. At present, when they are 10 years old, we are still in touch with 4351 children (92% of those who were enrolled in the 1946 survey and are still living in this country). They are fully representative of the whole population of children of their age.[1]

Questions about bedwetting were asked on three occasions by either health visitors or school nurses during home visits made when the survey children were aged 4¼, 6, and 7¾ years. At each visit the mothers were asked whether their child was wet by night and, if so, how often. On the second visit they were also asked whether he was wet by day. Information about methods used to cure the wet children was obtained when they were aged 6 and 7¾ years, and on the last visit the mothers were asked whether any of the sibs of the survey children had been bedwetters.

TABLE I—CHILDREN WET BY DAY

—	Wet by day only	Wet by day and by night	Total
Boys	7	30	37 (1·8%)
Girls	30	46	76 (4·1%)
Total	37	76	113 (2·9%)

In calculating these percentages a correction has been made for the fact that, whereas all children in the upper social groups who were born during the first week of March, 1946, were enrolled in the survey, only 1 of every 4 children in the manual working classes was enrolled (cf. Douglas 1951). This correction is made by giving the former groups a weight of unity and the latter a weight of 4.

We have excluded from this study all children whose histories at any of the three ages chosen were incomplete owing to temporary absence from the survey.[2] This reduced the number of children available from the original total of 4351 to 4294 (2268 boys and 2026 girls).

Children Wet by Day

Information about children who were wet by day was obtained when they were 6 years old, when 113 of them were reported to be wet by day. The numbers of boys and girls affected are shown in table I, the last column of which gives the prevalence for each sex.

Many more girls than boys are wet by day;[3] the sex difference is particularly striking among those who, although wet by day, were dry by night.

Owing to the relatively small number of affected children it is unprofitable to make a more detailed study of day wetting. All that need be said is that the variations in prevalence in the different groups of the survey population were, with the single exception of sex, closely similar to those reported below for bedwetters.

Bedwetting

Sex

We have divided the bedwetters (among whom were 3 mongols and 9 mentally defective) into those wet several nights a week (the regularly wet) and those wet less often (the occasionally wet). The proportion of children falling into these groups is shown in table II.

TABLE II—PREVALENCE OF BEDWETTING BY SEX (2268 MALES AND 2026 FEMALES)

—	Percentage frequency of bedwetting at age (yr.)		
	4¼	6	7¾
Regular bedwetters			
Male	3·69	4·00	3·55
Female	3·21	3·11	2·10
Occasional bedwetters			
Male	9·94	7·88	4·54
Female	7·34	5·31	4·11
Total			
Male	13·62	11·91	8·09
Female	10·55	8·42	6·11

Bedwetting, both occasional and regular, is consistently more frequent among boys than among girls. As regards regular bedwetting, the boys show no decline in prevalence during the survey period, whereas the prevalence among the girls drops by about a third. Thus the difference between the sexes, which is not quite significant at 4¼ years, is highly significant at 7¾ years.[4] The position is different for occasional bedwetters, among whom there is a steep decline for both sexes rather greater for the boys than for the girls. In this group the sex difference is highly significant at 4¼ and not significant at 7¾ years.[5]

4·3% of the boys and 2·8% of the girls were consistently wet throughout the whole survey period; most of them were reported as regularly wet on some occasions and occasionally wet on others.

TABLE III—PREVALENCE OF BEDWETTING BY PLACE IN FAMILY (REGULAR BEDWETTERS ONLY)

—	Percentage of regularly wet at age (yr.)			No. of children† (wet and dry)
	4¼	6*	7¾	
Firstborn	2·90	2·79	2·9[illegible]	[illegible]
Later born	3·76	4·02	2·9[illegible]	[illegible]

* $\chi^2 = 3{\cdot}68$ n = 1 $0{\cdot}1 > P > 0{\cdot}05$.
† There were 11 cards where information on place in family had not been punched.

When the prevalence of bedwetting in the two sexes is combined the proportion of children reported we no dislocation was present at first. He therefore recommended open fixation by wiring the spinous processes and bone grafting in all such cases; wiring alone was insufficient. Union was rapid and protection was required for three months only; there had been no deaths in 16 operations.

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[1] A detailed account of the losses through death, emigration, &c. will shortly be published as part of a comprehensive report on the health, growth, and environment of the pre-school child. For an account of the sample and methods of the inquiry see Douglas (1951).

[2] These temporary absences were due to illness or to removal of a family which was still untraced at the time of the survey.

[3] $\chi^2 = 18{\cdot}767$ n = 1 $P < 0{\cdot}001$.

[4] Comparing the prevalence of regular bedwetting among boys and girls:
At 4¼ years $\chi^2 = 3{\cdot}800$ n = 1 $0{\cdot}1 > P > 0{\cdot}05$.
At 7¾ years $\chi^2 = 7{\cdot}622$ n = 1 $P < 0{\cdot}01$.

[5] Comparing the prevalence of occasional bedwetting among boys and girls:
At 4¼ years $\chi^2 = 13{\cdot}000$ n = 1 $P < 0{\cdot}001$.
At 7¾ years $\chi^2 = 2{\cdot}239$ n = 1 $0{\cdot}2 > P > 0{\cdot}1$.

Mr **Barnes** said that in these cases he applied both deep and superficial wiring to his grafts; this gave such stability that only the lightest collar protection was necessary. He suspected that cases of unilateral locked facets were always irreducible by traction alone and needed immediate open reduction.

Stress Fractures of the Fibula

Mr M. B. **Devas**, with Mr R. **Sweetnam**, had seen 50 cases of stress fracture of the fibula, all in athletes. All their patients were already in training, and the chief cause appeared to be running on a hard surface. A ten day history was common, and the usual complaint was of pain behind the ankle. In some cases the onset was sudden; in rather more it was gradual. A few had noticed local swelling; this was always slight, tender, and soft at first and later hard. "Springing" the fibula produced pain. Diagnosis was made on clinical grounds and not from radiographs, in which the changes were slight even after a month. A fine crack appeared often affecting only the lateral cortex, and running upwards, inwards and forwards; the periosteal reaction was minimal. The scar in the bone might remain visible for years. The majority (29 cases) occurred between 4 and 7 cm from the lower end of the bone; the highest seen was 23 cm up. Two thirds of the cases had occurred in the winter months, perhaps because at that time official tracks were being saved and training done on roads. They believed that the stress was due to muscle action each time the ball of the foot struck the ground; they demonstrated by special radiographic technique that static contraction of the calf muscles without ankle movement caused the upper two thirds of the fibula to approximate to the tibia, although the lower part remained unmoved. Patients must stop all sport until free from pain and then take up training gradually. Strapping was useful but plaster was definitely contra indicated. If pain recurred the patient must again reduce his activities.

Mr **Newman** remarked that he had seen cases affecting the upper third of the fibula in parachutists.

Mr **McKee** had seen 1 case progress to non union requiring excision and bone grafting.

Mr **Devas** thought that the stress fractures of the upper third of the fibula in parachutists were of a different nature and were due to repeated relatively severe injuries.

BRITISH INSTITUTE OF RADIOLOGY

Radioactivity in Man and his Environment

In a presidential address on June 24, Prof. F. W. **Spiers** discussed the background or natural radioactivity of Man and his environment.

Professor Spiers pointed out that Man has always been exposed to ionising radiations; in fact, he has always lived in a radioactive world. It now seems likely that, at least in geologically recent times, there has been no great change in the radiation intensity to which Man has been exposed in his environment. But Man has now begun to produce artificial radioactivity and ionising radiations in abundance, and Professor Spiers considers it possible, and perhaps likely, that the increase in radiation background now taking place will be greater than any changes in the past.

The human body is naturally irradiated in two ways: by sources of radiation external to the body, which include terrestrial and cosmic radioactivity; and by internal radioactivity acquired by the body from air, food, and water. The radiation dose acquired in this way is known as the "background dose."

The main contributors to terrestrial γ-radiation are the members of the uranium and thorium series, together with naturally occurring radioactive potassium. Swedish alum shale is an example of a particularly highly radioactive rock; granites are less active, and sedimentary rocks are considerably less active than granites. Sea water has a low radioactive content, the equivalent radium content of sea water is about 100 times lower than that of sedimentary rocks. High radioactivity can occur in mineral waters and well waters. The radioactivity of tap water is much reduced by precipitation methods of purification.

The natural radioactivity of the air is due to radon and thoron arising from the escape of these gases from the ground. Their local concentrations depend on local atmospheric conditions, as well as wind, rain, dust, and, in the case of buildings, their ventilation and fabric.

The radium content of the human body has lately been established as $0{\cdot}05\text{–}0{\cdot}32 \times 10^{-9}$ g. Since there is only a slight correlation between the body-radium content and drinking-water, it seems probable that the major source of this radium is food. The other main contribution to internal radiation is from radioactive potassium; the ^{40}K body content is now established at about 0·2% of body-weight. Radioactive carbon as ^{14}C, though present, is such a weak β-ray emitter that its contribution to radiation dose, compared with radium and potassium, is negligible.

There are three components of external radiation background: local γ-radiation, cosmic radiation, and atmospheric radioactivity.

Rock radioactivity is responsible for most of the external γ-radiation background. Higher dose rates are recorded inside buildings than in the open air, particularly if the building fabric contains a high proportion of radioactive material—for example alum shale in concrete. In general, wooden houses do not have very dissimilar dose-rates from those in the open air; brick buildings are intermediate between wood and concrete or concrete shale structures. The dose rates recorded vary from 48 to 50 m rad[1] per year out of doors or in Swedish wooden houses, to 171 m rad per year for concrete buildings with a high proportion of alum shale in the concrete.

Cosmic radiation at sea level in Northern latitudes contributes 28 m rad per year. This intensity is increased by altitude, and diminished by absorption in the basements of tall buildings.

Atmospheric radioactivity under normal conditions with a radon atmospheric content of 3×10^{-13} curie[2] per litre contributes about 4 m rad per year. This is small, but if the highest recorded values from London of $2\text{–}3 \times 10^{-12}$ curie per litre are used the γ ray dose is of the same order as that from cosmic radiation.

The internal radiation background is due to radioactive potassium primarily in soft tissues, ingested radium in bone, radioactive carbon, and radon and its disintegration products in air.

^{40}K is the main agent of soft tissue irradiation and is estimated to contribute 20 m rad per year mean dose, the dose rates to individual organs being determined by their potassium content. ^{14}C contributes about 1 m rad per year.

Bone dosage is likely to be particularly heterogeneous, but if 82 m rem[3] per year is received from sources other than radium, and if an osteocyte is 5 µ in diameter, the radium contribution is estimated to be 39 m rem per year, making a total dose-rate of 121 m rem per year to the osteocyte.

The contribution to the internal background radiation made by radon and its daughter products arising from their inhalation is uncertain, and depends on the assumptions made. It is probably of the order of 2·0 m rem per between children in England and those in Wales and Scotland

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[1] rad is a unit of absorbed dose. It is 100 ergs per gramme (International Commission on Radiological Protection 1955.)

[2] curie is a unit of radioactivity defined as the quantity of any radioactive nuclide in which the number of disintegrations per second is $3{\cdot}700 \times 10^{10}$ (I.C.R.P. 1955.)

[3] rem is the absorbed dose of any ionising radiation which has the same biological effectiveness as 1 rad of X radiation with average specific ionisation of 100 ion pairs per micron of water in terms of its air equivalent in the same region. A dose in rems is equal to the dose in rads multiplied by the appropriate R.B.E. (relative biological effectiveness) (I.C.R.P. 1955.)

Effectiveness of Therapy

Of the 136 children regularly wetting their beds at $4^1/_4$ years 27 2% had become dry by the age of 6 years Of those regularly wet at 6 years 31 6% were dry at $7^3/_4$ years It is of interest to see to what extent the progress of these children is related to the measures taken to cure them We have no information about the earlier period, but, when the children were 6 years old, their mothers were asked about treatment The answers given were divided into the four broad groups shown in table VI, where they are related to the proportion of children cured and improved between the ages of 6 and $7^3/_4$ years

It might appear from this table that the best progress was made when there was no attempt at treatment, and the least progress when the child had been taken to a doctor or a clinic [11] It should be emphasised that we have no information about the selection of children for different types of treatment; it would, for example, be a sufficient explanation of these differences if only the children resistant to minor measures of reassurance and persuasion were taken to clinics or more actively dealt with by their parents

Discussion

The size of the problem of bedwetting is best shown if the percentages given above are used to calculate the number of children in the whole population who are affected at different ages at the current level of births Among children aged 4 years in Britain we would expect about 80,000 occasional and 30,000 regular bedwetters, and among children aged 7 years 30,000 occasional and 20,000 regular bedwetters At any one time there would be about a third of a million bedwetters aged $4^1/_4$–$7^3/_4$ years These numbers are based on the 1% Census Tables and on the prevalences given here, which agree closely with those reported by other workers—c f Bransby et al (1955)—and are, if anything, an underestimate

Comparisons of the prevalence of bedwetting in different social groups suggest that between a third and a half could be prevented by changes in upbringing and environment In other words, they show bedwetting as an important problem of public health Unfortunately, at present we have little knowledge of the various patterns of child-rearing in different sections of the community It is evident from the present inquiry that there are great social differences in the time that toilet training is started and control achieved, but, owing to the wide distribution of the sample, detailed histories of training are not available The poorest families start training latest and their children are also late in achieving control [12] In addition we find in each social group that early training is associated with a low prevalence, and late training with a high prevalence, of bedwetting at later ages [13]

These observations suggest that at least part of the social difference recorded is the result of different patterns of training That it is not wholly so is shown by the fact that among agricultural workers toilet training star late and the prevalence of bedwetting is low

The importance of bedwetting lies not only in its be a common source of worry and inconvenience to moth but also in its effects on the later adjustment of the chi This will be the subject of a further study, when we ha had greater opportunity to observe the progress of the children and to receive reports from their school teach and school doctors

Summary

The prevalence of wetting during the day and at nig among 2268 boys and 2026 girls drawn from all soci groups and from all parts of Great Britain is describ These children were observed throughout the first t years of their lives

At 6 years 1 8% of the boys and 4 1% of the girls we wet by day For both sexes together the prevalence day wetting was 2 9%

12 2% of all children aged 4 years wetted their bed and by the age of $7^3/_4$ years the proportion had dropp to 7 3%

At each age fewer girls than boys wetted their bed and among those severely affected—i e, who wett their beds several nights a week—the difference betwe the sexes increased with increasing age

These sex differences were most obvious (and on statistically significant) in the more prosperous familie

The lowest prevalence of bedwetting was found amon the well-to do and among agricultural workers Soci differences in prevalence were well marked for girls bu not for boys, and the high prevalence in the poore groups is partly explained by the large proportion of gir affected

More sibs of bedwetters wetted their beds than did th sibs of dry children

No significant differences in bedwetting were foun between firstborn and later born children, betwee children with younger sibs and those without, an between children living in different parts of Grea Britain

Bedwetting is an important problem for the child welfare and the school medical services since it appea that its prevalence could be considerably reduced b changes in upbringing or in environment But furthe research, particularly into patterns of child upbringin in the different social groups, is needed before effectiv preventive action can be taken

This survey is being made by a joint committee of the Institute of Child Health (University of London), the Societ of Medical Officers of Health, and the Population Inve ti gation Committee The chairman of the committee is Prof James Young the vice chairman Prof A A Moncrieff and the secretary Prof D V Glass The Nuffield Foundation has financed this inquiry during the pre school years and grants for continuing it in the primary school period have b made by the board of governors of the Hospital for Sick Children, Great Ormond Street through the Institute of Chil Health, and by the Ford Foundation Fourteen nationa hospital boards have also made grants to the inquiry fro their free moneys

We wish to thank the chairman and members of the join committee for their help and advice, the medical officers of health and the health visitors whose generous coöperation made the survey possible and the mothers in all parts of the country, who willingly answered numerous and detailed questions about their children s health

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[11] Comparing the proportions dry by $7^3/_4$ years χ^2 = 14 57 n = 3 P<0 01

[12] The proportions of mothers who did not start toilet training until after the sixth month were professional and salaried 8 7% black coated 9 8% manual 16 4% agricultural 14 9%

[13] For the whole sample the proportion of children regularly wet at $4^1/_4$ years was 2 8% for those whose toilet training was started during the first six months and 4 2% for those whose training started later The corresponding figures at 6 years were 2 6% and 4 2% and at $7^3/_4$ years 2 2% and 3 7%

Reviews of Books

Medical History of the Second World War

Royal Naval Medical Services Vol II Operations Edited by Surgeon Captain J. L S COULTER D S C, R N H M Stationery Office 1956 Pp 543 *57s 6d*

THIS second volume concludes the official history of the Royal Naval Medical Service in the late war by describing the medical aspects of naval operations From many thousands of reports the editor has chosen those which illustrate the *special problems of war* and has presented them as a clear and orderly account by grouping them into those ashore and those afloat, and by considering each group chronologically and geographically *Occasionally he gives a section to the special matters* they illustrate, such as the type of injury caused by different weapons

The opening chapter deals with the general duties of a ship s surgeon as recorded in a daily journal which covers the commissioning of a cruiser and her service in the Mediterranean and with a Russian convoy during the next eleven months *There follows a detailed consideration of the lessons learned* from these experiences, including an excellent commentary on morale This chapter occupies nearly a fifth of the volume and provides the first published account of the individual and specialised way of life of the naval surgeon Even the four pages given to a singularly uninteresting daily sick list are of value in establishing perspective and balancing the long sequence of epic accounts that follow Many of these are in the narrators own words a few have been skilfully paraphrased *and all are accompanied by shrewd comments or* frank and fair criticisms Brief tables or statistical summaries complete these records

The difficulty of illustrating such a book has been successfully overcome but the publisher s lay-out is uneven and only in the last two thirds of the book are quotations printed in smaller type The three page index is inadequate

Wherever possible the editor has traced the later hospital history of patients treated in action showing the value of the simple measures first adopted These footnotes and statistics represent *a formidable amount of* research, and Captain Coulter is to be congratulated on maintaining such excellent control over his material never confusing the main pattern of the book by irrelevant digressions Stories of extraordinary endurance are inevitably *restricted by space the tented hospital in* Crete the R.N Hospital Hong-Kong during the attack and after the fall the varied and exciting adventures of the light-hearted and courageous junior M O of H M S *Gloucester* at her loss and in his subsequent captivity in *Greece and Germany* · *the affair of the M O* parachuted into South Serbia and later engaged with the guerillas against the Japanese in the Malayan jungles

Several passages reveal how the Admiralty s view of security unfortunately excluded ships surgeons and the medical department *itself from taking* part in planning— to the Navy s detriment Thus, the naval surgeons at the Normandy landings *were sometimes unaware of what* was intended and could make little provision for what was expected of them, while their R.A.M C colleagues had been fully briefed It is however, reassuring that selected medical officers are now trained in staff duties at Greenwich

The final impression is of a work well done which successfully achieves the dual aim of a proud record and a reference for the future

Diseases of the Chest

H CORWIN HINSHAW M D PH.D clinical professor of medicine Stanford University School of Medicine L HENRY GARLAND M B B CH clinical professor of radiology Stanford University School *of* Medicine Philadelphia and London W B Saunders 1956 Pp 727 105s

THE number of textbooks on diseases of the chest which have appeared in recent years reflects the general activity in this branch of medicine and this work is a worthy addition to the list It is intended as a practical reasonably concise, up-to-date guide for the student and practitioner rather than as an exhaustive treatise and the authors have on the whole succeeded in their aim

The exposition is clear the text is amply illustrated with chest films of excellent quality, and there is a good bibliography which concentrates on modern articles of the first importance A fair balance has generally been maintained *in the space allotted to different subjects* but it is surprising that there is no more than a passing reference to influenza and a less lopsided account of xanthomatosis and ' honeycomb lungs ' would be an improvement

Not everyone will agree with the views expressed on some minor points for example the pessimistic pronouncement that at bronchography it is a rare feat adequately to fill both bronchial trees at one sitting , or with the opinion that radiotherapy has a place however small, in the treatment of simple lung abscess

The book is written by a physician and a radiologist. and the value of such a partnership in chest work is rightly *stressed* nevertheless the *importance of the* radiologist is harped on so insistently that the reader may recall the celebrated advice " Codlin s *the friend* not Short " In sum however this is an excellent textbook which should take its place among the standard works

New Directions in Psycho-analysis

The Significance of Infant Conflict in the Pattern of Adult Behaviour Editors MELANIE KLEIN, PAULA HEIMANN and R E MONEY-KYRLE London Tavistock Publications 1955 Pp 534 38s

BITTER controversy about Melanie Klein s theory of early mental development rent psycho-analysis in this country for more than a decade but it has now abated As this volume testifies there is a group of psycho-analysts composed in about equal proportions of doctors and non-medical members who accept her teaching and apply it to very diverse problems

The first part of the book contains twelve essays on schizophrenia depression and other clinical subjects in the second part literary æsthetic ethical, and social issues are considered Some of the writers put forward their views tentatively others *confidently but it is clear that all are convinced that* Mrs Klein s picture of the " positions and ' defences ' of infantile development is correct There are also two papers by Mrs Klein herself one giving the history of her *psycho*analytic play technique, the other exemplifying through a *prolonged analysis of a story by Julian Green her view of* projective identification

In his preface Dr Ernest Jones says with repetitive emphasis that Mrs Klein's work is firmly established. The book hardly confirms this. but bears out Dr Brierley's judgment that the series of hypotheses put forward by Mrs Klein call for lengthy and critical evaluation. rather than *outright* acceptance or rejection

The Medical Care of the Aged and Chronically Ill

FREDDY HOMBURGER, M.D research professor of medicine Tufts College Medical School *Boston* Little Brown London J & A Churchill. 1955 Pp 253 42s

Dr Homburger insists on the importance of preventing the long-term degenerative illnesses which afflict the old. His teaching is directed to the general practitioner. and he deplores the prevalent over-specialisation

> The splitting of the medical profession into the atoms of specialities has brought great progress and developed supreme skills but it is time to put the puzzle together once more *for the emergence of the supra specialist* the competent practitioner who can treat and likes to treat the patient as a whole and not merely as so many cases of this or that "

His advice on the diagnosis and treatment of the rather intangible maladies of old age is detailed and sound The chapters on senile osteoporosis and *malnutrition* for example, are excellent Of inoperable cancer he writes " it is therefore extremely poor medicine to adopt a completely fatalistic attitude upon the discovery of neoplastic metastases and to give up in despair And he gives many examples of ways in which the life of such a patient can *be made tolerable He is* convinced of the value of daily exercises for all chronically ill patients He deplores the use of the bedpan while a between children in England and those in Wales and Scotland.

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More sibs of bedwetters wetted their beds than did t sibs of dry children.

No significant differences in bedwetting were fou between firstborn and later-born children, betwe children with younger sibs and those without, a between children living in different parts of Gre Britain.

Bedwetting is an important problem for the chil welfare and the school medical services since it appe that its prevalence could be considerably reduced b changes in upbringing or in environment. But furth research, particularly into patterns of child upbringi in the different social groups, is needed before effecti preventive action can be taken.

This survey is being made by a joint committee of th Institute of Child Health (University of London), the Soci of Medical Officers of Health, and the Population Inv gation Committee. The chairman of the committee is Pro James Young, the vice-chairman Prof. A. A. Moncrieff, an the secretary Prof. D. V. Glass. The Nuffield Foundation h financed this inquiry during the pre-school years, and grant for continuing it in the primary school period have be made by the board of governors of the Hospital for S Children, Great Ormond Street, through the Institute of Chi Health, and by the Ford Foundation. Fourteen region hospital boards have also made grants to the inquiry fro their free moneys.

We wish to thank the chairman and members of the join committee for their help and advice; the medical officers o health and the health visitors, whose generous coöperatio made the survey possible; and the mothers in all parts o the country, who willingly answered numerous and detail questions about their children's health.

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[11] Comparing the proportions dry by $7^{3}/_{4}$ years: $\chi^2 = 14.57$; $n = 3$; $P<0.01$.

[12] The proportions of mothers who did not start toilet training until after the sixth month were: professional and salaried 8.7%, black-coated 9.8%, manual 16.4%, agricultural 14.9%.

[13] For the whole sample the proportion of children regularly wet at $4^{1}/_{4}$ years was 2.8% for those whose toilet training was started during the first six months and 4.2% for those whose training started later. The corresponding figures at 6 years were 2.6% and 4.2%, and at $7^{3}/_{4}$ years 2.2% and 3.5%.

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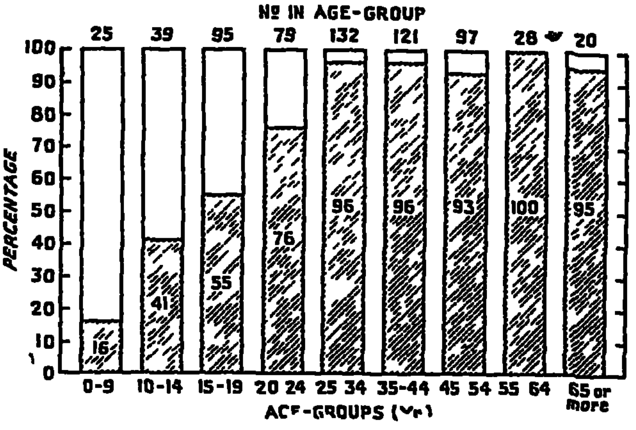

Fig 2—Results of tuberculin testing

led to recall for a full sized film again taken by the mass radiography unit In some cases the patient was too ill or too uncooperative for this to be done, in such cases the hospital portable apparatus was used In some patients it was necessary to make several exposures before a completely satisfactory film was obtained

Clinical and Bacteriological Examination —Where any significant abnormality was detected on the full sized chest radiograph the patient was examined clinically and as complete a history as possible was obtained Attempts were made to obtain sputum for examination by microscopy of the concentrated deposit and by culture for tubercle bacilli Many of the specimens obviously did not come from the patient's lower respiratory tract Whenever no sputum could be obtained an attempt was made to isolate tubercle bacilli from laryngeal swabs and fæces

Results

Tuberculin Testing —All 636 patients in the hospital at the start of the survey were tuberculin tested, and 512 (80 50%) were positive Fig 2 shows the result of tuberculin testing according to age groups 80 22% of males and 80 88% of females were positive in each age group the percentage positive was similar for males and females and the results are shown for both sexes together

Radiography —Of the 512 tuberculin positive patients at the start of the survey 6 left the hospital and 1 died of non tuberculous disease before the radiographic survey The remaining 505 positive reactors all had satisfactory chest radiographs and 32 of these were considered to be abnormal 25 of the 124 tuberculin negative patients were radiographed and 2 of these radiographs were abnormal Table II shows the result of the radiographic survey

Bacteriology —Specimens were examined bacteriologically in every case where tuberculosis seemed a possible diagnosis No tubercle bacilli were found in any specimen

TABLE II—FINAL RESULTS OF SURVEY

—	Males	Females	Total
Population surveyed	359	270	629
Abnormal lungs	26 (7 24%)	8 (2 96%)	34 (5 41%)
Non tuberculous lung disease	7 (1 95%)	1 (0 37%)	8 (1 27%)
Respiratory tuberculosis	19 (5 30%)	7 (2 59%)	26 (4 14%)
Significant tuberculosis	17 (4 74%)	6 (2 22%)	23 (3 66%)
Active tuberculosis	7 (1 95%)	4 (1 48%)	11 (1 75%)
Observation tuberculosis	10 (2 79%)	2 (0 74%)	12 (1 91%)
Insignificant tuberculosis	2 (0 56%)	1 (0 37%)	3 (0 48%)

Diagnosis and Classification —Final diagnosis in each case was reached mainly on an interpretation of the radiograph or a series of radiographs In many cases the diagnosis of tuberculosis was not considered beyond doubt until some months had elapsed and serial radiographs had been taken In all doubtful cases where the lesion may have been non tuberculous pneumonia the response to penicillin was assessed radiographically as a first step The response to antituberculous drugs also helped in reaching a diagnosis All the patients were allocated to two main groups—tuberculous and non tuberculous The tuberculous patients were grouped into those with insignificant and those with significant lesions, the latter being further divided into those thought to be active and therefore requiring treatment and those thought to be quiescent but still requiring careful observation Table II shows the final results of the survey classified as described

Discussion

The results of the present survey are similar to those already published Of 629 patients 23 (3 66%) showed significant tuberculosis, of which 11 cases (1 75%) were considered active 7 of the active cases were in males and 4 were in females 3 showed definite cavitation 6 of the cases of significant tuberculosis were previously known to the hospital authorities There is no reason to suppose that the prevalence of pulmonary tuberculosis in the hospital surveyed was any higher than in other similar institutions Oechsli (1949) has shown that the prevalence of tuberculosis in mental hospitals may be twice as great as in mental defective institutions

It is particularly appropriate that attention should be drawn to this state of affairs when the mental hospital service is undergoing development Not only is the problem serious for patients within the hospital, but also with the present improvements in treatment and the resulting high discharge rate of patients to their own homes measures should be taken to prevent the spread of tuberculosis in the general community by patients who have been discharged from mental hospital and have developed tuberculosis while in hospital In 1954, in England and Wales, 65,329 patients left mental hospitals and institutions for mentally defectives and returned to life in the general community the corresponding figure for Scotland is 6476

Control of Tuberculosis in Mental Institutions

The steps necessary for the control of tuberculosis in mental hospitals are well known and have been applied with encouraging results in several countries, particularly the United States With the advent of effective chemotherapy and its facilitation of sputum conversion even in chronic and advanced cases, it should be possible to produce better and more rapid results We suggest the following scheme of control

(1) Survey of all patients including tuberculin testing and radiography of positive reactors Where possible, negative reactors should also be radiographed

(2) Thorough investigation of all cases with abnormal radiographs and segregation of those with significant pulmonary tuberculosis

(3) B C G vaccination of all negative reactors to tuberculin once segregation of all possible sources of infection has been secured

(4) Annual radiography of all patients whether or not they have been radiographed in the preceding months

(5) Radiography and tuberculin testing of all newly admitted patients and immediate segregation of any showing abnormalities suggesting tuberculosis, and B C G vaccination of negative reactors to tuberculin

Possibly these measures could best be implemented by setting up special units for mental patients with

THE LANCET

LONDON SATURDAY, JUNE 2, 1956

"Anæmia" in Pregnancy

In a recent issue Dr Edgar and Dr Rice[1] raised the question whether it is desirable to give iron supplements to *all* pregnant women. They showed once again, how the hæmoglobin level in the peripheral blood falls during pregnancy; the mean hæmoglobin in their patients when the pregnancy was 5–8 weeks advanced was 91.8%, and at 33–36 weeks it was 76.7%. At the 5–8 week stage only 0.7% of the women had a hæmoglobin level of less than 70% (10 g. per 100 ml.). In their patients the mean corpuscular hæmoglobin concentration (M.C.H.C.)—a measure of iron deficiency—was 30.2%, a figure indicating, according to Discombe, iron deficiency short of anæmia. Edgar and Rice gave a daily supplement of iron in the form of tab. ferri sulph. co. gr. 9 (0.6 g.) daily; since the familiar green tablets have so often caused nausea or vomiting, they used white-coated tablets and only 5% of their patients reported intolerance. This dose of iron was given to a group of pregnant women of whom 89 were carefully followed through pregnancy. In 69 a normal hæmoglobin level was maintained throughout and the M.C.H.C. remained normal too; in the remaining 20 there were various degrees of falling away from normal.

The gradual fall of the hæmoglobin level in the peripheral blood in pregnancy has long been attributed to an increase in the plasma-volume, and the lowered hæmoglobin level was thus thought to be due to dilution rather than to anæmia. The calculation of the blood-volume has, in most investigations, been made indirectly from the venous hæmatocrit value and the estimation of plasma-volume by the Evans blue dilution technique. But Verel et al.,[2] who have reinvestigated this question, point out that the calculation depends on the assumption that the venous hæmatocrit bears a constant relation to the body hæmatocrit. In health the two figures are almost identical, but in disease and in pregnancy this is not necessarily the case. They therefore made simultaneous estimations of the plasma volume, by the usual Evans-blue method, and the red-cell volume, using radioactive phosphorus (^{32}P). They found that in pregnancy the ratio of body hæmatocrit to venous hæmatocrit varied unpredictably, and consequently it was necessary to re-examine the question of blood changes in pregnancy using separate estimations of red-cell and plasma volumes. Fortunately the new results do confirm previous views. Comparison with measurements made on a series of non-pregnant women showed that, when properly related to body-weight, the plasma-volume increased during pregnancy, and in addition the red-cell volume was maintained or even increased in 2 out of their 13 subjects. This maintenance or rise of the red-cell volume during pregnancy has received less attention than the dilution effect of the bigger increases of plasma-volume, but it has been recognised for some time. Caton et al.[3] found a definite rise in red-cell volume in their series of patients, though there was much individual variation. Wilson and Boyle[4] pointed out that the red-cell mass was increased in all their 5 patients, but the rise was proportionately not as large as that of the plasma-volume.

All these data suggest that the gradual lowering of the hæmoglobin level in the peripheral blood to about 10 g. per 100 ml. during pregnancy cannot be properly classified as "anæmia," if anæmia means that there is insufficient hæmoglobin to carry the oxygen the patient needs; for it is clear that the red-cell mass is either unaffected or actually increased. Clinical observation had, in fact, led to much the same conclusion; and many obstetricians consider as "anæmic" only those pregnant women whose hæmoglobin is less than 10 g. per 100 ml. (70%). With this definition, other observers have recorded figures very like those of Edgar and Rice. For example, Gatenby and Lillie,[5] in Dublin, found 24% of their pregnant patients to be anæmic by this criterion, and 9% of them were below 9 g. per 100 ml.; they noted too that symptoms attributable to the anæmia rarely become prominent at hæmoglobin levels above 6 g. per 100 ml. (45%). Edgar and Rice have therefore suggested that all pregnant women should have two hæmoglobin estimations, one when they first come to the antenatal clinic and the second between the 32nd and 36th weeks. Those with a hæmoglobin level of at least 70% are given a small dose of iron (gr. 9 of ferrous sulphate daily) to take throughout the pregnancy, but no further investigation is made. Those whose hæmoglobin level is less than 70% are sent for proper hæmatological investigation.

The form of this proper investigation is now established. Owing to the changes in the relations between plasma-volume and red-cell mass the colour-index is useless for diagnosis. We rely on the M.C.H.C. for the detection of iron deficiency and on sternal-marrow examination for the detection of the megaloblastic anæmia of pregnancy. Probably 9 out of every 10 patients with anæmia of pregnancy in this country are iron deficient. A fair proportion of these will respond quite satisfactorily to oral iron, and, as O'Sullivan et al.[6] pointed out, moderate doses of ferrous sulphate or ferrous gluconate will suffice. Increasing the dose beyond 0.6 g. daily of ferrous sulphate or 2 g. daily of ferrous gluconate brings proportionately much less benefit at the cost of a steeply rising intolerance-rate. It is better, in patients not responding to these doses of oral iron, to give parenteral iron, and, now that reliable intravenous and intramuscular preparations are available, such treatment should present no difficulties. But parenteral iron needs time to become effective; about 2 weeks elapse by either route before there is

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Tracing the Source of Infection

Swabs were placed in the sewer in three different places (1) near the manhole from which the sewage had escaped, (2) at a sewer junction about 200 yards away, and (3) at a pumping station half a mile away through which passed sewage from most of the houses on the south side of the town These swabs consisted of rolled-up pieces of gauze and were suspended in manholes at such a level that the sewage flowed over them They were left in situ for three days

The first examination produced negative results in all cases When it was repeated, however, the swabs from the sewer junction and the pumping station grew *Salmonella typhi*

Meanwhile I had looked through my records and found that in the previous 28 years there had been five cases of typhoid in Farnham Inquiries showed that one of these patients could not be traced, one had left the district, one was dead, and two were still living in Farnham One of these was the patient's uncle and had had typhoid 26 years ago He was immediately suspected, but he lived in a different house and had not seen the patient for some six to eight weeks before the onset of the illness

Fæces and urine from these two ex-typhoid patients were examined but gave negative results Because they might be excreting bacilli intermittently, swabs were placed in the manholes of the sewers from each of the houses occupied by these people Immediately, a positive result was obtained from the house occupied by one of the ex-typhoid patients, who lived on the south side of the town and had had typhoid 5 years ago The other specimens were negative Further positive results were obtained from the pumping station and a sewer through which the sewage from the affected house flowed

The man who had had typhoid was naturally thought to be the source of this contamination, but three consecutive specimens of urine and fæces all gave negative results

The only other occupants of the house were his wife and his mother-in-law, Mrs A Specimens were then obtained from them, and those from Mrs A gave positive results in urine and fæces

This woman, aged 74, had spent many years of her early life in India and Egypt, and although she had never to her knowledge had typhoid she did have some obscure and prolonged illness just previous to and after the birth of her daughter about 35 years ago This was probably typhoid 30 years ago her son had typhoid at the age of 3 years Her son-in-law Mr B, when he had typhoid 5 years ago, was living in a different house but stated that he often had meals with Mrs A

Cultures from the patient, the sewer swabs, and Mrs A all belonged to the same untypable Vi strain and were identical with that obtained from Mr B 5 years previously It seems reasonable to assume, therefore, that Mrs A had typhoid in Egypt some 35 years ago and has been excreting bacilli ever since and, as a result, infected her son 30 years ago, her son-in-law 5 years ago, and, lastly, the boy who had been paddling in the contaminated sewage

Points of interest are as follows

(1) The place where the boy was paddling was at least three miles from the original source of infection, and the sewage was heavily diluted with storm water

(2) Although Mrs A had probably been excreting typhoid bacilli for some 35 years she has so far as we know, infected only three people

(3) The swabs placed in the sewers gave consistent results

Treatment of the Carrier

The treatment of typhoid carriers is extremely unsatisfactory Recently, promising results were reported from America from using 3 mega units of penicillin every six hours together with probenecid 1 5 g twice daily for ten days (Parker et al 1953)

C A Rumball (Ministry of Health, personal communication), in dealing with R A F cases abroad used 2 mega units of penicillin three-hourly with 0 5 g of probenecid six-hourly for seven days, together with 5–8 g of sulphadimidine daily The essence of the treatment is to secure and to maintain a high blood penicillin level by combining it with probenecid, which temporarily inhibits the renal tubules The treatment has been used in this country in mental hospitals, where typhoid carriers are somewhat common

According to Dr Grant Nicol (personal communication), of the Ministry of Health, the results so far to hand have been very variable, but about 30% of the carriers treated ceased to excrete bacilli and remained free for a year or more Others relapsed as soon as the treatment was stopped The treatment is not without risk, particularly to people with damaged kidneys or a poor cardiovascular system

Before treating a patient it is advisable, therefore to investigate thoroughly the cardiovascular system and to make an electrocardiogram, besides testing the kidney functions (blood-urea level, urea concentration test, and alkali reserve)

Treatment would consist of 28 or 56 injections of penicillin according to the method adopted, and the blood-penicillin level should be checked after 24 hours and 3 days to see that a satisfactory concentration of penicillin is being obtained

The present carrier is a frail old lady aged 74, and I did not think it desirable to subject her to all this with only a 30% chance of cure, and instead gave her a course of tetracycline, which I recently found to be very effective in the treatment of Sonne dysentery It did not, however, have any effect

I should like to acknowledge the great help received from Dr G T Cook, of the Public Health Laboratory at Guildford in the pathological investigations

REFERENCE

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Contaminated Flour

The poison responsible for the outbreak[1] at Pontardawe, Glamorgan, has been identified as 'Endrin', an isomer of dieldrin, which is a constituent of certain pesticides and insecticides Further investigations are being made to discover how the flour became contaminated, but there is no evidence whatever that it happened during crop spraying or any other insecticidal measure Over 100 people were involved, and they became ill one to three hours after eating the poisoned bread Those most severely affected had epileptiform fits They all recovered

Spilled Virus

Four boxes of poliomyelitis virus were carried by aeroplane last week from Washington to Baltimore and when they arrived one was found to be broken and its contents spilled[2] The crew and cargo handlers were given injections of poliomyelitis vaccine and the aircraft was decontaminated At the suggestion of Dr Salk passengers were advised to have gamma globulin

Another Hazard of Smoking

The manager of a grocer s shop in Acton, London smoked his pipe while at the bacon slicer, with uncovered bacon and cheese nearby[3] He had previously been warned by a sanitary inspector that he was liable to prosecution under the new Food Hygiene Regulations[4] He was fined £10 and 2 guineas costs

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1 See *Lancet* May 19 1956 p 7[illegible]
2 *Times* May 28 1956
3 *Ibid* May 24 1956
4 See *Lancet* 1955 ii 1388 *Ibid* Jan 14 1956 p [illegible]

alike. Yet it is not clear why the recruit population should not have already acquired immunity to the virus nor is it known why epidemics have not been discovered among the civilian population. Furthermore DINGLE and FELLER[2] point out that although clinically similar syndromes among recruits and seasoned men are extremely common, the large majority are not caused by influenza or A.P.C. viruses. There is clearly a great deal of combined clinical and laboratory investigation still required in this field.

On the other hand, investigation of the cause of non-streptococcal summer sore throats has shown the rôle of at least three different viruses, which may well account for a large proportion of these conditions. Herpes-simplex virus causes herpetic stomatitis, some of the group-A Coxsackie viruses have been identified by HUEBNER and his colleagues as the cause of herpangina,[10] and now this same group of workers have found that type-3 A.P.C. virus is the cause of what they call 'pharyngo-conjunctival fever'.[6] This is an acute febrile illness, occurring particularly in children, in whom pharyngitis, occasional rhinitis, conjunctivitis (often unilateral), and cervical lymph-gland enlargement are the main features. Nowadays the interval between the discovery of a virus and the production of a vaccine against it grows steadily less, and although a good deal remains unknown about the disease-producing powers of the A.P.C. viruses it is encouraging to know that whatever disease emerges from this jungle of viruses there will almost certainly be a vaccine waiting to meet it. HUEBNER et al.[11] have prepared a vaccine from inactivated type-3 A.P.C. virus and injected it into human volunteers. The volunteers and uninoculated controls were challenged by inoculating live virus on to their conjunctivæ. An illness similar to the natural infection was produced in some of the volunteers and in a significantly smaller proportion of the vaccinated individuals. So far there have unfortunately been no confirmed reports of how to grow the common-cold virus or even how to make an efficient common-cold vaccine.

Fort mit dem Spray!

"In the year of our Lord 1536 Francis the French King sent a puissant army beyond the Alps. In the conflict there were many wounded on both sides with all sort of weapons but chiefly with bullets. I will tell the truth," PARÉ continues, "I was not very expert at that time in matters of Chirurgie. . . . I observed and saw that all the Chirurgions used that method of dressing which Vigo prescribes . . . that they filled, as full as they could the wounds made by gunshot with tents and pledgets dipped in scalding oyle at the first dressing. . . ."[12] And as befits the neophyte—for he was 27 and this was his first campaign—he followed their example assiduously. Then came his discovery:

> "I chanced on a time when by reason of the multitude that were hurt I wanted this oyle. Now because there were some few left to be dressed I was forced—so that I might seem to want nothing and that I might not leave them undressed—to apply a digestive made of the yolk of egg, oyle of roses and turpentine. I could not sleep all that night, for I was troubled in minde; and I feared that the next day I should find those whom I had not dressed with the scalding oyle dead, or at the point of death, by the poison of the wound. Therefore, I rose early in the morning; I visited my patients, and, beyond expectation, I found such as I had dressed with the digestive only free from vehemence of paine; but on the contrary the others that were burnt with the scalding oyle feverish and tormented . . . and the parts around their wounds were swolne."

No thunder, lightning, or other heavenly sign proclaimed to the world that the surgical Middle Ages had come to an end. The world remained intensely preoccupied with the petty squabbles of FRANCIS the French King and CHARLES the Emperor, while PARÉ jotted down the immortal summary: "Je le pansay, Dieu le guerit."

But PARÉ was not the first to revolt against the use of scalding oil and cauteries as a means of wound dressing. Over two hundred years earlier HENRI DE MONDEVILLE had written:

> "Wash the wounds scrupulously from all foreign matter, use no probes, no tents, except under special conditions; apply no oils or irritating matters. When your dressings have been carefully made do not interfere with them for several days. Do not pull your dressings about; Nature works better alone."[13]

More than a thousand years before him the physicians of Cos advocated not only gentle irrigation of wounds, to obtain primary healing, but also the careful cleansing of hands—and especially the nails—before operating. And (amid much cant and superstition) the compilers of the Ebers papyrus recorded in 1500 B.C. that their treatment of wounds consisted in simple apposition of the edges by linen bandage, held in place for three to four days by myrrh and honey.[14] Indeed the closer we look at medical history, the more we recognise the truth in old Sir 'Paddy' Cullen's mockery: "Modern science is a wonderful thing. Look at your great discovery! Look at all the great discoveries! Where are they leading to? Why, right back to my poor dear old father's ideas and discoveries. He's been dead now over forty years."

The other day we discussed experiments by PALUMBO et al.[15] from which they conclude that clean surgical incisions heal as well without dressings as with them. These observations recall some described forty-four years earlier by WEBB-JOHNSON[16] in the *Archives of the Middlesex Hospital*:

> "I have felt for some time that the careful application of layer after layer of dressings to closely sutured operation wounds was possibly an unnecessary waste of time, energy and material. An article by Mr. Reginald Alcock[17] on 'Iodine as the sole dressing of Operation Wounds' . . . therefore naturally aroused my interest. His results were so good that I felt not only justified but encouraged in giving the method a trial. . . . Not only has apparently unnecessary trouble been saved, but the patients have expressed themselves as being most comfortable. One or two patients who had undergone operations before and had experienced the discomfort of dressings and bandages were very pleased to be without these encumbrances. I consider that the wounds healed even better than when dressings are employed, and in no case in which I used the method did the slightest inflammatory reaction occur."

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Letters to the Editor

BURNS AND SCALDS

SIR,—Your editorials are so rightly esteemed for their sense of fair play and balanced judgment that I hope you will permit one who has made a close study of burns for more than ten years to offer comment which differs somewhat from the views expressed in your leader of May 19.

That leader was, in effect, a reply to a correspondent whose unhappy experience of his wife's scalded foot treated by exposure to air had left him unconvinced of the merit of that procedure; and the leader offered guidance to others (especially general practitioners) faced with the management of common injuries of this type. But was your guidance, Sir, very helpful? You told your readers that "the modern treatment" of burns is by exposure to air, and then went on immediately to mention certain undesirable features of that method—the pain involved "may be considerable," and there is good reason to question its efficacy as a means of preventing bacterial infection of the burned surface. In this last connection you rightly reminded readers that Lowbury and his colleagues[1] had shown that, while the dried surface of the eschar remained sterile or nearly sterile, its inner surface, next to the regenerating tissues, was often heavily contaminated by pathogenic bacteria. (Actually this was observed in all of six cases investigated.) Other observations pointed in the same direction—to the more frequent infection of burns treated by exposure. These workers concluded with the fair comment: "A place still exists for both kinds of treatment, and exposure is often indicated on clinical grounds or because adequate cover with dressings is impossible" (i.e., especially in burns of the face and buttocks).

What was the practitioner confronted with the scalded foot of an old lady to conclude from all this? Would he not ask himself: "Is there no surer way of avoiding infection, and all the pain of frequent dressings, the slow healing, and the poor final result which so often follows"? Your leader, Sir, offers him as the *only* alternative to the exposure method "ointments or picric acid"—treatments in vogue in 1930. There is no mention whatever of penicillin cream, which is still after ten years' experience with more than 3500 burned patients, regarded by the Birmingham workers as a most valuable agent for avoiding streptococcal infection. (Creams of some of the other antibiotics are equally valuable but very much more expensive.) Was this unique body of experience not even worthy of a passing mention? Nor the most illuminating fact that, in a carefully controlled clinical trial, Jackson et al.[2] had shown that, whereas only 1·7% of 58 burned sites (in 27 patients) acquired a streptococcal infection after the prophylactic application of penicillin cream, no less than 38% of 42 burned sites acquired such an infection in 19 patients not so treated. Surely, in view of the great importance of streptococcal infection in the burned patient, that observation was one of the most valuable signposts that has been set up in the past twenty years?

And it had particular relevance to your correspondent's scalded foot, since that is par excellence a lesion which can be effectively covered to protect it against both airborne and contact infection. (In Birmingham only 1·6% of all burns of the foot became infected by streptococci after treatment by penicillin cream and careful coverage.) After seeing some hundreds of such injuries so treated one may confidently hazard the guess that had the scalded foot of your correspondent's wife been covered generously with penicillin cream she would have had no pain at all from that time; her burn would almost certainly have escaped streptococcal infection; it would have healed in about three weeks (allowing for her age) if the injury was superficial, or it could have been grafted at an early stage with an optimal chance of success if that had been judged necessary.

Readers may well be asking: "Why did the leader not mention penicillin cream and the evidence of the Birmingham unit"? Why indeed? It appears that you had in mind the opinion of some plastic surgeons (*not* the whole Association of Plastic Surgeons) that the use of penicillin in this way entails "too great a risk of generalised sensitivity in the patient, or of insensitivity in the bacterial population." With reference to this opinion (which was, and I think still is, unsupported by any factual evidence based on experience of a large number of patients) I would refer your readers to the very informative letter by Bull and his colleagues[3] who stated that observation of more than 3000 inpatients at Birmingham had shown sensitivity to be "rare and transient." That is still their experience today. And perhaps I may recall, Sir, that your own wise comment[4] on this conflict of opinion was to the effect that readers who wished to arrive at the truth would choose between a clinical impression and a controlled trial. With regard to the other alleged risk of prophylactic penicillin—that it will favour the development and dissemination of organisms insensitive to that agent—Bull and his colleagues made the effective reply that this had already happened in many hospitals where prophylactic applications were not being used.

In conclusion, may I suggest that the most urgent need for the better treatment of the many burns which could be dealt with at home is of a penicillin preparation for local application which is stable at ordinary temperatures, or of another equally effective and inexpensive antibiotic. The exposure method has been on trial all over the world for seven or eight years, and most surgeons now recognise its considerable limitations. The time has come for a return to wisely directed local prophylaxis, combined, when possible, with dressing in clean air and other measures calculated to reduce the chance of infection. We should no longer be complacent about infection. Let us get rid of it.

Farnham Royal, Bucks. LEONARD COLEBROOK

SIR,—The letter from your correspondent "Unconvinced" (May 19) raised several points, some of which were answered very clearly in your editorial. The difficulties in diagnosis of the depth of burns and scalds are well known: the clinical appearance on admission is often grossly misleading, and the pin-prick test demands good cooperation from the patient at a time when he is least likely to give it. It may prove possible to devise tests for burn depth by the intravenous injection of suitable dyes or radioactive isotopes. Indeed, one such dye is under investigation at this hospital. But I would suggest that an accurate history of the accident and the immediate first-aid measures employed may give a good lead as to the depth of the burn or scald.

The popular misconception that a scald is less serious than a burn is still widespread amongst both medical and lay workers. Yet our experience at the regional burns centre for Wales shows that a considerable proportion of the scalds sent to this hospital require skin grafting. For instance, of 108 cases of domestic scalds admitted during 1955, 54% required grafting. During the same period, 118 domestic burns were treated, of which [illegible] needed grafting.

The types of scald that are likely to prove serious are:

(1) Those in which the boiling liquid falls on to uncovered skin—e.g., hands, forearms, legs, and neck.

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[1] Lowbury, E. J. L., Crockett, D. J., Jackson, D. M. *Lancet*, 1954, ii, 1151.

[2] Jackson, D. M., Lowbury, E. J. L., Topley, E. *Ibid*, 1951, ii, 705.

[3] Bull, J. P., Jackson, D. M., Lowbury, E. J. L. [illegible] 1951, i, 161.

[4] *Ibid*, p. 298.

Neither conclusion can be accepted without comment, and it is instructive to seek the reason for their differences. The American workers, with much larger numbers, compare mortality-rates but do not discuss duration of life in relation to treatment. Moreover, their comparison is made not between treated and untreated patients but between those who have received more or less than an arbitrarily defined "adequate" dose of arsenic. This method, though hallowed by tradition, particularly in American studies of syphilis, is of doubtful validity, because no-one really knows what constitutes adequate treatment for cardiovascular syphilis, and doses of the same drug above or below an arbitrary minimum "adequate" quantity may not be very different in their effects. Gamble gets over this difficulty by selecting for comparison totally untreated patients and those who received at least 3 g. of arsenic, and he goes to great lengths to ensure that his treated and control groups should be comparable in other ways. Unfortunately, in doing so, he is forced to discard large numbers of cases, so that his final conclusions are drawn from very small groups, the largest of which contains only 17 cases, and this makes his results rather less convincing. Finally, both studies suffer from the defect that the treatment was deliberately chosen by the doctor in charge and was not selected at random.

In the arsenical era to which these papers relate it was a matter of importance to decide whether life was prolonged in cardiovascular syphilis by a treatment which carried a considerable risk of poisoning or exhausting the patient. Since the introduction of penicillin, however, with its indisputable effectiveness in other forms of syphilis, with its safety and ease of administration, the question whether to give or withhold specific treatment is no longer a live issue. Although no drug can be expected to deal with the mechanical problems of a damaged aorta or an incompetent aortic valve, it seems possible that the process may be retarded by penicillin, and it now remains to be decided what is the proper dosage of this antibiotic. The difficulties of clinical trials in cardiovascular syphilis may mean that the ultimate answer is provided not by the clinician but by the pathologist, and there is need for further work on the histological criteria of active syphilis in the aorta. Such studies might reveal the need to continue treatment for longer than has been customary hitherto.

NON-CELLULAR HISTOLOGY

HISTOLOGY has always been recognised as a little bit of science and a lot of art, and some would say a pretty mystical art at that. Even books bearing the title of *histochemistry* seem full of formulæ for revealing the distribution in cellular sections of sphingolipides or glycoproteins. But cells are no longer the only preparations with proteins and lipoids and carbohydrates distributed throughout their bulk. Every paper electrophoretic strip (and thousands must be produced each day) confronts the biochemical analyst with the same question that faces the histologist: "what is the distribution of interesting components throughout this preparation I have made?" The methods used to reveal, with varying degrees of specificity, the required components on the paper strip are often those of proved histological worth—azocarmine for proteins, Sudan Black for lipides. But Uriel and Grabar[1] go one better: they prepare their electrophoretic medium as a thin transparent film of agar, and the components of the solution under investigation are finally distributed along the strip in a pattern determined by their electrophoretic mobilities and relative amounts. The agar film is then treated like a tissue section, fixed, dehydrated, mounted on glass, and stained by histological procedures. The resulting strip is like a large histological slide, permanent and easily handled, and transparent so that direct photometry is possible.

Perhaps the strip could be more truly likened to a photographic colour transparency, and it might be possible to project the pattern like a lantern slide if it was protected against the heat. Uriel and Grabar do not mention counter staining of their agar films, but it should not be beyond the ingenuity of those who combine organic chemistry with histological magic to produce multi-coloured electrophoretic strips. A 3-dimensional presentation may confidently be expected.

OBSTETRIC ACUTE YELLOW ATROPHY

THE name "obstetric acute yellow atrophy" was first used by Sheehan[1] in 1940 to describe a condition found at necropsy in 6 patients out of a series of 400 maternal deaths. The clinical features were those of acute yellow atrophy of the liver—namely, vomiting, epigastric pain, jaundice, mental disturbance, coma, and death. The absence of liver-cell necrosis, however, was a conspicuous feature. The most striking histological abnormality in all 6 cases was severe fatty infiltration of an unusual kind; the affected cells were distended with fine fatty droplets which showed no tendency to form the large globules commonly found in fatty infiltration of the liver. Only a narrow rim of cells around the portal tracts looked normal. Despite the very severe involvement of the affected cells, nuclear changes were insignificant and inflammatory reaction absent or slight.

Between 1940 and 1955 only 7 more cases of this kind were reported, but recently Ober and Le Compte[2] have given 3 further examples. These were clinically indistinguishable from fulminant infective hepatitis, and the final diagnosis in each case was made only at post-mortem examination. The histological changes conformed closely to the original description by Sheehan. A remarkable feature of the cases so far described is the smallness of the liver (800–900 g.) despite the absence of histologically recognisable necrosis. As the remaining liver cells were obviously enlarged by their abnormal fat content, the true loss of hepatic substance was even greater than the weight suggests. Since the size of the individual lobules seemed normal, each lobule must have contained fewer than its normal complement of cells. It is remarkable that so great a loss of liver cells can take place in so short a time without leaving a more obvious inflammatory reaction.

As with other manifestations of pregnancy toxæmia, the greatest difficulty is to find the cause. None of the known exogenous causes of severe fatty infiltration seems to be involved, and there was no history of nutritional deficiency, alcoholism, or exposure to hepatotoxic agents. In the absence of any such satisfactory explanation, it must be concluded that endogenous factors are chiefly responsible. Hormonal imbalance, although more often the result than the cause of liver disorder, can at least in experimental animals lead to severe fatty infiltration: Graef et al.,[3] for example, have shown that such a change is often found in hypophysectomised dogs. Although nothing in the history or clinical features of these cases indicated a hormonal upset as profound as that, some less drastic hormonal disturbance may be responsible for the fatty infiltration. Much severer grades of fatty infiltration, however, occur both in man and animals without severe hepatic insufficiency. The problems presented, therefore, by this group of cases concern not only the cause of the fatty change but the associated loss of hepatic tissue and the almost invariably fatal hepatic failure.

Most of these obstetric cases showed a fatty infiltration of the proximal convoluted tubules of the kidney, as which it was immersed, as though this episode had a universal validity for every case of neurological disaster after spinal anæsthesia He assures us also that he has first-hand information (of some presumably unpublished experiments) that such a carbolic solution as was allegedly responsible for paraplegia in two cases recently the subject of a High Court action, when injected intrathecally into "higher animals," produces the lesions believed to exist in these two cases

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[1] Uriel, J., Grabar, P. *Ann. Inst. Pasteur*, 1956, 90, 427.

[1] Sheehan, H. L. *J. Obstet. Gynæc., Brit. Emp.* 1940, 47, 49.
[2] Ober, W. B., Le Compte, P. M. *Amer. J. Med.* 1955, 19, 743.
[3] Graef, I., Negrin, J., Page, I. H. *Amer. J. Path.* 1944, 20, 823.

He does not give us any details of the clinical course or nature of the symptoms in the experiments he refers to, and without this information his reference is meaningless The point is important since carbolic acid is a corrosive poison with immediate destructive effects upon living tissues That, injected intrathecally, it should lead not to immediate and striking symptoms, but only—as is characteristic of paraplegia following spinal anæsthesia—to a symptom-free latent period of hours or days and then to a subacutely developing syndrome over further days or even weeks, is something I find no grounds for believing

Yet in the cases referred to, this is what the court was invited to believe, and also that it was negligent in an anæsthetist who, using a then accepted method of sterilising his ampoules, did not see in them hypothetical and invisible cracks

In the event, the court accepted the first plea, which was incompatible only with toxicology, but rejected the second which was contrary to common sense

We must regret that Sir Robert Macintosh still seeks to hide the very serious nature of this problem in his invisible cracks, which in fact do not hide it, for all the evidence indicates that there is some special risk inherent in spinal anæsthesia

To maintain there is none such, means that whenever a neurological disaster follows spinal anæsthesia—and there is no reason to think that they will not recur from time to time—the unfortunate anæsthetist involved lies open to a charge of negligence In the present attitude of the public, a scapegoat will be sought, and if it be authoritatively held that the method properly used is without special risk, patients and anæsthetists will be exposed to dangers from which they should be protected

Anæsthetists might well give themselves to some research upon this matter, since a naïve optimism is not a substitute for knowledge

London W 1 F M R WALSHE

ACUTE AND LATENT PORPHYRIA

SIR,—We can support the opinion of Dr Whittaker and Mr Whitehead, in their interesting paper of April 28, that acute porphyria is more common than is generally realised We have encountered five new cases [1] in two years from a population of approximately 300,000, and almost certainly many remain undiagnosed

One of our patients, with paralysis had taken butobarbitone (Soneryl) for the first time just before the onset of the illness and she was inadvertently given the same drug again later, the abdominal pain returned for a day or so but there were no further neurological developments and she recovered

As regards the pathogenesis we suggested that there seems to be a sudden and probably widespread arterial disturbance—perhaps a kind of allergic vasculitis and curiously reminiscent in some respects of polyarteritis nodosa—operating in those with an inherited error of pyrrole metabolism, drugs precipitate this in some cases but in many no causal factor can be found

C E ASTLEY
Middlesbrough A ALUN WILLIAMS

SIR,—We agree with Dr Pathy (May 12) that barbiturates can occasionally precipitate an attack of acute porphyria, one patient under our care was given barbiturate by her practitioner for the relief of insomnia and this induced an attack of acute porphyria We regret that this point was not made clear in our article

Our special interest in the relationship between the neurological complications of acute porphyria and the administration of barbiturates arose from a personal communication from Dr A Goldberg, who drew our attention to Waldenstrom's [1] original observation that barbiturates might precipitate neurological manifestations in patients who might otherwise suffer only from the abdominal symptoms of the disease Goldberg and Rimington [2] develop this theory experimentally, and we trust that they will soon elucidate further the role of barbiturates in acute and latent porphyria

S R F WHITTAKER
Warwick Hospital T P WHITEHEAD

ALDOSTERONE

SIR,—We read your annotation last week with great interest There can be no disagreement with the main conclusion that at present diagnosis and management of primary aldosteronism must rest on clinical findings and metabolic disturbances without depending on the measurement of the hormone in urine or blood However, in the annotation there are certain inaccuracies of fact and emphasis which we feel, if ignored, would tend to delay understanding of the condition

In our experience, the yield of free aldosterone from urine is increased *10 to 30 fold* by hydrolysis at pH 1 not threefold as you quote one of us as saying

The main problem in the study of cases of primary aldosteronism would appear to be that in two examples investigated in detail—that reported by Dr Chalmers and his colleagues (Jan 21) and that described by Dr M D Milne at the Royal Society of Medicine on April 25—the urinary excretion of aldosterone, as measured by our group and Dr G T Mills respectively, although raised above the normal mean value is almost within the range of values for twenty healthy subjects In contrast, certain cases of secondary aldosteronism excrete the hormone in much greater amounts The following possible reasons for this were investigated in the case reported by Chalmers et al

1 That renal excretion or mode of conjugation of the hormone was abnormal However, the concentration of free compound in blood and the ratio of free to conjugated aldosterone in urine was not found to be outside the normal range This explanation, therefore, seems unlikely, as does the advanced in your annotation—that the conjugate may not have been hydrolysed This latter hypothesis would imply the presence of an inhibitor of pH 1 hydrolysis in the urine of cases of primary aldosteronism There is no evidence for this, and in any case the values of free aldosterone in blood and urine were not greatly raised

2 That the condition was due to another adrenal compound However the urine from the case of Chalmers et al was extensively fractioned by partition column chromatography under conditions which would lead to little loss of most neutral steroids The fractions were then bio-assayed with respect to their effect on the urinary Na/K or Na or K excretion of adrenalectomised rats No activity was found other than in the fractions containing aldosterone There is thus as yet no evidence for the existence of such a cortico

3 A recent publication by Luetscher,[3] which is supported by the results of the analysis of rat adrenal venous blood by Singer and Stack-Dunne,[4] reports that normal humans depleted of potassium with plasma potassium concentrations of 1 5–2 5 m eq per litre, show markedly depressed excretion of aldosterone This raises the question as to whether subjects with normal intake and plasma values of electrolytes are the appropriate controls for cases of primary aldosteronism These results indicate that cases of potassium losing nephritis without adrenal tumour showing low potassium and normal

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[1] Astley, C E, Williams A A Univ Leeds med J 1951 3 116

[1] Waldenström J Acta psychiat Kbh 1939 14 37

[2] Goldberg A Rimington C Proc roy Soc B [illegible] 143

[3] Luetscher J A jun Curtis R H Fed Proc 19[illegible] 14

[4] Singer B Stack-Dunne M J Endocrinol 19[illegible] 12 1

aspects of a case were often brought to light and in general the staff obtained a new understanding and insight which they were then able to apply in dealing with other patients in their care Mackenzie's paper shows that this way of working is a valuable advance in preventive mental health and a pointer to further progress

ELECTROLYTES AND THE ELECTROCARDIOGRAM

THE importance of the electrocardiogram (E C G) in the detection of disorders of electrolyte balance is now generally accepted The process of ventricular activation is influenced by the ionic concentration of the extracellular fluid bathing the cells of the myocardium, and also by local electrolyte changes in the cells themselves There is generally a fair agreement between the serum concentration of certain electrolytes and the development of electrocardiographic changes The electrolytes which produce changes in the E C G are potassium and calcium Alterations in serum sodium levels may also indirectly produce E C G abnormalities by inducing acid-base imbalance and altering the potassium sodium ratio in the extracellular compartment

Electrocardiographic changes due to a low serum-calcium develop when the level falls below 7–8 mg per 100 ml There is an increase in the iso electric line between the Q R S and T deflections, the T wave is unaffected, but the duration of systole (Q–T interval) is greatly prolonged [1] By contrast, hypercalcæmia shortens the Q–T interval, virtually abolishing the ST segment [2] Hypokalæmia produces depression of the ST segment, flattening of the T wave, and large U waves [1–3] Conduction defects and arrhythmias are common The Q–T interval is prolonged but often difficult or impossible to measure because of the disappearance of the T wave into the U wave [4] By contrast, hyperkalæmia is associated with greatly augmented positive T waves, and conduction defects in severe cases

Bellet [2] has closely studied the E C G changes in electrolyte imbalance He points out that the prolonged Q–T interval in hypocalcæmia can be brought back to normal by the intravenous administration of calcium, and that, although the patterns of low calcium and low potassium states are usually strikingly different, combined deficiencies of the two electrolytes produce atypical pictures He has examined the E C G s of 125 patients with hypokalæmia from various causes and has described four patterns Pattern I consisted of ST-segment depression and a prominent U wave, pattern II included various degrees of T-wave inversion, associated with prolongation of the Q–T interval, and a prominent U wave, and patterns III and IV consisted of positive T waves of various shapes followed by one or more U waves The diagnostic E C G appearances were most common at levels of serum-potassium below 3 0 m eq per litre Measurements of intracellular and extracellular potassium showed that the E C G pattern correlated better with the extracellular than with intracellular levels But there was not always close agreement between serum-potassium and the E C G , because of variations in the normal range, and because of other factors, such as the administration of digitalis, which shortens the Q–T interval and distorts the ST segment By contrast, cardiac ischæmia, subendocardial infarction, and myocarditis could produce E C G changes similar to those seen in hypokalæmia, while potassium intoxication has been shown to produce currents of injury resembling acute cardiac infarction or pericarditis [5] Bellet [2] has also shown that hyperkalæmia may cause the inverted T waves of myocardial infarction to become deeper, and Sharpey Schafer [6] noted the same result after giving potassium by mouth to patients with inverted T waves from the same cause When the T-wave inversion was due to ventricular preponderance, however, potassium caused the T waves to become upright

Bellet has described four stages in the development of the E C G signs of hyperkalæmia in the dog Stages 1 and 2 consisted of elevation of the T wave with narrowing of the base, and cardiac irregularity due to sino auricular block (serum potassium 6–9 m eq per litre) In stage 3 the ventricular complexes were widened, and the ventricular rate slow (serum potassium 10–13 m eq per litre) Stage 4 showed slow idioventricular rhythm, and further widening of the Q R S (serum potassium 14–18 m eq per litre) The cause of death was usually ventricular standstill, but occasionally fibrillation (at a level of 16–18 m eq) in the normal dog The stages in man were very similar, but less well demonstrated The effects of hyperkalæmia on the E C G of cardiac infarction were variable, either causing the T wave to become larger and further inverted or to revert to a positive deflection In patients with subendocardial ischæmia, potassium produced a diphasic T wave which was not typical of hyperkalæmia Bellet concludes that the electrocardiographic detection of hyperkalæmia is difficult in the early stages Certainly augmented positive T waves in precordial leads can result from posterior infarction and pericarditis, and may be the prelude to an anterior ischæmic episode [7]

Careful attention to the changes in serial electrocardiograms can yield valuable information about electrolyte disorders, but interpretation must take account of the many other factors which may obscure or counterfeit specific changes

VASCULAR HEADACHE

IT is now well established that the headache of migraine is usually due to distension of arteries, probably both intercranially and extracranially But, by their quality and accompanying symptoms many headaches which do not form part of a true migraine syndrome seem to be vascular in origin Indeed, adequate investigation of headaches of uncertain cause now includes full exploration of the response to vasomotor drugs, both constrictor and dilator By this means it is often possible to reproduce the spontaneously occurring headache and so plan rational treatment Wolff [8] and his colleagues have done a great deal in the past few years to clarify these vascular headaches One of their many contributions is to the technique of recording changes in the extracranial arteries They have designed an instrument,[9] essentially similar to Mackenzie's polygraph, for recording the arterial pulse-wave via an electronic amplifying system on a direct ink-writer This device clearly demonstrates changes in the pulse contour in a variety of spontaneous headaches and in those induced by vasomotor drugs The recorder can be easily applied to the temporal arteries and its branches and to the occipital vessels Moreover, simultaneous bilateral recording can help to elucidate the mechanism of unilateral headaches Such investigations have confirmed that changes in vascular tone and calibre—both distension and constriction—may be responsible for headaches Tunis [10] has given further illustrations of the application of this method to the study of headache and of the effect of allegedly vasomotor drugs There is no doubt that it provides objective evidence of changes in a field where subjective symptoms are often particularly difficult to assess

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[1] Merrill, A J *Amer Heart J* 1952 43 634
[2] Bellet S *Arch intern Med* 1955 96 618
[3] Bellet S Steiger W A Nadler C S Gazes P C *Amer J med Sci* 1950 219 542
[4] McAllen P M *Brit Heart J* 1951 13 159
[5] Levine H D Wanzer S H Merrill J P *Circulation* 1956 13 29
[6] Sharpey Schafer E P *Brit Heart J* 1943 5 80
[7] Brink A J Goodwin J F *Ibid* 1952, 14, 331
[8] Wolff H G Headache and Other Head Pains Oxford 1948
[9] Tunis M M Wolff H G *Amer J med Sci* 1952, 224 565
[10] Tunis M M *Canad med Ass J* 1956, 74 185

PERFORATED ACUTE AND CHRONIC PEPTIC ULCER

SIR,—We would like to reply to some of the points raised by your correspondents on this subject Like Mr Moore (April 28) we practise vigorous resuscitation measures in patients with grave peritonitis and include among these drainage of the peritoneal cavity at the earliest practicable moment Mr Moore, however, doubts our description of 7 patients as "moribund" before treatment and implies that more vigorous management might have saved some of them Mr Gilmour (May 5) considers that consecutive admissions of cases of perforation to his beds on his receiving day constitute an unselected series of cases comparable to our own We therefore put forward brief descriptions of our 7 moribund cases to illustrate our attitude to these problems

1 Man, aged 67 perforated duodenal ulcer, blood pressure unrecordable on admission Dextran and blood transfusion, peritoneum drained under local anæsthetic Died within 24 hours of admission

2 Man, aged 63 perforated duodenal ulcer, very emaciated, chronic bronchitis, œdema of ankles, and bedsores Immediate response was good but collapsed and died 16 hours after admission

3 Woman, aged 77 perforated gastric ulcer, blind and deaf, bedridden for 15 years Became unconscious soon after admission and made no response to treatment Necropsy showed pulmonary embolus in addition to peritonitis

4 Man, aged 83 perforated carcinoma of the stomach with secondaries

The next three patients were all admitted to the medical wards

5 Man, aged 74 admitted with uræmia and bleeding duodenal ulcer, perforated after admission Perforation did well with conservative treatment but patient died after five days from uræmia, due to pyelonephritis in only functioning kidney

6 Man, aged 69 admitted with severe bleeding from duodenal ulcer and gross anæmia While he was being resuscitated the ulcer perforated In spite of vigorous treatment he never recovered sufficiently to undergo operation

7 Man, aged 77 admitted as a case of collapse and died in a few hours Diagnosis of perforated duodenal ulcer made at necropsy

We hope that Mr Moore will admit that "moribund" is not an exaggerated description of these cases We hope that Mr Gilmour will agree that our mortality figures include more deaths than those in "cases admitted to the beds of a surgeon on his receiving day" The last 3 cases would not have been included on Mr Gilmour's definition of an unselected series nor would 2 at least have been likely to appear under the main heading of "perforations" in the lists of a hospital records officer We find a great difference between mortality in that group of cases which find admission to surgical wards and the total admissions to the hospital collected *as the cases arise* as a matter of special interest Avery Jones found the same discrepancy, with less than half the mortality in the operated cases

Mr Downie (May 19) asks what proof exists that our 200 cases were in fact perforations 75% of the cases showed gas under the diaphragm on radiography, and we have regarded that as proof The incidence of intraperitoneal gas is roughly the same as in published figures of operated series where the diagnosis was confirmed at operation We feel, therefore, that our clinical diagnoses in the 25% without gas are not far wrong apart from the collected group of errors we have described There is, of course no proof, but cases have only been accepted as perforations with the full distinctive clinical picture the series does not include doubtful "leaks" or painful exacerbations of the ulcer The question is of course an academic one Our claim is that within the conditions set out in our paper the patients whom we diagnose as suffering from perforated ulcers do remarkably well if they have only a short history of dyspepsia, but are well enough—like the sutured cases in other hospitals—if they have suffered from indigestion for years

We do not wish to enter into a discussion on the place of immediate partial gastrectomy in the treatment of perforations Our experience teaches us that no sort of operation has any place in perforated *acute ulcer* but that neither suture nor aspiration is completely satisfactory, in the long view, in cases of perforated *chronic* ulcer Where it is feasible, we believe partial gastrectomy to be the treatment of choice for perforated chronic ulcer Nevertheless, if the condition of the patient precludes partial gastrectomy, operation merely to close the perforation offers no advantages where the stomach can be kept empty by aspiration

London Hospital, E 1

HERMON TAYLOR
RICHARD P WARREN

SMOKING

SIR,—In connection with cancer of the lung and cigarette smoking there is much talk of alleged "carcinogenic factors" in tobacco smoke Research is going on in the hope of finding such factors, and—presumably—eliminating them from the tobacco so that people can go on smoking (and coughing their heads off) immune from the danger of bronchial carcinoma

Perhaps the *coughing* is the clue to the riddle? The heavy cigarette smoker who presents with cancer of the lung has had "a smoker's cough" for years—and an inflamed, irritated respiratory tract, the lining cells of which are under a constant stimulus to replace themselves with undamaged cells It is not to be wondered at if some fine day the replacement process shows signs of wear and tear and carcinoma cells are produced

If this theory of irritation is correct the search for presumed "carcinogenic factors" in tobacco is superfluous Cancer of the lung could result equally from smoking brown paper or cabbage leaves

In pipe-smoking there is conspicuously less irritation of the throat, less coughing, and less carcinoma of the bronchus

London, W 1

J A BRUCE YOUNG

HOME CONFINEMENT

SIR,—I should like to mention another argument in favour of home confinement, or better still return home after completion of labour as in the scheme suggested by Dr Sluglett and Dr Walker (May 12) Much has recently been written about the effects of maternal deprivation on young children[1] A young child needs to have and to *feel it has* persistent parental affection and protection to give it emotional security[2] How disturbing it must be for the firstborn to be separated from his mother while she goes into maternity hospital and on her return to be presented with a mewling infant who monopolises much of her time

It appears that most children survive the trauma with little reaction except jealousy of the newcomer and "difficult" behaviour, but it is conceivable that harm might be done and that from a mental health point of view the increasing number of hospital confinements may not be a desirable cultural pattern

Cardiff

JULIA FOREMAN

SIR,—I am sure that all G P obstetricians will welcome the inquiry into the maternity services which has been set up as a result of the findings of the Guillebaud Committee's report and will await the emergence of a comprehensive and unified midwifery service with patience

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1 Bowlby J Maternal Care and Mental Health Geneva 1951

2 Edelston H Earliest Stages of Delinquency Edinburgh 1952

TABLE IV—PREVALENCE OF BEDWETTING BY SOCIAL GROUP (REGULAR BEDWETTERS ONLY)

Social group	Percentage regularly wet at age (yr.)			Wet throughout the period (%)*	No. of children (wet and dry)†
	4¼	6	7¾		
Professional and salaried	2·21	1·95	1·68	2·07	768
Black-coated	3·27	2·72	1·90	2·08	1102
Manual	3·64	3·81	3·47	2·84	1757
Agricultural	2·74	2·74	1·68	1·99	474

* These percentages include children wet regularly at some periods and occasionally at others.

† 193 children had fathers who were self-employed or engaged in miscellaneous occupations.

was 12·2% at 4¼ years, falling to 10·3% at 6 years and 7·3% at 7¾ years. The corresponding figures for regular bedwetters were 3·5%, 3·6%, and 2·9%. The proportion consistently wet throughout the period was 3·2%.

Since regular bedwetters give the greatest trouble to their parents and their doctors we have considered them alone in tables III–VI.

Family Size

The usual impression that bedwetting is more common among children from larger families is only partly borne out by the present study. Table III shows the proportion of bedwetters who were firstborn and later-born children.

When both sexes are taken together there is no significantly greater prevalence of bedwetting among the later-born, although at both 4¼ and 6 years there is a slight but not significant excess of bedwetters among them. When sex also is considered this excess is seen to be greater for the boys than for the girls.[6]

TABLE V—SEX DIFFERENCES IN BEDWETTING BY SOCIAL GROUP*

—	Percentage regularly wet at age (yr.)			No. of children (wet and dry)
	4¼	6	7¾	
Non-manual workers				
Male	3·81	3·41	2·51	897
Female	1·71	1·26	1·03	873
Manual workers†				
Male	3·83	4·27	4·05	913
Female	3·43	3·43	2·84	844

* Comparing males and females among non-manual workers: $\chi^2 = 21·46$, $n = 3$, $P<0·001$.
Comparing males and females among manual workers: $\chi^2 = 2·93$, $n = 3$, $0·5>P>0·3$.

† Excluding agricultural workers.

The birth of a younger child has been regarded by some as a factor in the ætiology of bedwetting. This view receives no firm support from the present evidence. The prevalence of regular bedwetting among children aged 4¼ years was 3·7% when there was a younger sib and 2·9% when there was none—a difference in the expected direction but of no statistical significance.

Bedwetting among Sibs

In 1953 the mothers of all our survey children were asked to give details of any of their other children who had wetted their beds at night even if they had later become dry. The answers relate to 3536 sibs aged from 5 years to 14 years 11 months in 1953.[7]

Of the 264 sibs of regularly wet survey children 28 (10·6%) had a history of bedwetting and of the 3272 sibs of dry or occasionally wet survey children 189 (5·8%) had a history of bedwetting.[8]

In addition 480 sibs occasionally wetted their beds, of whom 9·6% had been bedwetters—a proportion that is about twice as great as that among the 2794 sibs of entirely dry children (5·1%).[9]

Thus it appears that the familial element is equal in regular bedwetters and in occasional bedwetters. This does not necessarily imply that there is a genetic basis for bedwetting; it could equally be explained by a common pattern of upbringing.

Social Group

It was expected, from the evacuation experiences of the 1939–45 war (Titmuss 1950, Women's Group on Public Welfare 1943), that there would be a social gradient in bedwetting, and this was found in the present survey (see table IV).

TABLE VI—PROGRESS OF CHILDREN GIVEN DIFFERENT TYPES OF TREATMENT FOR BEDWETTING

—	Type of treatment given (as reported at 6 yr.)			No treatment†
	Clinic	Reward or punishment	Other active measures	
No. regularly wet at 6 yr.	41	67	32	26
Percentage dry by 7¾ yr.	19·5	20·9	31·3	57·7
Percentage improved*	24·4	28·4	28·1	11·5
Percentage unchanged	56·1	50·7	40·6	30·8

* i.e., only occasionally wet at 7¾ yr.

† No treatment was admitted by the mother, but it is likely that all the parents tried various methods at different times even if no consistent method was used.

The lowest incidence of bedwetting was among children of the relatively prosperous professional and salaried groups and among the children of agricultural workers. The greatest prevalence was among the manual workers, whereas the children of black-coated workers occupied an intermediate position, being nearer the manual at 4¼ years and nearer the salaried at 7¾ years. The gap between the social groups widened with increasing age and was only significant at 7¾ years.[10]

The proportion of children wet throughout the period was similar in each social group, and the excessive number of bedwetters in the poorer groups was apparently made up of children becoming wet for relatively short periods.

We have already remarked on the high prevalence of bedwetting among boys. This sex difference was largest and only significant in the professional and black-coated groups, and part of the unfavourable position of the children of manual workers seems to be explained by the high prevalence of bedwetting among the girls (see table V).

Geographical

There were no significant differences in the proportion of children reported as bedwetters for the various regions of England; nor were there any significant differences

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[6] The excess among later-born boys is significant at 6 years: $\chi^2 = 4·773$, $n = 1$, $0·03>P>0·02$.

[7] Owing to certain sorting difficulties, sibs under 5 were excluded from the following analysis. Sibs of 15 years and over were also excluded because many of them had left home and thus had made it impossible to define with any certainty the complete population of these older children.

[8] Comparing these two groups of sibs: $\chi^2 = 9·891$, $n = 1$, $P<0·01$.

[9] Comparing these two groups of sibs: $\chi^2 = 15·332$, $n = 1$, $P<0·001$.

[10] At 4¼ years $\chi^2 = 3·886$, $n = 3$, $0·3>P>0·2$.
At 6 years $\chi^2 = 7·144$, $n = 3$, $0·1>P>0·05$.
At 7¾ years $\chi^2 = 11·685$, $n = 3$, $P<0·01$.
When non-manual workers are compared with manual workers, significant differences are found in each year.

Obituary

JOHN DEMPSTER FRASER

T D, M B Glasg, F R F P S, D O M S

Dr J D Fraser, who died while he was giving expert evidence in court on May 21, had been surgeon to the Glasgow Eye Infirmary for only a short time but it was long enough for him to win the friendship of his colleagues and the admiration and respect of his patients He was born in 1913, and educated at Hillhead High School and the University of Glasgow After graduating M B with honours in 1936 he held resident appointments under Sir John McNee, Prof A J Ballantyne and Mr Roy Young His postgraduate training was interrupted when he was mobilised as a regimental medical officer to the 6th Battalion of the Highland Light Infantry, but in December, 1939 he was posted to the China Command as an ophthalmic specialist As a prisoner-of-war in Hong-Kong he was allowed to continue his work as the ophthalmic specialist to the British Military Hospital until the end of hostilities For his war service he was mentioned in despatches and in *1946* he read a paper to the Ophthalmological Society of the United Kingdom on the ocular manifestations associated with malnutrition, based upon his personal observations carried out in the military internment camps in Hong-Kong

After the war he resumed his work as a clinical assistant in the Glasgow Eye Infirmary and in the university eye department at the Western Infirmary When the Ophthalmological Society of the United Kingdom met in Glasgow under the presidency of Professor Ballantyne, Fraser acted as local secretary and impressed the members by his enthusiasm and efficiency His flair for this kind of work developed, and he became the Glasgow secretary of the Scottish Ophthalmological Club His interests within the specialty lay in pathology and neurology For ten years he worked as ophthalmologist to the neurosurgical unit at Killearn Hospital

"In that position," writes J S , " he gained an authoritative knowledge of the neurology of the eye which can rarely have been equalled by one so young Not only the quality of his advice but also the confidence with which he gave it made his neurological colleagues rely on him to an ever greater extent Although the number of patients seen by him in consultation grew week by week not only did he investigate them all most carefully but he got to know each patient as a human being with a job and a family Weeks and months later he might recall the details of an optic fundus and remember where the man lived and worked and how many children he had We shall miss his counsel, his human warmth his great practical common sense and his humour "

As W J B R says, " his loss is a most serious one not only to Glasgow and the West of Scotland but to a wider medical public which was beginning to appreciate his calibre He spoke well and with assurance at a meeting in London the month before he died His work was of the highest quality and he possessed great manual dexterity."

Dr Fraser is survived by his wife, a daughter, and a son

GUSTAV HERRNHEISER

M D Prague

Dr Herrnheiser, consultant radiologist to the Connaught Hospital London, and a former professor of the German University of Prague, died on May 13

He was born in 1890 in Prague, and studied medicine at the German University there, and at Munich After graduating M D in 1914 he spent seven years in postgraduate work in Prague at the morbid anatomy department under Ghon and at the department of internal medicine under Jaksch In 1920 he joined the radiological department under Holzknecht in Vienna Five years later he returned to Prague as *Dozent* in radiology to the German University In 1931 he was appointed to the chair of radiology His early work included investigations on the anatomy of the blood-vessels of the lung but later his main interest was in radiological diagnosis of diseases of the chest and gastro-intestinal tract

In 1939 political events forced him to leave Pra where he had lived and worked for the best part of l life, and where he had built up the X-ray departm at the university clinic He went first to Palest where he became chief radiologist to the Hadass Hospital, Tel-Aviv, an appointment which he held u 1942 when he left for Egypt to become chief radiolo to the King Fuad Hospital and the Jewish Hospital i Alexandria He settled in this country in 1948 F the first time after many years he felt at peace agai writes M E G , 'and England became a second ho to him one which he loved and where he was happ once more He soon became active again, and in a ve short time made many new friends He was respect by all who met him, and realised his qualities h sincerity and deep knowledge, his innate modesty a unceasing search for the truth

Professor Herrnheiser leaves a wife and two daughte

Dr J M D OLMSTED a former professor of phys logy at the universities of Toronto and California h died at the age of 70 He shared in the research whi led to the discovery of insulin, and he was a co-edit of several editions of *Macleod's Physiology in Mode Medicine* He was also interested in the history of h specialty and had published monographs on Clau Bernard (1938) and on François Magendie (1945)

Diary of the Week

JUNE 3 TO 9

Monday, 4th

POSTGRADUATE MEDICAL SCHOOL Ducane Road W 12
4 P M Dr W Ritchie Russell Spastic Paraplegia
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY Chelsea Hospital for Women Dovehouse Street S W 3
4 30 P M Mr Kenneth Bowes Intersex
INSTITUTE OF NEUROLOGY The National Hospital Queen Square W C 1
5 P M Dr Ludo van Bogaert (Belgium) Genetic [illegible] and Necrosing Acropathy in Neurology

Tuesday, 5th

THE WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY St Mar Hospital Medical School, W 2
5 P M Prof C H Stuart Harris Recent Studies in [illegible] Respiratory Disease (Almroth Wright lecture)
INSTITUTE OF DERMATOLOGY Lisle Street W C 2
5 30 P M Dr R H Meara Xanthomatosis

Wednesday, 6th

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
5 15 P M *History of Medicine* Sir Zachary Cope Fl Nightingale and the Doctors (Presidential address)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Prof G L Montgomery Morbid Anatomy of Coron artery Disease
INSTITUTE OF DISEASES OF THE CHEST Brompton S W 3
5 P M Mr T Holmes Sellors Congenital Heart disease
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Differential Diagnosis of My Infections
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
NOON (Queen Charlotte's Hospital Goldhawk Road W *Mr A L Gunn* The Use of Kielland's Forceps
MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8 30 P M (Royal College of Surgeons 18 Nicolson Street Edinburgh) Mr Douglas I Savill The Painful Foot

Thursday, 7th

ROYAL SOCIETY OF MEDICINE
5 P M *United Services* Surgeon Commander J W L Cro ll Drowning
POSTGRADUATE MEDICAL SCHOOL OF LONDON
5 P M Dr Paul Wood Diagnosis and Treatment of [illegible] Paraplegia
SOCIETY FOR ENDOCRINOLOGY
5 30 P M (University College Gower Street W C 1) Dr C N H Long (Yale University) Experimental Obesity
UNIVERSITY OF ST ANDREWS
5 P M (Queen's College Small's Wynd Dundee) Sir Harry Platt The Backache-Sciatica Problem

Friday, 8th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A M Mr Norman Capener Tumours of the Bony Chest Wa
2 P M Mr K Morris (Melbourne) Mediastinal Goitre
4 P M Dr Russell Fraser Metabolic Bone Disease
ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington W 2
5 P M Mr J B Blaikley Impressions of Obstetrics and Gy cology in the United States
INSTITUTE OF DISEASES OF THE CHEST
3 30 P M Prof H J Ustvedt (Oslo) Usual and Un Reactions to B C G Inoculation
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330 Gray's Inn Road W C 1
3 30 P M Mr A I Dingley Hoarseness

University of London

The following have passed the final examination for the degrees of M B B S

Honours —F W I Brown (*b*) St Thomas's J W Carter (*a*) King's College Hosp B G Child (*d*) Charing Cross D H Elliott (*e*) Bart's Florence P Forsythe (*b*) Guy's, C J W Hunter (*e*) Bart's R F Jewkes (*d*), Charing Cross, Ann F Johnson (*e*), Univ Coll Hosp W G G L Jones (*c*) King's College Hosp S F Jost (*e*) Middlesex, Mary C Munday (*a d university medal*) Middlesex R W Portal (*b*), Middlesex K T Tighe (*d*) Guy's

(*a*) Distinguished in pathology (*b*) distinguished in medicine (*c*) distinguished in applied pharmacology and therapeutics (*d*) distinguished in surgery, (*e*) distinguished in obstetrics and gynæcology.

Pass —J A Abraham C D Addo, Peter Adlington, Barbara A Alcock M J Andrews Christos Angeli, C R N Ashbee Rosemary R Ashby Lyn Ashworth Solomon Vacchus A I M Bailey, G R Ball Armaity Bamboat R O Barnard, R M Barnes Elaine Y Barraclough R D E Basden, J D G Baxandall M A Beale I S Beales M E I Beard A W L Beatson, M A Bedford P J Bekenn J D L Bell Phyllis J A Bell R L Belsey Robin Bendall R J I Bennett R V Berry John Bertram L J Binnie B P Bliss T W Bolton J R Bowles, L B H Boxall, K W Braybon R S Britton, C P Broad, Susan M Brocklesby I F Brooks W B J Broom Helen R L Brown K W Browne Y R Bruce D M Bruton A G Bryer D W Bullman D R Burcombe Maureen Y Burrage A L Bussey K A Butler M B Butler R M C Butler R P Callaghan D I Campbell F P A Capps R J Carmichael G B Carter Malcolm Chapman, Davina C Cherry, C D Chilvers T G C Christopher, M D Churcher J M Clark A I Clement Elmer Clissold Dulcie V Coleman, Delia E Coney D B Connell Joseph Connolly, Neville Conway, P L Cook Bryan Corrin M H Cox Frank Cramer, P J Creaven A H Crisp Nickel Crombie J G Cruickshank B I Cuddigan J B St Clair Cumberbatch, J M Cundy J, R Curtis, D F Davies, R D Davis, B P Day, J J de Jode P L G G Delva Gillian R Diamond J A Easton Helen F Economides I M Edwards M A Edwards Alan Elsworth, E F Ely, D M Entwistle I M Evans Joy Evans Rachel G Evans J O O Fajemisin Parviz Faridian Aragh I W J Fearne G M D Fleming, P G T Ford, P A French M I N Frohn P L G Gallwey G B Gillett A B Gilmour Margaret A Gordon Watson R A Gould Fiona M Graham C B T Grant R H F Grant Ann B Gray, J M Gray I D Green G H Griffith P D Griffiths P D J Griffiths Ajeet Bans Lall Gulati, Teresa M Gurrin D M Harris J M Harry T D Haskins, G W Hatcher, P R Hawley, Benjamin Hecht, R S Henderson Diana K Henry R L Hewer Jennifer L B Hicks Thomas Hillier, I R Hobbs A G Hocken Pamela M Hogg, J G Holmes Milner C V Horn Jennifer M Hubble I D Hudson Pauline M Hughes, D I Hughes Davies J W Hunt Ann L Hunter, J D Hurley H F Inniss Palmer G W Jenkins, Trefor Jenkins Jane G Jenkinson Barbara D Jones W F O Jones A J Jordan A J Jouhar J M Kennedy M G Kielty, Barbara C King Margaret King, T J King R E Knight, Pamela F Kordik Y A Kumoji G D Langham R J K Law Marian F Le Couilliard, P F S Lee D S Leede I R Leeds B L Lees S C Lennox A W E Lettin D J Lewis W G Lewis, T M C Lindsay, Patricia F Linnell D B Lloyd Louis M Loury J N Lunn M A C Lyon B C McDermott Bertha S McGill, M B R MacKenzie, D M MacLaren R E Maclaurin Angela de la Condamine Main P D Marsden P B Martin Edna Matthews Faith E Maurice Williams Ann P Melville G B Middle Jerzy Mikolajewski E J C Millard Malcolm Millest W F Millner R E Mills P H Mine B A I Mindham R M Moffitt Ann H Montford, D A Montgomery Gwyn Morgan J A Morgan K H Morgan M T Morgan G M Morris I R Morton P A Mounfield, Janice H Mount G G Muir Barrie Murphy, J K Murphy, Pamela M Mylward P H Nankivell A I C Napier, F J Nash M A Nelson A I E Nichini, F R Nye, N W I Oliver C M O'Neill Pamela D Osborn D A Packham Hosep Pambakian D R J Parrott D L Parry Margaret R Paton, Jose Pavan R S Peachey R L V Pearce W S Pease D E Pegg P A Pelham Eifion Phillips Hazel M Phillips, T T Phillips Ann P Pickering B N Pickering G E Pickup J F G Pigott P W Pitt Iris C Platt I H Porter C I Powell Smith John Price Anna Pridal Glyn Priddle Valerie J Prior John Quantrill M C Rang, Shirley G Ratcliffe W D Rees, D E Rendle Kathleen M Rich D A Richardson F I Roberts A R Robertson R H Robinson W D Roche R K Rondel P O Rosanwo I G Ross Charmian A Russell D G L K Russell I A Russell Mary G Russell R D Sandfield, Winifred Sanford J V Sandy Bryan Scaife Elizabeth A Scharff P M Schiller M P A Scott P J Scott A K Seeram H T Shacklock Malcolm Sharp A I H Shepherd M C Sheppard Margaret F Shields Michael Shillito C D G L Shimmin C R Silver P J C Simons E C Smart D C Smith G I Smith Jean M B Smith Marguerite F Smith P G Smith R B E Smith Elizabeth A Spence D M Stainton Ellis R E Steel A S Y Steele M D B Stephens D O Stewart P I Stiles Susan Stonestreet A J Sutton, G R Swift A R Tanser C G Taylor D J Terry P H I Theobald A A L Thomas D B Thomas G D Thomas C R Thompson G J Thorpe A C Ticehurst I E Tindle Dileas M Tinkle J W Turner Jennifer M Vann W R C Walker Margaret M Walshe W J Walton Judith C R Wardle Edna M Watson R R Welsh Harry Westbury C T Western David Whitby A C Whitmore P C Wilkinson P I K Will D O Williams E J Williams I A Williams D I Willsher D W Wilson E D Wilson P E H Wilson P J F Wilson Shirley J Wilson Donald Winstock Anne Winterton A J Wood C D Wooding F K W Woolacott J A R Worthy B C Wyatt P R Wykes Grace O Yoloye R C Young Barbara K Zamoyska

Biochemical Society

A joint meeting of this society with the Scandinavian biochemical societies will be held in the Department of Biochemistry Tennis Court Road, Cambridge from June 28 to 30

Cambridge Graduates' Medical Club

The annual meeting and dinner of this club will be h Queens' College on Friday, June 22 Further particulars be had from Dr T B Anderson 1, Huntingdon R Cambridge

Prison M O s' Conference

The annual conference of prison medical officers a psychologists was held at the Home Office on May 2 w Dr H K Snell director of the medical services of the Pri Commission in the chair The opening address was given Sir Lionel Fox, chairman of the commission and ot speakers included Dr W E Lloyd and Dr F H Brisby

Harveian Society of London

At the society's Buckston Browne Gray Hill dinner h on May 25 at the Royal College of Surgeons the preside Dr Maurice Long, spoke of plans for celebrating next yea tercentenary of the death of Harvey These included scientific meeting and a visit to Folkestone and it wa hop that the occasion would be one of the most memorable scien events of 1957 Dr Long was replying to the toast of Th Society, cordially proposed by Dr Charles Hill Dr Lo recalled that it was now 100 years since the society's memb first dined together, but he did not say whether the presen of ladies for the first time at this year's dinner was an innovation to mark the centenary *At all events Dr Hill congratu*lated the society on this change in custom Dr D Geraint James an honorary secretary, welcomed The Guests, for whom Colonel Conn Milburn medical attaché to the U S Embassy replied

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CORRIGENDA —*Paraplegia Following Spinal* [illegible] —In line 11 of the case report by Dr J P Payne and D S E Bergentz (May 12 p 666) the concentration of cinchocaine hydrochloride should have read 1/1500 and *not* 1/500

Iodine and Fluorine —In our report of May 19 (p 741), we wrongly stated that 5 mg per litre was an adequate iodine level for drinking water The correct figure is 5 μg per litre

Appointments

MCGRATH P G, M B Glasg, D PSYCH whole time consultant Broadmoor Institution Crowthorne

RITCHIE E A, M B Lond M R C P D P M asst psychiatrist St Augustine's Hospital, Canterbury

Birmingham Regional Hospital Board

ANSON F P M B Manc F R C S whole time senior casualty officer Dudley and Stourbridge group

HOLZER R S, M D Berne part time asst geriatrician (S H M O) Birmingham (Dudley Road) group

SAVAGE C R M B Lond, F R C S part time consultant genera surgeon South Warwickshire group

East Anglian Regional Hospital Board

CANDY JOHN, M B Lond F R C S senior surgical registra Ipswich and East Suffolk Hospital

PARTINGTON M W M B PH D Lond pædiatric registrar Jenny Lind Children's Hospital Norwich

SMITH M N M B Lond pædiatric registrar Peterborough area

THOMAS D I C, M D Lond D P M consultant psychiatr Suffolk mental hospitals

VOISEY M M M B Lond anæsthetic registrar United Norwich Hospitals

South-Western Regional Hospital Board

CONWAY H J M B N U I D P M asst psychiatrist Roundway Hospital Devizes

CRAFT M J M B Lond M R C P E deputy medical superintendent Royal Western Counties Institution Starcross

ENGLAND E J M B Adelaide surgical registrar Gloucestershire Royal Hospital Gloucester

GALLA THOMAS M B Edin D P M asst psychiatrist Bristol mental hospitals

ROBINSON R M M B Lond surgical registrar Weston super Mare General Hospital

[illegible] B E M B Manc F F A R C S D A senior anæsthetic registrar Frenchay Hospital Bristol

WEEKS K F M B Lond D P M asst psychiatrist Moorhaven Hospital Ivybridge S Devon

Births, Marriages, and Deaths

BIRTHS

MURPHY —On April 29 to Inez wife of Eugene F Murphy M B M R C P I Seacroft Hospital Leeds—twin daughters De Gratias

DEATHS

REVELL —On May 26 following an operation at University College Hospital London Rowan William Revell M D D P H [illegible] officer of health for [illegible] dearly beloved husband of [illegible] Revell pulmonary tuberculosis, as suggested by Early (1950), who estimated that about 2·5% of the regional mental hospital beds should be formed into one tuberculosis unit, the optimal size of which would probably be about 150 beds.

Summary

Tuberculin and radiographic surveys were made in an institution for mentally defectives.

3·66% of the patients were found to have significant pulmonary tuberculosis, half of which was considered to be active.

These figures agree closely with published surveys made in similar institutions.

Suggestions are made for the control of tuberculosis in mental institutions.

Thanks are due to Dr Reginald Bailey, physician-superintendent, Gogarburn Hospital, for his willing cooperation, which made this survey possible; Dr P. W. Tait, medical director, mass-radiography unit; and Dr A. T. Wallace for bacteriological investigations.

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[illegible] (19[illegible]) [illegible] 277.

GENERAL MEDICAL COUNCIL

At the opening of the council's 192nd session on May 29 Sir DAVID CAMPBELL, the president, remarked that in the recent elections of direct representatives of the medical profession to the council 41% of the electorate in England had voted. It was a matter of concern that 2380 (4½%) of the voting papers issued in the English election were returned as dead letters, with the consequent disfranchisement of the practitioners to whom they were sent. Apparently the tendency of addresses to become inaccurate still moves nearly as fast as the process of correction. In the long run a high level of accuracy would be achieved and maintained only by the cooperation of every member of the profession in making sure that his registered address was one at which letters would reach him.

The executive committee had lately decided to recognise the degrees of the University of Baroda in respect of the Medical College, Baroda; the degrees of the University of Nagpur in respect of the Medical College, Nagpur; the degrees of the University of Rajputana in respect of the Sawai Man Singh Medical College, Jaipur; and the diploma of membership of the State Medical Faculty of West Bengal in respect of persons who had studied at a medical college affiliated to the University of Calcutta.

At its last session the council had adopted new rules as to courses of study and examinations for diplomas in public health. These rules, superseding those adopted in 1945, made no provision for a certificate in public health but in other respects did not differ substantially from the previous rules. The new rules would come into operation on Oct. 1, 1956.

A Bill for consolidating the Medical Acts and statutory provisions passed between 1858 and 1950, of which there were more than twenty, was now in an advanced state of preparation, and was indeed likely to be presented in the House of Lords almost at once.

The President referred to an appeal by a practitioner to the Judicial Committee of the Privy Council against a decision by the Medical Disciplinary Committee to erase his name *from the Register*.[1]

"The Disciplinary Committee will . . . no doubt wish to consider at an early date the desirability of widening one or more of their existing rules in the manner which their Lordships have been so good as to indicate. I must add, however, that under section 16 of the Medical Act, 1950, it will be necessary for the committee to consult with certain outside bodies before amending the rules."

On July 1, when the Dentists Act, 1956, would come into operation, the responsibilities of the council in regard to dentistry would cease. These had lasted for 78 years, and it was hard nowadays to picture the situation as it was when they began. On the one hand dental surgery was historically a branch of surgery; on the other there were many persons at that time who with a limited practical training were occupied with dentistry as a trade or craft rather than as a profession. The first Dentists Register published by the council in 1879 contained the names of 483 licentiates, and no graduates, in dental surgery, together with 4806 persons who on their own declaration were stated to be engaged in the bona fide practice of dentistry. The 1922 Register, the last Dentists Register published by the council, contained the names of 1768 licentiates or graduates in dental surgery. Today there were 15,895 names on the Register, including 12,521 licentiates or graduates. At the end of its long period of trusteeship the council handed over its remaining responsibilities in the dental field with the greatest good will to the new General Dental Council. The G.M.C. would not lose all contact with dental education and examinations, for under the new Act it was to nominate six of its number to act and vote for those particular purposes as members of the General Dental Council.

Public Health

TRACING A TYPHOID CARRIER
BY MEANS OF SEWER SWABS

F. BIRD HOBBS
B.A., M.D. Camb., M.R.C.P., D.P.H.
MEDICAL OFFICER OF HEALTH, FARNHAM U.D.C.

On Jan. 10, 1955, a boy aged 7 years was admitted to the isolation hospital with a diagnosis of ? encephalitis. He had been taken ill five days previously with a sore throat and a rash and was at first thought to have scarlet fever. He had a swinging temperature up to 105°F and was very drowsy.

During the next seventeen days this high swinging temperature continued and he was extremely ill. His motions were loose and incontinent, and this was at first thought to be due to the aureomycin with which he was being treated. Blood culture, Paul Bunnell, and other tests were negative, and it was not until Jan. 22 that the Widal test was found to be positive and typhoid bacilli were found in the stools, and the case was first notified to me.

On investigating, I found that the patient had not been out of Farnham except to visit Harringay Circus on the day previous to the onset of the illness. He had eaten no ice cream, shell fish, watercress, &c., and since the other inmates of the house were quite well, food did not appear to be the source of infection. His mother, however, told me that he, together with two other boys, had been playing in a field where there had been an overflow of sewage during the recent heavy storms, and that he had come home with his boots covered in sewage. This seemed to be a very likely source of infection, so I decided to take samples of sewage for bacteriological examination.

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[1] See *Lancet*, May 5, 1956, p. 641.

to exact sciences than does medicine But there is still hope, I think, for the student who cannot think logically when he first enters the hospital wards, for many such eventually become surprisingly good doctors In fact the scientific method of thought can be developed in the wards no less than in the laboratory I would therefore plead that preclinical teachers should resist the temptation to press for the exact maintenance (or even extension) of their present share of the student's time and energies

The third objective is the acquisition of *empirical knowledge* Only as experience grows will the student develop clinical judgment

Processes of Learning and Techniques of Teaching

The student must learn to observe and reason and must acquire empirical knowledge Observation he can learn only by long practice this requires the use of the senses but no great mental effort The ability to reason, on the other hand, can be gained only by using the mind These are two entirely different processes of learning Furthermore, it is not easy to combine the two, and it can be very confusing to try to do so, particularly at first It follows that the arrangement of studies must facilitate learning by enabling the student, so far as possible, to use one process at a time Each is assisted by different techniques of teaching, one transmitting information passively and the other activating thought Thus the technique of teaching should always be relevant to the process of learning This is, in fact, vital to the successful study of medicine which contains so much factual material, for if timing is wrong, or the wrong methods of teaching are used, the student has little alternative but to commit the facts to memory without understanding This is more likely to happen in medicine than in other subjects because medicine includes so much that is not yet understood by anyone, and where knowledge is empirical it can be acquired only by memory, aided by experience Too early exposure of the student to random experience is an incentive to practise memorisation and discourages his efforts to learn by understanding Hence unlimited vocational experience and teaching should be restricted to the later stages of his education

No one, however, can think in a vacuum, and learning the method of rational thought requires some knowledge to start with In the earliest stages of his education, therefore, the student must be given selected facts It is essential that his mind should work upon orderly problems rather than chaos He will be helped by systematising the material which he must learn, and in the early years, some integration of subjects is necessary for this reason His experience of clinical problems—i e, of patients—should, likewise be systematic at first Recognition of this, and action to ensure it, is of the utmost importance I do not believe this is fully understood

Techniques of teaching require further experiment and research To standardise them would certainly be a mistake for they are much affected by environment and by the widely differing attitudes of students Thus there is a great need for individual selection, by and for each student, of the most appropriate technique, and our present educational system fails to recognise or cater for this need We have already at our disposal a considerable array of methods of proved value What is wanted is a closer study of their efficacy and especially of their application to different stages of medical education We have the didactic lecture, the clinical theatre demonstration, traditional outpatient teaching, bedside demonstration, teaching in the wards to a small group, the individual tutorial with or without patients the discussion group, the clinical pathological conference in these, according to circumstances and the habits of the teacher, teaching predominates, or there is mutual interchange of ideas or the student may take an active part Then we have practical duties—the medical clerkship, the apprenticeship in the outpatient clinic Then again, the stude may learn for himself by extracting knowledge fr textbooks and original papers, or by analysing ca records, or writing essays, or doing a piece of resea All these are learning techniques which need to b arranged more deliberately to serve a definite education purpose at each stage of the educational plan Onl experiment with different methods, can enable us t arrive at the best possible arrangement

An Educational Plan

So little is known of the processes of learning and little have the techniques of teaching been studie that it is impossible to claim that, of the several pla on which medical education could be based, any particul one will prove to be the best It is, however, undenia that each must endeavour to ensure that medical educ tion becomes a continuous process of learning, progress by interlocking stages, each with its own education objective and techniques of teaching relevant to i In the light of experience I would favour a sequence stages as follows

The study of the normal
The study of the causes and effects of variation from norma
A short introductory course in clinical method
A period of practice of clinical method—i e, an orde clinical clerkship
A stage of consolidation—designed to combine the stud of special pathology and the systematic study of clinic medicine
A stage of more general experience mainly in the ward by attachment to firms
A stage of special outpatient teaching and of midwife and pædiatrics
A stage of practice under supervision, both in the ou patient department and outside hospital
A stage of responsible practice under supervision—i e the provisional registration appointments

That is the skeleton which I now propose to clothe though very sketchily I must make it plain, however that I am not trying to describe a curriculum I am describing a plan which could become the curriculum in my own medical school (or any other) only if all the teachers required were available at the right time, and all the necessary facilities, both clinical and non clinical could be found Even then, after the plan had been put into effect as a curriculum, it might well prove to be wrong as regards the duration of its stages, or their sequence, or the methods of teaching employed

Study of the Normal

The study of normal would be an *introduction* to anatomy, physiology, biochemistry, and psychology—a systematised and, as far as possible integrated, introduction Such interdepartmental teaching would not be difficult to achieve, and in Birmingham a course of this kind exists, though on a bigger scale Perhaps it integration at staff level, each teacher knowing what his colleagues are teaching, that is most important, and at this level there is usually much more integration in our present preclinical departments than in the clinical field

To illustrate what I mean by introduction, I will take anatomy as an example *The whole body would not* be dissected, and it would be useful to experiment with dissection of the fœtus More detailed study of certain areas of the body would be left to later periods when it could be related to clinical work, for instance, th pelvis would be studied with midwifery It might however, prove sensible to study one system in detail at this early stage, and the central nervous system is the obvious choice—and rewarding because of the ease by which anatomy and physiology can be integrated in this system and their application to clinical medicine demonstrated In helping the student to understand the normal the departments of medicine and surgery would take part

In England Now

A Running Commentary by Peripatetic Correspondents

For many years it has been my lot to stick needles periodically into other people's children—but last week found me at the other end of the needle. I arrived at 9.30 A.M. at a welfare centre in North London with my eight-year-old son and sat in company with a dozen other ladies and their children waiting with identical appointment cards for our first injection against poliomyelitis. It was a curiously assorted gathering, reminding me of hours once spent during a pregnancy at a launderette. Conversation established that the birthdays of all children present fell in March or November. No further confidences were exchanged, because my neighbour asked me in a ringing tone if I were not scared, adding that she nearly hadn't come herself. At once I too experienced unreasonable terror, but glancing at the faces of the elder children and seeing the stony look on my son's, I explained that the know-all to whom I am related by marriage considered us to be in the category of (small) football-pool winners. I got the impression that not even my son believed me, and the evidence of our ears now proved that some of our predecessors behind the closed door shared my neighbour's views.

Soon it was our turn to enter this door and roll up the left sleeve. The injection (most expeditiously performed) was followed by advice to take no violent exercise for a week—no swimming in particular. The first signs of distress now appeared, and my offspring's eyes filled with tears. "No cricket?" asked this little Briton. The lady doctor's voice took on a more strongly Continental note. "Ah, cricket," she said musingly, "cricket is something I do not understand—but not a very violent game, I think."

* * *

"Cambridge should be a man's university" was the creed graduates and undergraduates of my generation held in the 20s. Women had been enfranchised; they had gained equality in all the other British universities, and they should be content. Members of Girton and Newnham attended lectures and were like ordinary undergraduates until they came to the end, when they were allowed to take their degrees by diploma and (lucky beggars) did not have to pay graduation fees. Their chief grievance was that they could not hold university posts.

The crisis came, so we thought, in 1921 when a grace before the senate recommended that women should be admitted to degrees and given representation on the council of the senate. The hackneyed phrase "controversy ran high" was an understatement. Clergymen, who rarely left their parishes, were coming up to vote, and doctors who were supposed to be absolutely opposed to the idea, were travelling in force despite great inconvenience. Such were the rumours founded on hearsay and sometimes not even on that. The great day arrived and 1602 graduates voted. The figures were given from the Senate House: PLACET 694, NON PLACET 908. The crowd, on hearing that the non placets had defeated the grace and kept the women in their place, rushed to Newnham. The gates were closed against us. Tree trunks were quickly collected from nowhere and used as battering rams against the wrought-iron gates. (Vandals rarely know the beauty of the things they mutilate and it was a shock to all of us to find that these gates were of great artistic value.) The authorities had phoned the police, who arrived expeditiously, and the word quickly went round, "The police have drawn their truncheons." It is 35 years ago, but I can still remember doing my right-about turn and sneaking off like a dog with his tail between his legs. Retribution in kind was offered at once, but true retribution came later, and as it came slowly led to conversion.

Marriage, an educated wife, and two daughters as worthy of our university education as my son, have all played a part. So has women graduates' ready acceptance of the responsibilities of educated citizens.

In 1947 women were admitted to full membership of Cambridge University, and equality and equity were achieved, if we except their ineligibility for the office of proctor and esquire bedell. All would now be well if Girton and Newnham could take all the eligible women who want to have a Cambridge University education, but they cannot, and these two colleges and all the men's colleges have tried to remedy this by helping in their divers ways to found a third women's college, New Hall. It will want help from every quarter if it is to become a seat of learning like its Victorian sister colleges, and my hope is that many of my generation who enjoyed their years at Cambridge will help to give more women the benefit of what we all feel Cambridge provides, the best education in the world.

* * *

Wandering round an exhibition of historical documents at Portsmouth the other day I noticed a letter from one John Aylward sending the overseers of the poor of Portsmouth an account for medicines and attendance provided from Nov. 20, 1784, to March 15, 1785, by Edward Hale and John Cotman, two surgeons living at Hambledon. The bill came to £6 [illegible]s. and it is endorsed by the surgeons of the Portsmouth Workhouse as follows: "We have examined the within bill and are of the opinion that forty shillings may be deducted therefrom, with propriety." The charges included 2s. 6d. for "a nervous mixture" and 5s. for "a journey." A second more sympathetic endorsement runs: "We whose names are hereunto subscribed are much astonished to see the signatures of two gentlemen of the Faculty so very improperly placed to this Bill, intimating an Imposition in the Charge, as they are very certain they themselves wd have made it double for so long an attendance even at their next door." Mileage and prescription charges always seem to have been live issues.

* * *

Personally I prefer our Aylesburys wrong side up with a full dish of green peas alongside, so until last year the final quack had been silenced by Christmas. It was only a bid by a farmer neighbour for the future stud services of a particularly fine specimen of English duckhood that saved Sir Francis from a macabre visit to the potting shed. The possible immorality of leaving him alone in the feminist stronghold of the henhouse led to Corluvia's reprieve, and so the winter snows were printed with a double set of deltas. With the coming of spring she disappeared from the garden, and although we suspected a poacher's dirty work Sir Francis remained surprisingly complacent in his isolation. In fact he seemed puffed up with unaccustomed pride. We were getting rather worried about Corluvia until one evening our old bloodhound lumbered up and began breathing heavily into a crevice in the wood pile. A flurry of white shot out. Monitor put his stern between his legs and fled, with a wicked yellow bill snapping dangerously near a tender spot. We took advantage of the chase to investigate the nest. There sure enough were ten warm eggs. Our daily help is a natural pessimist, casting doubt upon the fertility of the clutch. She shook her head: "I've never seen Sir Francis acting like a proper gentleman." But I have attended so many clinical examples of the magic of the waterside meadows in our village that I am putting in five extra rows of peas this year.

* * *

I now have a perfect reply to philistinism. Passing from the room with the French impressionists at the Tate to the last, most modern one of the current exhibition of German painting, we stopped to examine one of the striking large canvases. It was a representation of round, oval, and irregularly shaped splashes of vivid colour and no identifiable message. My wife wondered aloud if our Peter could achieve something like it. This was overheard by a middle-aged, stocky, bearded man who observed with perfect charm: "May I respectfully suggest, Madam, that he tries."

* * *

May I intrude upon the musing of the peripatetic shuftiscopist and, with respect for the sanctity of the wondrous revelations of auscultation to the physician, suggest that we rename the stethoscope, the Accessory Oracle?

Premedical Education and Postgraduate Training

The plan I have outlined for undergraduate medical education depends on what goes before it and what comes after I am certain that a balanced general education and a sound foundation in basic science can be achieved only by relaxation of the excessively high academic standard now demanded for entry into medical schools No authority ought to require more than three subjects to be taken at advanced level, and one of these should be non-scientific

At the other end of undergraduate education postgraduate training must be arranged in continuity, according to the specialty which is to be practised Provisional-registration house appointments are a part of undergraduate education—a period of *responsible* practice under supervision—but they are a vital link with postgraduate training As such they need careful examination and control so that they may provide the necessary experience †

Postgraduate training after registration is as important for the general practitioner as for anyone else Part of it must clearly be as a trainee assistant, but it should also include *non resident appointments* in hospital departments—e g , psychiatric, ophthalmic, and dermatological The present tendency to give such appointments only to men who are going to specialise in these subjects is most unwise There should also be appointments, probably of the "rotating" type, especially contrived for those who wish to take up general practice, and for young practitioners who have discovered a weakness in their experience, or a special interest which requires a firmer basis It is unjustifiable to discredit future general practitioners by suggesting that they would be less willing than others to prepare themselves properly for their work This branch has for centuries attracted many of the finest men in medicine, and it will continue to do so

Reasons for Choice of Plan

I have three reasons for preferring to any other the plan I have described

Firstly it forms a continuous process which is in the beginning entirely educational and then becomes progressively more vocational

Secondly, it should surely be a guiding rule in any education that uniformity of the curriculum is avoided so far as possible not only individual schools but also individual students in a school, should be free to differ from each other This plan makes possible the easy absorption into clinical schools of students from the universities of Oxford and Cambridge, and it enables students in any university to diverge from the main stream at the completion of the first stage in order to take an honours degree in medical science The first stage means a considerable reduction in the content of anatomy and physiology as at present taught—although, of course students would meet these subjects and teachers in later stages I believe such a reduction is essential for many students, but a large number are capable of going further and it is right for them, and imperative for future advance in medicine, that they should be able to do so The present proportion of those who now take the B SC is too small

But though we must allow "divergence" of students, any arrangement by which they were separated into two streams on arrival at medical school would be utterly wrong Students should be free to diverge not only for an honours degree in the preclinical sciences, but in pathology, and (one would hope), some day in clinical science also

Thirdly, the plan pays due regard to the importance and the difficulty of acquiring a sound basis in clinical technique When the student is first introduced to this he should be as free as possible to concentrate upon the method of learning which it requires and should receive instruction from those expert in giving it

The alternative system—inclusion of clinical technique from the start, so that the student learns how to examine each part of the body while he is learning its normal structure and function—has been in operation in Western Reserve University for nearly four years I do not think it helps the student to acquire any better basis in clinical method and I think it may result in one not so good Because it is capable of enlivening the study of anatomy and physiology, it is often suggested as a necessary reform, but this seems to me an insufficient reason for an arrangement that may weaken the foundation in clinical medicine It is the less convincing because where anatomy and physiology are taught well and under good conditions—as at Western Reserve—they are not dull

I do not wish to disparage in any way the great service this university has done to medical education everywhere by its courageous and radical experiment—one that had to be made Moreover the change in curriculum is not the only, and not the most important experiment at Western Reserve There is also an experiment in interdepartmental teaching, which is I think successful There is a successful experiment in a tutorial system And above all, there is an experiment in the ability of a medical school to conceive, adopt and put into action an agreed educational plan This last has been an unqualified success, and the form of the curriculum which this school develops is of little importance compared with the immense stimulus its staff have received in its development The deficiencies of any curriculum can be remedied by the concerted efforts of an enlightened and interested teaching team, and Western Reserve has given us a lesson in medical education which we cannot afford to ignore

Educational Requirements

Any medical school in this country could take immediate steps to devise an educational plan, and it would then see what additional facilities it would need to put the plan into effect The curriculum which it might eventually adopt would be the product of the available facilities as much as of the plan itself

We can envisage some of the difficulties which would be encountered

The provision of proper accommodation would almost seem axiomatic, but it is surprising how hard it can be to get space at appropriate times for all the various learning and teaching methods I have described Clinical theatres, suitable outpatient consulting rooms, rooms for tutorial and group discussions, facilities for laboratory investigation by both staff and students—all these are essential to education but they are seldom easily found Since the patient is no longer indifferent to and uninterested in remarks at the bedside, there must also be rooms for ward teaching away from the patient

A more obvious need is for clinicians to be able to give more time to teaching I have mentioned the American system of geographically full time consultants and the extraordinary difficulties the National Health Service has placed in the way of our having a similar system But no adequate plan can be fulfilled unless this problem is tackled

Finally under the heading of facilities for teaching we come to the question of clinical material I have referred to the distortion and fragmentation of the student's clinical experience, but specialisation in teaching hospitals is not the only problem There

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† Many of these posts already differ greatly for various reasons from pre-war house appointments, and it is unfortunate that the newly qualified are often given advice on their postgraduate training which fails to take this into account

In England Now

A Running Commentary by Peripatetic Correspondents

For many years it has been my lot to [illegible] other people's children—but last week found me at the other end of the [illegible]. I arrived at [illegible] a.m. at a welfare centre in North [illegible] with my eight-month-old son and sat in a [illegible] with a [illegible] other mothers and their children waiting with [illegible] appointments for our first [illegible]. It was a [illegible] Christmas [illegible] established that the [illegible] present [illegible] November [illegible] were [illegible] a [illegible] if I were [illegible] that she [illegible]. At [illegible] I [illegible] but [illegible] the [illegible] of the other children and seeing the [illegible] I [illegible] my arms. I explained that the [illegible] to which I am [illegible] by [illegible] to be in the [illegible] I [illegible] even my son [illegible] me, and the [illegible] that some of our [illegible] the [illegible] my [illegible].

[illegible] was our turn to enter this [illegible] left [illegible]. The [illegible] was [illegible] to take [illegible] exercise for a week—[illegible]. The first signs of [illegible] and [illegible] eyes filled with tears. "No [illegible]" asked this [illegible]. The [illegible] confidential [illegible]: "[illegible] is something I do not understand—but [illegible] a very [illegible] I think."

* * *

"Cambridge should be a man's university" was the cry of graduates and undergraduates of my generation back in the '20s. Women had been [illegible] that had gained equality in all the other British universities and they should be content. Members of Girton and Newnham attended lectures and were like ordinary undergraduates until they came to the end, when they were allowed to take their degrees by [illegible] and [illegible] because [illegible] did not have to pay graduation fees. The chief [illegible] was that they [illegible] not [illegible] posts.

The crisis came, so we thought, in 1921 when a [illegible] of the senate recommended that women should be admitted to degrees and given representation on the council of the senate. The [illegible] phrase "[illegible]" was an understatement. Clergymen who rarely left their parishes were [illegible] to vote and doctors who were supposed to be [illegible] the [illegible] were travelling in from [illegible]. Still was the [illegible] and sometimes not even on that. The great day arrived and [illegible] graduates voted. The figures were given from the Senate House: [illegible]. The news [illegible] that the non-placets had defeated the grace and kept the women in their place, rushed to Newnham. The gates were closed against us. The trucks were quickly collected from porters and used as battering rams against the [illegible] gates. (We [illegible] know the beauty of the [illegible] then, and it was a shock to all of us to find that these gates were of great artistic value.) The authorities had [illegible] the police who arrived expeditiously and the [illegible] quickly [illegible] "The police have drawn their truncheons." It is [illegible] years ago, but I can still remember [illegible] my [illegible] and [illegible] off like a dog with his tail between his legs. [illegible] was [illegible] but true [illegible] came later and as [illegible] slowly led to conversion.

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In 194[illegible] women were admitted to full membership of Cambridge University, and equality and [illegible] were achieved. [illegible] except their ineligibility for the office of proctor and [illegible]. All [illegible] will be well if [illegible] Newnham [illegible] take all the [illegible] who want to have a Cambridge University [illegible] but [illegible] and [illegible] this by [illegible] to found a third women's college. New Hall [illegible] seat of learning like its [illegible] and [illegible] hope is that [illegible] Cambridge will help to [illegible] Cambridge provides the best [illegible] in the world.

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[illegible] an exhibition of historical documents at [illegible] the other day, I [illegible] a letter from [illegible] the [illegible] Nov. [illegible] to March [illegible] [illegible]. The [illegible] signatures of [illegible] gentlemen of the [illegible] the Church [illegible] at their [illegible] always [illegible] been [illegible].

* * *

[illegible] I [illegible] a [illegible] Christmas. It was only a [illegible] by a [illegible] particularly [illegible] specimen of English [illegible] that saved Sir Francis from a [illegible] the [illegible]. The [illegible] of the Lady [illegible] and so the [illegible] with a [illegible] set of [illegible]. With the coming of spring our [illegible] and [illegible] the garden, and [illegible] Sir Francis [illegible] in his [illegible]. [illegible] up with [illegible]. We [illegible] until [illegible] and [illegible] began [illegible] heavily [illegible] a [illegible] in the [illegible]. I [illegible] him for his [illegible] between his [illegible] a [illegible] and [illegible] a [illegible]. We took advantage of this [illegible] to investigate the [illegible]. [illegible] is a natural [illegible] of the church. She [illegible] "[illegible] seen Sir Francis [illegible] a proper gentleman." But I have [illegible] of the [illegible] of the [illegible] that I am [illegible] this year.

* * *

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* * *

May I [illegible] upon the [illegible] of the [illegible] and, with respect for the [illegible] of the [illegible] to the physician, suggest that we rename the [illegible] the [illegible] of [illegible]?

function of doctors—as it must, not least because medical care is now part of the economic life of the nation

The third step in the reform of medical education is, therefore, to establish a means whereby it can itself be studied   Research is necessary in three things—in learning, in teaching, and in the pattern of medical practice   On the first two depends the future improvement of medical education   On the last depends the nature of the work students are eventually going to do   All three are the vital concern of the university medical schools   Their investigation requires a focus from which stimulation as well as correlation can come   A body capable of providing this focus must be found in the form of either a national council or an institute of medical education   Here is a supreme opportunity for collaboration between the Royal Colleges and the medical faculties of the universities—a collaboration at the educational level which would inevitably form a basis for wider cooperation in all fields of medical practice

EFFECT OF OXYGEN ON EXERCISE ABILITY IN CHRONIC RESPIRATORY INSUFFICIENCY

USE OF PORTABLE APPARATUS

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THE effective control of acute respiratory infections in patients with chronic pulmonary disease has probably increased the number of such patients who progress to breathlessness on the slightest exertion   When such patients breathe oxygen, their arterial oxygen saturation is restored to normal (Comroe and Dripps 1950), their uptake of oxygen during exercise is increased (Valentin and Venrath 1952), the ventilation for standard exercise is reduced (Zorn 1940, Altschule 1954), and sometimes their ability to exercise is greatly improved   Therefore it seemed possible that portable oxygen equipment might have a use   Suitable apparatus has become available as a result of the development of equipment for supplying airmen and mountaineers with oxygen (Cotes 1954)   We describe here an attempt to assess its usefulness in the symptomatic treatment of men with chronic respiratory failure

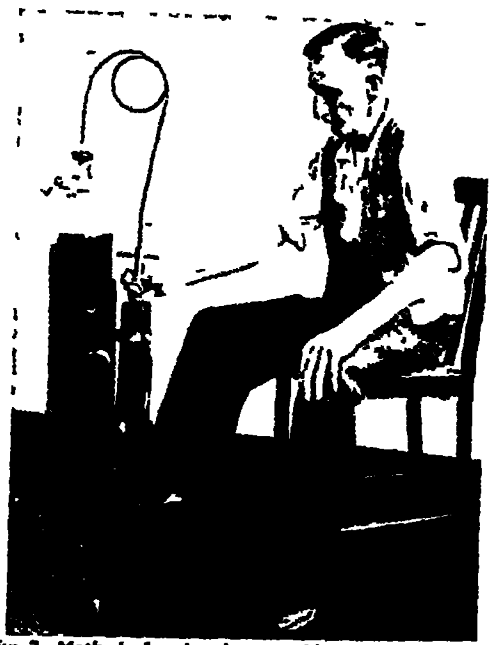

Fig 2—Method of recharging portable oxygen apparatus

Apparatus

One or more small light weight steel cylinders containing 50–120 litres of oxygen at a pressure of 120 atmospheres are connected to a pressure gauge, a reducing valve, and a flow selector   The complete apparatus for 120 litres of oxygen weighs $2^1/_2$–$3^1/_2$ lb   More oxygen can be stored by using multiple cylinders but the weight is not increased in proportion, since the cylinders share a common pressure regulator

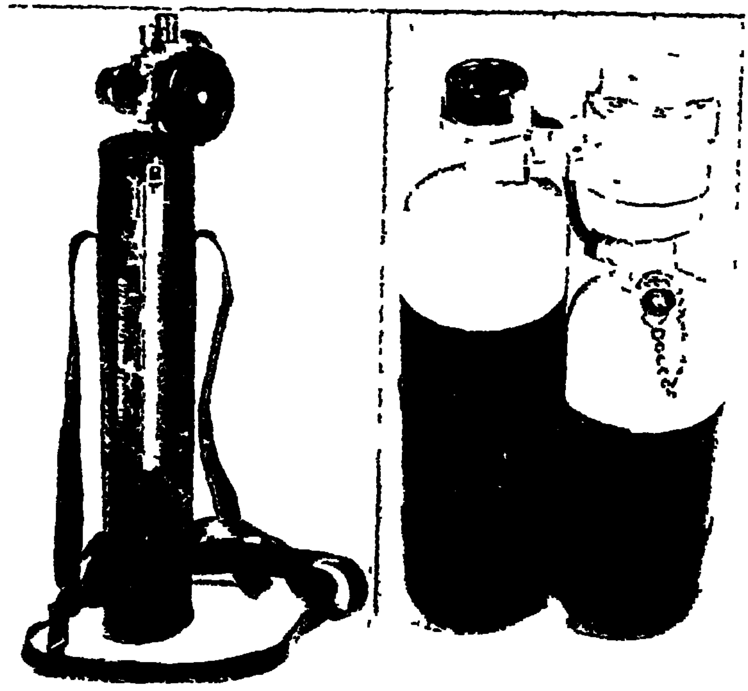

Fig 1—Portable oxygen apparatus

Two types of apparatus are illustrated (fig 1)   In one the oxygen flow is controlled by an on off cock, and two flow settings are available   This apparatus can be carried comfortably on the shoulder   In the other, the squat two cylinder type which goes into a pocket, the on off cock and flow selector are combined into a single switch, which can be turned from "off" to any one of five preselected flows

Charging has been done from a standard cylinder with a simple jig which can be operated by the patient (fig 2)   This is not entirely satisfactory, because the pressure in the charging cylinder will remain high enough to transfer a useful quantity of oxygen to the smaller cylinder for only a limited number of refills (fig 3), however since those who benefit from the portable apparatus often use standard cylinders at home the half charged ones can be used for this purpose   Sets are being developed with detachable cylinders which could be charged at a central depot and supplied to dispensaries by the dozen in manageable packages for distribution   Domiciliary recharging of portable sets would then be avoided and the difficulty of distributing unwieldy oxygen cylinders to private homes overcome in many cases

(2) Those in which there is considerable delay in removing clothing which has been saturated in boiling liquid Most of these scalds occur in the region of the axilla and upper arm, or in the groin—both sites where hot liquid tends to "pool" In our survey last year we found 15 cases, all in children, in which there was definite delay in removing clothing after a scalding injury All of these children required skin grafting, 5 needing two, and 2 needing three, grafting operations In all these children, woollen garments, such as cardigans and knickers, were worn at the time of the accident, and it is our impression that these knitted garments hold the heat much longer than other materials

The importance of early removal of clothing from scalded patients is not widely appreciated, and the Ministry of Health advice note 5/54 states that "in the event of a burn or scald no attempt should be made to pull the clothes off the skin " This is no doubt put forward in order to prevent further shock by rough handling of the patient, but certainly in the case of scalds retention of sodden hot clothing may cause unnecessarily deep destruction of the skin

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MICHAEL N TEMPEST

RESPIRATORY INVOLVEMENT IN POLIOMYELITIS

SIR,—We welcome the discussion on the management of bulbo respiratory complications in poliomyelitis which has taken place in your journal, and particularly the consideration given to the correct place of tracheotomy It is timely that experience in this field should be pooled at the beginning of the poliomyelitis season as it is no longer necessary to be guided by the data collected during the Copenhagen epidemic of 1953, which was responsible for the great increase in the method in the U K

Dr Scott and Dr Knox (April 21), in an interesting discussion on their experience in transporting twelve cases of bulbo respiratory paralysis last year, suggest that it might be better to perform tracheotomy before the journey, so that the trachea can be protected by the cuffed tube from aspiration from the pharynx, and positive pressure respiration can be given by the same tube if necessary Dr Crampton Smith and Dr Spalding (May 5) reply suggesting that for the period of transport it is better to use an *oral* cuffed tube passed under local anæsthesia, and to perform the tracheotomy once the patient is "under good conditions on arrival at the final hospital" We should like to support the first part of the latter recommendation but to add that by the time the patient has reached "good conditions" one of the two major hurdles—namely, transport—is already passed, and that instead of performing a tracheotomy on arrival the resources of the hospital should be directed to avoiding this intervention if at all possible Thus, while the oral tube is in place the patient can be prepared for its removal, and for the use of negative pressure respiration by (*a*) emptying the stomach and lower bowel (vomiting, associated with restlessness, is probably the other major hurdle), (*b*) effective sedation, (*c*) transfer to a cabinet respirator to be maintained in a steep head down tilt after removal of the tube, and (*d*) the establishment of effective replacement therapy If necessary the lungs can be cleared by direct vision with a bronchoscope, and of course effective suction must be constantly available to keep the pharynx clear

It has been our unfortunate lot for the past eighteen months to observe what a tragic complication a tracheotomy can be in a condition such as poliomyelitis, which may leave behind severe residual respiratory paralysis Such patients have virtually no cough, and chronic pulmonary infection appears to be an inevitable consequence of the stoma This infection reduces both the effective ventilation obtained by the residual respiratory power, and also the area of healthy lung tissue available for respiratory exchange Consequently the recovery of spontaneous respiration is severely handicapped, and, so long as the stoma and therefore the chronic infection persist, weaning from aid may be impossible Yet closure of the stoma is fraught with danger because of the chronic infection in the absence of a useful vital capacity and effective cough The patient is, in fact, trapped in a vicious circle, and the period of rehabilitation is either grossly prolonged by months or even years, or closure, and consequently rehabilitation, may have to be abandoned altogether, with the result that the patient may be condemned to permanent stay in hospital for the rest of his days There are, in fact, a number of cases with severe respiratory paralysis now living in relative happiness at home for whom such a solution would have been impossible had a tracheotomy been performed in the acute stage, and some of these cases would have been in real danger of this complication had they fallen into less conservative hands at that time

Obviously, the decision to perform a tracheotomy in a particular case must rest with the man on the spot Our object in writing is simply to pass on to him the product of our own experience in managing such cases of severe respiratory paralysis complicated by stomata in the recovery period, so that he may take our viewpoint into consideration when making his decision In practice, we believe that the suggestion made by Dr Crampton Smith and Dr Spalding—that the danger period of transport should be tided over by means of an oral endotracheal tube—should be extended to tide over the rest of the acute episode, and that both "prophylactic" tracheotomy and tracheotomy for the sake of administering artificial respiration by positive pressure should be almost limited to patients who fall ill beyond the reach of full hospital facilities and thus have mainly a "geographical" indication

The time for which an oral tube can be left in situ is still, we understand, sub judice Figures varying from eight to forty eight hours or more have been cited to us by different authorities Certainly in one case a duration of forty eight hours was risked with impunity The danger period in poliomyelitis is fortunately often relatively short, and for this reason one should be the more reluctant to superimpose a complication which may have such lasting serious consequences if there is any hope that it can be avoided

Nuffield Orthopædic Centre,
Oxford

J TRUETA
M AGERHOLM

PARAPLEGIA FOLLOWING SPINAL ANÆSTHESIA

SIR,—Dr Payne and Dr Bergentz (May 12) do well to draw attention once more to the well established clinical fact that paraplegia ensuing upon spinal anæsthesia may appear only several days after this procedure, and may then progress slowly for a further period of days or even weeks

Their case exemplifies also another established fact—that the immersion of ampoules of spinal anæsthetic in toxic solutions for purposes of sterilisation is by no means a constant factor in recorded cases of neurological complications after spinal anæsthesia

The only factor common to all these cases is the use of a spinal anæsthetic

The relevant literature makes it clear that the patient has often severed his ephemeral connection with the anæsthetist before his neurological syndromes—particularly the less severe ones—develop Therefore what the anæsthetist does not hear about may nevertheless have happened

Sir Robert Macintosh returns from Africa, not "with something new," but with the old story that what he has not heard about has not happened In his letter last week he cites again his single experience of the ampoule contaminated through invisible cracks by the coloured fluid in chest infection or of right heart-failure The remaining 12 were admitted for the series, of whom 9 were found to benefit by active medical treatment before beginning graded exercise on the treadmill

In 22 of the 29 patients the walking distance was at least doubled when they were breathing oxygen, compared with air (table I) In most cases this result was obtained with a mouthpiece or mask of the oxygen-reservoir type, but 2 men (cases 15 and 28) got little benefit until a nasal catheter (*flow 6–8 litres a minute*) was substituted Of the remaining 7 patients exercise was limited in 2 (cases 2 and 23) by giddiness and in 1 (case 18) by pain in the chest 2 (cases 6 and 19) showed only a small improvement on oxygen (34% and 22% respectively), and 2 (cases 3 and 17) showed no change

Minimal Effective Oxygen Flows and Influence of Design of Oxygen Mask

In 6 patients an attempt was made to determine the minimal effective quantity of oxygen by varying the oxygen content of the inspired gas and the method of its administration (table II) Tests were so arranged as to allow for the effect of order of tests on exercise ability and for day-to-day variations

The first patient to be studied in this way (case 21) did 6 walks on each of six days, breathing 20%, 25%, 30%, 50%, and 100% oxygen through a mouthpiece and using a portable oxygen set with flows of 2, 3, and 4 litres a minute delivered to an oronasal mask The results (fig 4) suggest that this patient paused for breath when his exercise ventilation exceeded 14 litres a minute, and that sensations arising as a result of changes in arterial oxygen saturation were not themselves directly responsible for his stopping From the findings it appeared improbable that 25% oxygen in the inspired gas mixture would be sufficient for patients in this condition, and this mixture was not considered further

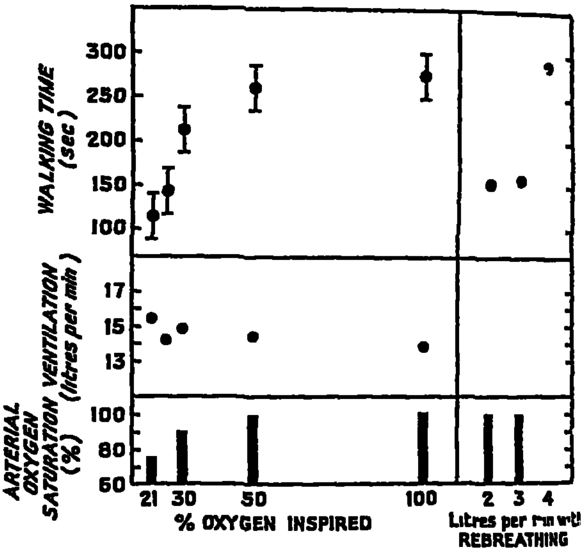

Fig 4—Effect of oxygen on walking time (case 21)

When the lines drawn about a pair of points do not overlap the difference between the points can be said to be significant

The relative efficacy of the seven remaining combinations was determined in triplicate in 2 further patients (cases 4 and 7) The results (fig 5) are in agreement with

TABLE II—EFFECT OF OXYGEN ON WALKING TIME, EXERCISE VENTILATION, AND ARTERIAL OXYGEN SATURATION

		Case no							
		21	4	7	4 and 7	8	12	26	8, 12 and 26
Treadmill Speed (m p h) Gradient (%)		 [illegible] 5	 1½ 10	 [illegible] 0		 1½ 10	 [illegible] 0	 1½ 10	
Oxygen	Index								
% O₂ in inspired air									
21	Walking time (sec)	113	128	148	138	114	157	116	1[illegible]9
	Ex vent (litre/min)	15 3	23 3	24 1		27 7	18 6	18 7	
	% Art O₂ satn	75				[illegible]	85	63	
25	Walking time (sec)	142							
	Ex vent (litre/min)	14 1							
	% Art O₂ satn								
30	Walking time (sec)	213	193	303	248	319	298	264	2[illegible]0
	Ex vent (litre/min)	14 7	25 0	21 3		29 5	17 5	18 6	
	% Art O₂ satn	90				98	91	92	
50	Walking time (sec)	260	369	336	302	300	291	306	309
	Ex vent (litre/min)	14 3	23 1	21 5		2[illegible] 8	16 0	16 9	
	% Art O₂ satn	99				101	100	100	
100	Walking time (sec)	277	283	313	298				
	Ex vent (litre/min)	13 8	23 2	20 6					
	% Art O₂ satn								
Mask with rebreathing O₂ flow (litre/min)									
2	Walking time (sec)	146	122	92	107				
	% Art O₂ satn	100							
3	Walking time (sec)	148	157	195	176	131	220	204	1[illegible]
	% Art O₂ satn	99				101	95	99	
4	Walking time (sec)	307	200	218	209				
	% Art O₂ satn								
Mask without rebreathing O₂ flow (litre/min)									
1	Walking time (sec)					164	290	275	237
	% Art O₂ satn					99	91	97	
Minimal difference in walking time significant at 5% level		13*			9				31·0

* Applies only to O₂/N₂ mixtures

or raised plasma-sodium values might excrete abnormally low amounts of aldosterone In that case slightly raised excretion of aldosterone under these electrolyte conditions may be diagnostic for the presence of tumour Thus the values in the case of Chalmers et al as measured some time before the operation could be explained by a combination of aldosterone secretion by a tumour relatively autonomous to electrolyte control together with that from normal adrenal tissue which is depressed by the prevailing state of potassium depletion This depletion would have given rise to a low excretion of aldosterone for a subject with a totally normal gland This could also explain the great decrease in aldosterone excretion after removal of the tumour down to values found in totally adrenalectomised patients whereas the cortisol values are only halved and presumably one gland remains intact In our opinion this speculation which can be investigated experimentally, would appear to be the most fruitful approach to the problem at the present time

It should be emphasised that this suggested reduction in aldosterone excretion in potassium-losing nephritis without tumour would not be due to nephropathy caused by hypokalæmia as reported in your annotation, but to a selective effect of the mineral environment on the adrenal secretion of aldosterone

O Garrod
S. A Simpson
J. F. Tait.

Middlesex Hospital Medical School
London W 1

COMPOSITION OF FLOUR

Sir.—According to the Panel on Composition and Nutritive Value of Flour, whose report you summarised last week the millers and bakers claim " that if people can obtain only bread made from 80%-extraction flour they may eat less bread and more of other manufactured foods which may not be so nourishing " It does not appear to have occurred to the industry that it would be better for the public health to engage in proper milling and baking that is, milling to leave in all the germ and resist its subsequent sterilisation by whatever process has superseded agene, while in baking such things as anti-staling agents and all chemicals should be left out so that bread is only flour and yeast Then English bread would again have a pleasant taste and substance and a crisp crust, instead of being the worst bread gastronomically in Europe The consumption of bread would improve as it gave pleasure to the public, dividends would improve and health would improve

London W 1 Franklin Bicknell

FATS AND DISEASE

Sir,—In spite of forty-three years of single-minded experimentation the dietary theory of atherogenesis has remained pure speculation All that has been shown is that the levels of certain serum-lipid fractions are raised in many cases of atheromatosis, it is a far cry from this to a causal relationship These increased levels may mean no more than that atherosclerotic plaques contain lipids—hardly a very striking contribution to knowledge

Even if it could be shown that these abnormal blood levels are indeed an important causal factor in human atherogenesis, it would still remain to be proved that they were due to feeding habits. Numerous bodily reactions affect the blood-lipid balance, each one of which might be inculpated with equal, and most with better, justification Myocardial infarction itself is one of these many causes of lipæmia [1]—a fact which illustrates strikingly the weakness of the dietary theory

The war-time decline in the incidence of coronary disease is cited in support of this theory as if a low fat content were the only characteristic of a war-time diet With much better justification one might speculate about the hypotensive effect of a low-calorie and low-protein diet on the population and on its obese contingent in particular These effects are well attested as is the atherogenic effect of hypertension

Do general practitioners really eat twice as many eggs as their consultant colleagues ?[2] Do bus conductors refuse to share sunflower cakes with their drivers ?[3] In spite of widespread publicity nothing has yet come to light to suggest that diet plays an important part in any but a small fraction of the people who come to grief as the result of atherosclerosis

Edinburgh Erich Geiringer.

TREATMENT OF SUPERFICIAL SEPSIS

Sir.—Dr Bauwens and his colleagues are to be congratulated on their valuable and interesting paper last week The general adoption of the methods they describe however, would lay an additional burden on already overworked departments of physiotherapy Any evidence concerning the efficacy of physical methods as a routine measure in the treatment of minor sepsis should, therefore be examined with care

It is for this reason that I venture to suggest that their control and treated groups are not strictly comparable. The wounds in the treated groups were dressed with tulle gras or tulle gras and aureomycin powder while in the control group 1/1000 proflavine was applied The use of a different dressing, whatever its nature for the control group would alone appear to detract from the validity of their findings. In addition there is evidence that proflavine in dilutions as high as 1/120,000 exerts an inhibitory effect on the growth of fibroblasts and macrophages [4] It is conceivable, therefore, that the use of proflavine, particularly its repeated use may have delayed the healing-time in the control group

While the methods advocated are of undoubted value in cases of minor sepsis which fail to respond to accepted measures it is doubtful on available evidence whether they should be used in every case

St George's Hospital
London, S W 1 Michael E. Fearnley.

TREATMENT OF TETANUS

Sir —Professor Lassen and his colleagues (April 28) describe two cases of severe tetanus in which protracted administration of 50% nitrous oxide and 50% oxygen led to fatal aplastic anæmia, caused, they suggest by the nitrous oxide

Is it not possible that the oxygen, rather than the nitrous oxide, was the cause ? It is known that anoxia is the usual stimulus to red-cell formation and living at high altitudes leads to polycythæmia in compensation for the reduced partial pressure of oxygen Conversely, with high pressures of oxygen the formation of red cells is depressed [5] With administration of 50% nitrous oxide and 50% oxygen the partial pressure in the alveoli is raised some three and a half times, and it is possible that over a period of days this partial pressure of oxygen removes the natural stimulus of anoxia to red-cell formation The agranulocytosis in the cases described by Professor Lassen and his colleagues would not rule out this thesis, if in fact the hæmocytoblast is the common precursor of both the red cell and the granulocyte.

A further trial would seem to be indicated using 20% oxygen with 80% nitrous oxide or, better still (since only one factor would be varied), 20% oxygen, 30% nitrogen, and 50% nitrous oxide

Queen Alexandra Military Hospital
Millbank London S.W 1 Charles Sanders

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[1] Adlersberg D Drachman L E., Schaefer S R Circulation 1951 4 465

[2] Morris J. N Heady J A. Barley, R G *Brit med J* 1952 i 503

[3] Morris J N Heady J A. Raffle P A. B Roberts C G, Parks J W *Lancet*, 1953 ii 1053

[4] Jacoby F Medawar P B Willmer, E. N *Brit med J* 1941, ii 149

[5] Wright S Applied Physiology London 1952, p 194

tution of cartons of small cylinders of the type used in portable equipment (weight 25 lb per 48 c.ft capacity) for the 48 c.ft cylinders (weight 35–45 lb) in present use. This change would also greatly ease the burden, which in our experience usually falls on the dispenser, of transporting oxygen to the patient's home and of carrying it upstairs to the bedroom.

To make the best use of portable oxygen and any domiciliary supply, an accurate leak-free pre-set flow selector is essential (fig. 7). The regulator developed for the portable equipment could be used on the standard cylinders and would save much oxygen. For maximal economy a well-fitting mask of the oxygen-reservoir type, with a check valve to prevent rebreathing, should also be used.

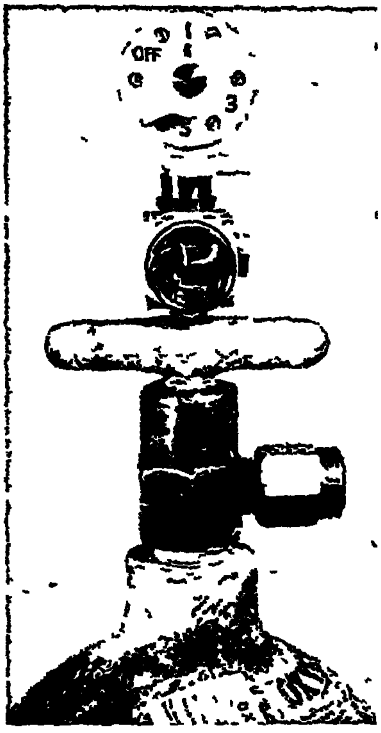

Fig. 7—Oxygen regulator and flow selector adapted to fit standard oxygen cylinder.

Discussion

Our results show that, in a fair proportion of patients with chronic respiratory infection and severe respiratory disability, a further useful increase of exercise ability above that produced by intensive chemotherapy can be produced by breathing 30% oxygen.

It is our impression that such patients gain in exercise ability by breathing oxygen only if they are prepared to exercise to the point of some visible respiratory distress while breathing air. Some patients do so constantly, and others may wish to do so after treatment and rehabilitation, but some patients apparently cannot exert themselves so far. This variation is a manifestation of the patients' attitude to their disease and need not represent any difference in the underlying pathology, though this cannot be excluded. It is likely to be the major factor affecting the success or failure of portable-oxygen therapy in the individual case.

The increased exercise ability when the patient is breathing oxygen is probably due to a reduction towards the normal levels of the ventilatory requirements for exercise as a result of the relief of anoxia. The reduction of ventilation causes a rise of the arterial carbon dioxide tension (Haldane and Priestley 1935), which could lead to loss of consciousness (Donald and Davidson 1954). This complication has not been observed, and the risk can be reduced by restricting activity to essential tasks and by using minimal effective oxygen flows. Addiction to oxygen is a more serious risk, but it is one to which many of these patients are already exposed when using domiciliary oxygen and is probably not increased by making the equipment more portable; but it is a reason for limiting the use of oxygen to those who get real benefit from it.

Portable oxygen should be regarded as an integral part of domiciliary oxygen therapy. A review of existing equipment and the cost of supplies is needed. This might be expected to lead to much improved equipment and to the more effective use of oxygen, with an ultimate saving of cost to the National Health Service. Demand is likely to increase because an ageing population is likely to contain more people with chronic respiratory failure.

Summary

Breathing oxygen usefully increased exercise ability in most of 29 patients selected as having severe chronic respiratory insufficiency. The effect was measured by the increased time they could walk on a treadmill.

From detailed studies of 6 patients it is concluded that 30% oxygen in the inspired gas is not greatly inferior to 50% and 100% oxygen in increasing exercise ability. An effect similar to 30% can be obtained from an oxygen flow of 4 litres a minute delivered to a well fitting oxygen mask, with an oxygen reservoir bag protected by a check valve to prevent rebreathing. Exercise ability is significantly impaired by the omission of this valve.

Portable oxygen equipment is described which has been used successfully by 4 patients in their homes.

The need for improved portable and domiciliary oxygen equipment is emphasised.

It is a pleasure to acknowledge our indebtedness to Mr F. Purse, of the Prescription Pricing Bureau, Wales, for information on the supply of domiciliary oxygen equipment to dispensaries; to our colleagues, in particular Mr P. D. Oldham, for help with the design of the experiments and with the statistical analysis of the data; to Dr J. A. L. Gorringe, Dr C. B. McKerrow, and Dr J. B. West for the clinical care of our patients; and to Mr A. J. Merrick, Mr F. Meade, and Mr R. T. Harris for technical and photographic assistance. Messrs Walter Kidde & Co. Ltd., Northolt, Middlesex, and Messrs Normalair Ltd., Yeovil, Somerset, provided the portable oxygen equipment.

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BRONCHIAL CARCINOMA

EFFECT OF RADIOTHERAPY ON SURVIVAL

J. R. Bignall
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There is no indubitable evidence that radiotherapy prolongs the life of patients with lung cancer.

No clinical trial has been recorded in which patients were allocated at random to treated and untreated groups; and, since it is generally agreed that the treatment can improve or relieve certain distressing symptoms, it is doubtful whether such a trial would be justified. But with a large number of case records and a knowledge of factors influencing survival it might be possible to construct groups sufficiently comparable to demonstrate differences in survival, if they are large enough to be practically important.

In this report the survival of 207 patients treated by radiotherapy is compared with that of 248 who were not so treated.

As a G P obstetrician in the London area I can only hope that the county authorities have little or no part to play in the new organisation At present the antenatal and postnatal clinics in my district are staffed by L C C medical officers, and their sole duties in the maternity services are those of antenatal and postnatal care, they are completely divorced from all other aspects of midwifery There appears to be no liaison between the clinic doctor and the G P obstetrician I cannot recall receiving any communication from the clinic doctors during the last ten years, although I undertake the care of many midwifery cases

While I am certain that these medical officers give care of the highest order, I am equally certain that it is not right for this vital part of the service to be so cut off from the actual labour and puerperium, and conversely it is equally wrong that the G P obstetrician should have to treat emergencies in the mother's home at all hours of the day and night despite the fact that he is not considered to exist during the antenatal period

It seems to me that the district midwives, the G P obstetricians, and the obstetric hospitals in the area should be responsible between them for all midwifery in that area, both hospital and domiciliary They could form a team in the real sense of the word, and in this team there would be no place for the splendid isolation of the local health authority

I realise that the local health authorities employ the district midwives and health visitors and others, but they, too, could come under the unified control and be part of the team

London S W 11 **IAN SAMUEL**

RHESUS (D) FACTOR IN SARCOIDOSIS

SIR,—Dr Cudkowicz has reported (April 21) that of 32 cases of suspected sarcoidosis 21 (66%) had rhesus (D) negative blood He suggested that a larger series should be analysed I have investigated this point in 80 cases of clinical sarcoidosis at King's College Hospital The results are as follows

Rh (D) factor		*ABO group*			
Pos	*Neg*	*A*	*B*	*AB*	*O*
68 (85%)	12 (15%)	36 (45%)	6 (7·5%)	4 (5%)	34 (42·5%)

All but 2 of the 80 cases had pulmonary and/or hilar-node involvement

Thus the prevalence of Rh (D) negative blood in our 80 patients was 15% This figure is in accordance with the prevalence in the general population and is at variance with that found by Dr Cudkowicz

In my opinion Rh (D) negative blood has the same prevalence in patients with sarcoidosis as in the general population

King's College Hospital
London S E 5 **H C SMELLIE**

ANÆSTHESIA IN OBSTETRICS

SIR,—Dr Coleman and Dr Day (May 19) are to be commended for drawing our attention to the complications due to aspiration of stomach contents during obstetric anæsthesia They have obviously anæsthetised their patients with great skill and care, and their results are due to this rather than to the technique they adopt which courts the very dangers they seek to avoid

By their method Dr Coleman and Dr Day steer clear of the Scylla of vomiting, but in so doing head straight for the whirling Charybdis of regurgitation For, if the stomach be full, the omission of the passage of an œsophageal tube before giving a paralysing dose of relaxant, and inflating the lungs, however gently, is flirting with disaster This danger of regurgitation overcome, only a fickle laryngoscope bulb and pious hopes of a normal epiglottis stand between easy intubation and those few moments of anoxia that may mean all the difference between life and death to the fœtus

We all pass through the phase of using large doses of relaxants and universal intubation but where two lives are at stake, surely would it not be better to ensure that one person at least is breathing spontaneously? To say that the anæsthetic problem involved is similar to that in a case of intestinal obstruction is incorrect, for full abdominal relaxation is needed for the latter, whereas even for a cæsarean section only very moderate relaxation is sufficient We must not be so blinded by our magic drugs and chromium-plated gadgets that we fail to recognise the essential requirements of our partners the surgeons

I have lately described a very simple and safe general-anæsthetic technique that I have found most satisfactory for all obstetric cases[1] Alternatively, as far as forceps deliveries are concerned there is much to recommend caudal or (dare I mention it?) low spinal anæsthesia

Gravesend and North Kent Hospital **PAUL AZZOPARDI**

SIR,—Dr Coleman and Dr Day have done a great service in again drawing attention to the dangers of vomiting during the administration of anæsthesia for obstetric operations The method they advocate is doubtless safe in their capable hands, but I feel that attention should be drawn to the feeling that many anæsthetists have about the danger of giving any relaxant and especially succinylcholine in a case where the stomach may be full

They say "attempting to pass a Ryle's or œsophageal tube on a woman in labour increases her fear and distress" This may be so, but the remark would apply equally to a case of intestinal obstruction or ileus Would they agree to omitting the passage of such a tube in these cases? I feel that any woman in labour must be treated as a potential case of ileus, and a full stomach anticipated even if no food has been taken for many hours Surely the passage of a large bore Ryle's tube should be a routine in all such cases?

It is possible to intubate a patient harmlessly without the use of a relaxant It was done before relaxants were introduced into anæsthetic practice, and I believe should be done in any case where vomiting is anticipated

Worthing **F R GUSTERSON**

SIR,—Great attention is being paid to this subject at present, and endotracheal intubation with a cuffed tube is often advocated as a protection against inhalation of gastric contents The relative safety of different methods of producing suitable conditions for endotracheal intubation are still sub judice, and even experienced anæsthetists sometimes cannot perform the intubation itself as rapidly as they would like Moreover techniques safe in hospital practice may be dangerous outside hospital

If it is considered that general anæsthesia with no artificial airway, except perhaps a nasopharyngeal tube, is hazardous the cuffed gastric tube described by Fisher[2] might be of value This is a small stomach-tube with an inflatable balloon situated distally After this end has been passed into the stomach the balloon is inflated and drawn firmly against the cardiac orifice, thus preventing reflux of stomach contents Anæsthesia is then induced

This technique is simple Patients who will not tolerate attempts to pass the tube will probably empty their own stomachs by vomiting during this time It is unpleasant for the patient, but some anæsthetic techniques that do not proceed without a hitch are unpleasant for the fœtus as well as the mother

It would be interesting to know what experiences practitioners have had of this method

St Albans **J W R MCINTYRE**

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[1] *Brit med J* May 19 1956 p 1171

[2] Fisher C W *Anesthesiology* 1953 14 506

TABLE II—DURATION OF SURVIVAL AFTER FIRST ATTENDING THE HOSPITALS

—	Total no.	Proportion (%) surviving after (yr.)		Proportion (%) surviving (mos.)				
		1	2	0–5	6–11	12–17	18–23	24–
No mediastinal metastases								
1000–3900r	49	30	6	37	33	12	12	6
Untreated	148	20	5	54	25	11	4	5
4000r or more	54	35	15	22	43	15	5	15
Untreated	126	24	6	47	29	13	5	6
Mediastinal metastases								
1000–3900r	63	19	3	46	35	11	5	3
Untreated	100	25	8	45	30	12	5	8
4000r or more	39	38	13	20	41	15	10	13
Untreated	89	28	9	38	34	14	5	9

groups probably contained more patients in an advanced stage of cancer who, although having no demonstrable distant metastases, were yet considered too ill to withstand radiotherapy. Their number is unknown. But there are known to be differences between the groups in the proportions considered to be in too poor a condition to withstand pulmonary resection. For instance, in those without evidence of mediastinal metastases the proportions were 27% in the untreated and 11% in the treated patients. It seems fair, however, to conclude that the groups are not so grossly biased that a large difference in survival could not reasonably be attributed to treatment rather than to selection for treatment.

Survival

The experience of each radiotherapy group was compared with that of its corresponding untreated group. The duration of life after first attending hospital was preferred to the total duration of illness. The interval between attendance and death can be accurately recorded, but, since the length of illness before diagnosis is almost always approximate, the total duration of illness is inaccurate. Furthermore, the duration from first attending hospital is a more clinically useful expression of the experience of the patients. But the comparison is only valid if there are no large differences between groups in the estimated duration of illness before attendance. The differences are in fact small. Moreover, the effect of the previous duration of illness has been eliminated as far as possible by comparing, in addition, the experience of patients with histories of similar duration.

One-year and Two-year Survival-rates

In the group treated with less than 4000r the differences in the proportions surviving two years from first attendance were insignificant (table II). Among those without metastases 30% of the treated lived more than a year, compared with 20% of the untreated. The difference of 10% with a standard error (S.E.) of 7% is small. So also is the difference of 6% between the treated and untreated patients with metastases. The differences at one and two years are only slightly greater in the groups treated with 4000r or more. In those without metastases 35% of the treated and 24% of the untreated lived for a year or more—a difference of 11% (S.E. 8%). There was still a small difference of 9% (S.E. 8%) in those surviving two years. In those with metastases the differences are of the same order—10% (S.E. 9%) after one year and 4% after two years.

Pattern of Survival

The pattern of survival judged by the proportions living for successive six-month periods, was not greatly different in the treated and untreated patients (table II). In the untreated patients the largest proportion of deaths took place in the first six months, and the pattern of survival of those treated by less than 4000r is similar. In the group with mediastinal metastases the patterns are, *in fact, almost identical*. But fewer of those without metastases died within six months of first attendance—37% compared with 54%—a difference of 17% (S.E. 8%).

The differences in the group treated with 4000r or more are larger, and the biggest number of deaths among treated patients took place in the period between six and eleven months after first attendance. The differences in the proportions dying within six months were 25% (S.E. 7%) in those without metastases and 18% (S.E. 8%) in those with them.

The probabilities that the observed differences in the patterns of survival were due to random-sampling variations are more than 1 in 20, except in the case of patients without metastases treated with 4000r or more, where the probability is less than 1 in 100.

Previous Duration of Symptoms

Survival after first attending hospital is affected by the duration of previous illness.

Groups of treated and untreated patients with approximately similar durations of symptoms were therefore compared. 35 of the 54 patients without metastases who received 4000r or more had had symptoms for less than six months; 27 (77%) lived six months and 11 (31%) a year, compared with 51% and 21% of the corresponding untreated group. In those with symptoms for more than six months there were similar differences: 79% of the treated living six months and 42% a year compared with 56% and 28% of the untreated. Further subdivision according to length of symptoms produces groups that are too small for valid comparison, but the trend throughout is the same: whatever the length of symptoms the treated patients lived a little longer than the untreated. Thus 16 had been ill for three to five months; 13 survived six months and 6 a year. In the corresponding untreated group of 31 only 13 lived for six months and 4 for a year. In both those with metastases and those without, the differences between treated and untreated patients were smallest in the groups with the shortest previous illness. Indeed, in the case of patients with mediastinal metastases treated with small doses the corresponding untreated group with symptoms for less than three months fared a little better than the treated group; 55% of the 36 untreated survived six months and 22% a year, compared with 18% and 17% of the 29 treated.

Discussion

There are several reports of comparisons between the course of bronchial carcinoma in untreated patients and in patients treated by radiotherapy, but in none has an *attempt been made to study the comparability of the two* series or to balance them by selection.

Most workers have compared the mean durations of life from the first symptom (Chandler and Potter 1927, Maxwell and Nicholson 1930, Vinson 1936, Steiner 1940, Tenzel 1941, Shorvon 1947, Harnett 1952). Longer mean duration has been reported in the treated patients, the differences ranging from 1½ months (Steiner 1940) to nine months (Shorvon 1947). LaDue (1955) compared 470 treated patients with 133 untreated and concluded that irradiation led to a 5–15% increase in the survival rate from the start of symptoms; half of the 470 given radiotherapy died during the first year compared with 68% of the untreated. Leddy and Moersch (1940), Farberov and Barlow (1941), and Hilton (1945) reported that treated patients lived longer after diagnosis, as did Widmann (1944), but he rightly commented that

Notes and News

FEEDING IN MENTAL HOSPITALS

A CONFERENCE on feeding in mental hospitals was convened by King Edward s Hospital Fund for London on May 2, under the chairmanship of Prof S J COWELL

Dr T P REES emphasised the psychological value of giving patients in mental hospitals a say in the choice of their food This is achieved at Warlingham Park Hospital by means of weekly meetings between the catering officer and representatives of patients, one from each ward as far as possible

Miss J GUTTERY spoke of the need for a proper balance in menu planning In her experience the dietary often has too much starch and not enough protein, and insufficient attention is paid to balancing of flavours between sharp and bland, appearance and colour, and consistency She urged that breakfasts should always include a protein dish, and that marmalade should be provided daily with breakfast and jam with tea Her conclusion, which was well received, was that food should be purchased according to the requirements of the menu, instead of the menu being fitted to the food purchased

Mr G J STORMONT drew attention to the disproportionate ratio of boiling pans and steaming and draw plate ovens to boiling tops, salamanders, fish fryers, and roasting ovens in the equipment of the average mental hospital kitchen, which of course adversely affects the standard of menu He went on to emphasise the need for correct layout and proper balance of the preparation cooking, and service areas in the main kitchen in mental hospitals, which, owing to the numbers that have to be fed, are usually so large as to make proper supervision difficult, if not impossible A higher standard of cooking would undoubtedly be achieved if all meals were prepared in ward and villa kitchens, but the problem of staffing control would be insuperable in present conditions, and in his view the best compromise would be a kitchen with a maximum output of 1000 meals which would afford scope for sectionalisation and which, under the present Whitley scale, would be large enough for the employment of adequately qualified staff

Mr W G WILSON, speaking mainly in the light of his experience in a mental deficiency hospital, advocated the use of insulated food boxes in preference to electrically heated food trolleys, for the transport of food between kitchen and wards He argued that, intelligently used, insulated food boxes retain heat effectively and at the same time are much cheaper to operate For towing Mr Wilson favoured electric trucks as cleaner steadier, and more manœuverable than petrol driven vehicles

Miss E H JOHNS said that even today there are many difficulties in providing a satisfactory meal service, such as badly equipped ward kitchens, inadequate crockery and cutlery, and, above all, lack of staff Miss Johns urged that priority be given to the upgrading of ward kitchens installation of refrigerators and modern tea making equipment, redecoration and refurnishing of dining room areas, and the provision of more domestic help This last is perhaps the greatest need, in order to reduce the atmosphere of haste which prevails in so many large wards where two or three nurses have to look after seventy or eighty patients, many of whom may require individual attention at meal times Her final plea was for properly appointed tables with tablecloths, tumblers and when the menu requires it, fish knives and forks, so that patients may be encouraged to behave as they would in their own dining rooms

ROYAL COLLEGE OF MIDWIVES

ON May 24 Queen Elizabeth the Queen Mother laid the foundation stone of the college s new and enlarged head quarters at 15, Mansfield Street, London W 1 Since it was founded as the Midwives Institute in 1881 the work of the college has steadily expanded and every year 2000 students now take its courses It receives no Government grant, and to complete the new building and endow it an appeal for £150,000 has been made So far £42,000 has been raised

CASUALTY CENTRES AT SWINDON

Two casualty centres have been opened at the Swindon works of the Western Region of British Railways These centres are to be used for dealing with injuries sustained at work by any of the 12,000 employees in the works and offices, and for renewal of dressings and follow up Each centre comprises a waiting room, first aid treatment room, and rooms for doctor and nurses

GENERAL MEDICAL COUNCIL

THE results of the recent elections for 11 members to sit for five years were as follows

ENGLAND AND WALES

Election of 1 member as a person resident in Wales—The only candidate nominated was Dr W V Howells, who was accordingly elected

Election of 7 other members—The result of the voting was as follows

Dr JANET AITKEN	16,501
Dr H GUY DAIN	15 729
Dr L D CALLANDER	15 277
Dr O C CARTER	14 758
Dr J A BROWN	14 424
Dr S N SCOTT	14 128
Dr E A GREGG	13 936
Dr Stanley Dillon	8615
Dr C T H Whiteside	7911

Dr Aitken, Dr Brown Dr Callander Dr Carter Dr Dain, Dr Gregg, and Dr Noy Scott, were accordingly elected

SCOTLAND

Election of 2 members—Two candidates only were nominated, Dr I D Grant and Dr G W Ireland, who were accordingly elected

IRELAND

Election of 1 member—The result of the voting was as follows

Mr WILLIAM DOOLIN	1376
Dr M B Conlon	485

Mr Doolin was accordingly elected

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on May 26, with Mr Charles Read, the president, in the chair, the following were elected to the council

As representatives of the fellows—Frank Cook, S W Maslen-Jones J A Stallworthy D M Hart

As representatives of the members—Dorothy M Shotton Matthew Garrey

The following were admitted to the fellowship

V H Barnett Gavin Boyd J E Giesen A D T Govan S W J Harbutt Stanley Henderson Derek Jefferiss N K B Kimbell Parvati Malkani K A McGarrity A H McLennan J D Murdoch E L Nicolson L B Patrick I M Robertson Jane B Roy G J Strean W H Tod

The following were admitted to the membership

E A Agius D G Bonham Reginald Bowman R J M Byrne J K Craig C A Cussen R P De Bond R R Elvidge J W G Evans L A J Evans Jack Eyton Jones Winifred J A Francis C O Fung Kee Fung J G Furber R H Gelb Anne L M Graham R G Harbison, G F W Hossack, G F Jolly, Anna R Kemp Edward Lacy J D Llewellyn Jones F V Mackay John Mander, M D Manion Brian Mensday Nirupama P Nayak R W A Nel J P O Neill G M Parkin H E Reiss L L Relf Freda M Roberts S B Robertson A W Russell Jean M Sharpe P F Venter L M Wolf

Society of Apothecaries of London

At recent examinations the following were successful

M M S A—A S H DeSilva E S Linton B G Pickles A H Saddler I H F Swain, M H Turner

L M S S A—A M Marcus M A C Lyon P L Pratt R S Kjestrup S R Harris H Bezzi G Wood, P J Sandison, J B Middleton R A Harlow H Pambakian J B B Milne D H Brennan C L Wagstaff, B L Dodson W L P Gould P G C Beney A J D Souza D A Gilchrist, D J Dale D G Thomerson B J P Wright G V Lewis, E P Jackson A B Gilmour

Royal College of Physicians of London

On Thursday, July 5, at 5 P M, at the college, Pall Mall East, S W 1, Dr Ivan de Burgh Daly, F R S, will deliver the Bertram Louis Abrahams lecture when his subject will be intrinsic mechanisms of the lung

An R A M C War Memorial

On June 17, at 3 P M at R A M C T A Centre, Upper Chorlton Road, Manchester 16, Major General Thomas Young, colonel commandant of the corps will unveil the R A M C Territorial Army memorial to those who fell in the late war Relatives and past and present members of the R A M C units and attached corps may obtain tickets from the centre

RADIOTHERAPY OF CANCER OF THE LUNG

RESULTS IN A SELECTED GROUP OF CASES

JOSEPH SMART
M A , M D Camb , F R C P
PHYSICIAN, LONDON CHEST HOSPITAL

GWEN HILTON
M B , B Sc Lond , F R C S , F F R
DIRECTOR, RADIOTHERAPY DEPARTMENT, UNIVERSITY COLLEGE HOSPITAL, LONDON

THE treatment of carcinoma of the lung has hitherto been limited to surgical treatment by pneumonectomy or lobectomy, radiotherapy and chemotherapy in inoperable cases, and the combination of surgery and preoperative and postoperative radiotherapy

The five years survival rate of operable cases varies according to different authors The figures given by Bignall and Moon (1955) in a survey of cases operated on at Brompton Hospital and at the London Chest Hospital showed that out of 531 cases there was a 32% over-all survival-rate of five years or longer, which continued to fall gradually to 21% in an approximately ten-year follow up of a limited number of cases The survival-rate following surgical treatment has improved with technique but is still disappointing

The results of radiotherapy in cases considered unsuitable for surgery are even more disappointing Hilton (1935) reports that only 8 of 203 patients selected for radiotherapy survived five years, and at the Christie Hospital, Manchester, Paterson et al (1950) report that 7 of 234 patients survived five years Dobbie (1944) and Shorvon (1947) give an over all survival-rate of up to 2% for five years These figures suggest that the treatment of bronchial carcinoma by X rays alone has no real place, but it must be borne in mind that these figures for X ray treatment refer to cases considered unsuitable for surgery because of spread of disease to the mediastinum and elsewhere Hence it is quite unrealistic to compare the figures with the survival rate for cases operated on

In 1942 one of us (J S) saw a patient with a carcinoma of the bronchus who, on bronchoscopy, was deemed inoperable in view of the involvement of the phrenic nerve and paralysis of the diaphragm, and in whom biopsy showed an undifferentiated carcinoma This case was treated by X rays at St Bartholomew's Hospital, and, although there was gross X-ray fibrosis of the right lung, the patient was still alive, well, and working thirteen years later, when he developed an infection in his fibrotic lung, which was subsequently drained surgically He still remains well and working although there is a permanent drain into his infected space

2 other cases, seen by one of us (G H), were considered by surgeons operable from the purely technical point of view—i e the growth was situated in such a position that pneumonectomy was possible and no secondary deposits were found—but 1 patient refused operation, and the other was unsuitable because of chronic bronchitis Both these patients were treated by radical X-ray treatment and survived for more than five years

In the light of these 3 cases we felt that it would be justifiable to treat a series of selected cases by radiotherapy alone

Selection

Each case was judged suitable on the following grounds the general condition was good the lesion was localised and situated in such a position that surgery could be undertaken, and there was no evidence of mediastinal glandular involvement either clinically radiologically or on bronchoscopy In each case definite histological proof was secured by bronchoscopy and histological section, or by a positive sputum for new growth cells before radiotherapy was started

Material

So far 33 cases have been treated, the first eight years ago Of this series 19 were squamous cell carcinoma and 6 anaplastic carcinoma , in 8 cases the diagnosis was determined by carcinoma cells in the sputum—4 were squamous, and in 4 the precise nature of the cells was not determined, making it impossible to state dogmatically whether these were squamous or anaplastic carcinomas

Preparation

Careful preparation of the patient before irradiation was an essential part of the treatment Measures were taken to improve the general condition and to increase the percentage of hæmoglobin if it was at a low level If necessary, sepsis was dealt with, infected teeth were removed, and infection in the mouth and upper respiratory tract was attended to Infection in the lung was treated by postural drainage and with appropriate antibiotics In some cases several weeks were spent treating the infection before radiotherapy was begun

Supervision

The patients were kept under close medical supervision throughout the course of treatment They were admitted to hospital if possible, especially during the winter They were given a well balanced high calorie diet and full doses of iron and advised to take plenty of rest Sedatives were given to ensure adequate sleep and to suppress any non-productive cough

Radiotherapy

Great care was taken in localising the tumour and assessing the volume to be irradiated, because it was considered that one of the chief causes of failure of radiotherapy in bronchial carcinoma was insufficient dosage to the whole of the cancerous tissue The whole range of radiological methods was used to assess this *The size and disposition of the treatment fields depended on the size of the tumour bearing area* Multiple small field technique was used only if the growth was a squamous carcinoma If the growth was an undifferentiated or oat cell tumour the treatment fields were increased to cover the whole of the mediastinum The inclusion of so large an area was considered necessary because of the almost certain involvement of many of the mediastinal glands

A dose of 5000–5500r was delivered to the tumour if the carcinoma was squamous cell, but only 4000–4500r if it was undifferentiated The length of the treatment and the amount of radiation to be delivered each day was not prearranged at the beginning of the course The patient was seen daily by the radiotherapist, and his temperature chart, pulse rate, respiration rate and general condition were studied before deciding the amount of radiation to be given on that day If there was a rise in temperature or an increase in pulse rate or respiration rate, either the dose was decreased or treatment was suspended for a day or two Great importance was attached to varying the daily dosage according to the *patient's condition* The whole course of treatment usually lasted seven to eight weeks

Follow-up

Of these patients 12 have been followed up for five years or more, 4 of whom are still alive and well 3 of these 4 had squamous cell carcinomas and 1 an anaplastic carcinoma In this same group 1 other patient survived three years 2 survived two years *or more*, and 5 died within the first two years Over this period in a very limited number of cases this gives a survival rate of 33%, which figure is similar to the surgical results

CHANGES IN MEDICAL EDUCATION*

JOHN R ELLIS
MBE, MA, MD Camb, FRCP
ASSISTANT PHYSICIAN TO THE LONDON HOSPITAL, SUB DEAN OF THE LONDON HOSPITAL MEDICAL COLLEGE

(concluded from p 818)

ALL too often attempts to improve medical education are concerned primarily with the curriculum, but the first essential surely, is to define the aim Having translated this into educational objectives, we can then decide what processes of learning the student must employ and what arrangement of his studies will enable him to employ the right process at the right time This arrangement of the right process at the right time is not the curriculum it is an educational plan We know too little about the processes of learning to be sure of what the best plan is, but we know enough to outline the possibilities most likely to be successful

Whatever plan is adopted is, however, no more than an ideal For learning has to be aided by suitable techniques of instruction, and these in their turn require facilities that are bound to vary from school to school and can never be perfect Only when the ideal educational plan is matched against the available facilities does the curriculum emerge In the words of Dr Hale Ham "The curriculum is the course through which the student travels, it is a definition of limitations as well as opportunity"[6] For this reason recommendations confined to the curriculum are tackling medical education at the wrong end and do little more than tinker with the time-table

These then are the essential steps in building up the curriculum

1 A statement of the *aim*—what we are trying to achieve in the period of undergraduate training

2 A formulation of *educational objectives*—what kind of discipline we must teach to achieve it

3 An analysis of the *processes of learning* which the student should employ to master this discipline, together with *techniques of instruction*

4 The framing of an *educational plan* in which these processes and techniques are arranged at the most suitable stages of the student's development

5 Implementation of this plan by translating the theoretical ideal into a feasible *curriculum*

The Aim

The aim of medical education was formerly defined as the preparation of the student for efficient general practice on qualification Though for many years this aim has been obviously unattainable there has been reluctance to admit the fact Even in 1944 the Goodenough Committee said that "the training must fit [students] to enter practice as general practitioners, and must also provide a sound basis upon which those who wish to become teachers and specialists can found the postgraduate training and experience they will require"[7] But since then the practice of medicine has greatly changed, and general practice has itself become clearly a specialised branch of it Within the pattern of the National Health Service postgraduate training for this specialty has developed in the form of trainee assistantship, which most have come to accept as desirable if not essential

It is now clear that the aim of medical education must be to give the student a foundation upon which he can later build a training for any branch of medicine This can be achieved only if he is "groundedly learned" in (1) clinical observation, (2) method of thought, and (3) empirical knowledge, and if he learns how to learn for himself—which is the only basis for lasting efficiency and safety in practice

Abandonment of a comprehensive training in favour of a basic education does not imply a mere reduction in the amount to be learnt It means rather that, throughout medicine, a purely vocational training should give place to education in method of thought and clinical method I do not believe this basic education would be less safe than the present training which is intended to be comprehensive but inevitably leaves out much that has to do with safety

These considerations apply particularly to the general practitioner whose work is affected by advances in almost any part of medicine The standard of medical care in this country depends upon the standard of general practice, and medical schools must regard it as their first duty to ensure the best possible undergraduate education and postgraduate training for their students who will take up general practice, irrespective of whether these are a large or small proportion of the total The sure way to fail in this duty would be to base the undergraduate curriculum on what appears to be the present knowledge needed for general practice, and allow this to be acquired by purely vocational methods But it is also essential that *every* student should see medicine as a whole—both in relation to the patient as an individual and in relation to medical care as it affects the community

The suggestion, often made, that an education which aims to give students an understanding of scientific method is beyond the capacity of most of them is, in my opinion, quite invalid No serious attempt to give it has been made in this country in the past thirty years, though many students have acquired it for themselves "Scientific method" is not a laboratory process but the process of rational and critical thought If we discover that the majority of medical students are indeed incapable of acquiring it, after a university education directed to that end, then we are not attracting suitable people into the profession, and, if we cannot find others more suitable, then there will be no alternative but to have two grades of doctors and alter the pattern of medical practice accordingly

What we have to do, then, is to work out a foundation which will be a sound basis for all forms of medical practice This foundation will continually change, for its content will always be selective, but it will not expand with the additions to medical knowledge The strain of expansion will be transmitted to the postgraduate stage, where it can be relieved—as indeed is already happening—by specialisation within the specialties

Educational Objectives

The first objective is to cultivate in the student the power of *accurate observation* The teaching of clinical observation has always held a high place in English medical education, and the technique of history-taking and of physical examination was a basic feature of the apprenticeship system The clinical introductory course has, I believe, put instruction in this technique on a surer foundation

The second objective is to develop the power of *logical thought* This is necessary for the interpretation of what is observed—although we have to recognise that in clinical medicine it is often effective only when allied to experience

Now there is considerable controversy on when and where the student learns or should learn this habit of logical thought Some hold that it can be learnt only in preclinical or even premedical departments, since these deal with subjects which approximate more nearly to the 11th right rib) to a left oblique approach to the splenic vein (from umbilicus to the bed of the 10th left rib) (fig 1)

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* The Goulstonian lectures for 1956 delivered before the Royal College of Physicians on Jan 17 and 19

[6] Ham T H *In* An experiment on Medical Education at Western Reserve University New York 1954 p 13

[7] Report of Interdepartmental Committee on Medical Schools H M Stationery Office 1944 p 173

We concluded that the dorsal position gave us the best exposure and enabled us to obtain standard splenic and portal venograms Our problem was what to do with the arms In these circumstances the arms may be defined as rigid articulated structures interfering with the approach to the side of the body To extend them in the cruciform position was no solution, because that would prevent the vital third assistant from standing headward of the surgeon To fold the arms on the patient's chest in the usual way did not leave enough room for all surgical manipulations, and we wished to be unrestricted

We solved the problem by flexing and raising the patient's arms so that they crossed his face as in the start of the hornpipe dance arms flexed to a right angle and in a plane as nearly as possible perpendicular to the long axis of the body The hands come to rest more or less on opposite shoulders, but small pads may be necessary to prevent pressure on the chin or to support one of the forearms on the upper part of the chest Good fixation can be obtained (as in fig 2) by using elastic adhesive strapping fixed down the dorsal or ulnar surfaces of upper arm, forearm, and hand and extended on to a convenient point of fixation on the side or undersurface of the operating table

Fig 2 shows that the endotracheal tube, the blood-pressure cuff, and the intravenous-infusion needle are concentrated in as small an area as possible The anæsthetist can attend to all the patient's requirements without having to move and therefore favours the position Respiratory movements are in no way impeded There appears to be no risk whatever of any brachial plexus palsy The arms, however, must be prevented from falling upwards if the patient is tipped into the Trendelenburg position

We have now used this position more than 150 times to great advantage Care and a little ingenuity are all that is required in fixing the patient quickly and without special apparatus X-ray cassettes can easily be manipulated in and out of a lateral cassette tunnel—a matter of vital importance in all operations when radiography of either the portal tree or the biliary tract is essential The costal margin is raised, and the inferior angle of the scapula is rotated forward, improving the exposure in the upper abdomen and opening out incisions wh cross the costal margin

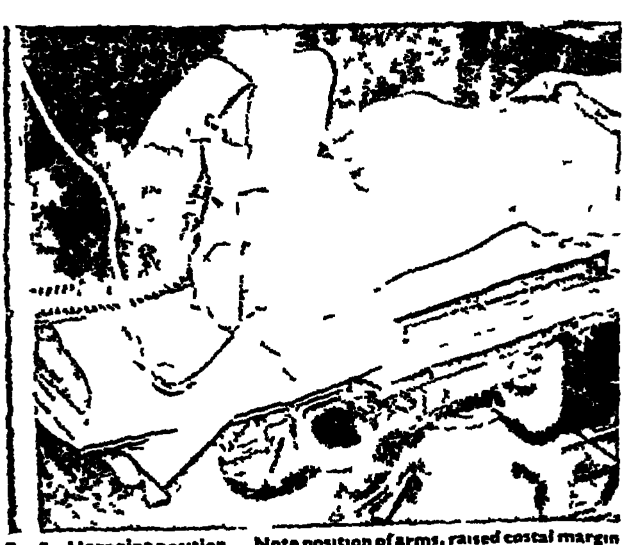

Fig 2—Hornpipe position Note position of arms, raised costal margin forward rotation of scapula freedom of approach from front and sides blood pressure cuff on right arm intravenous needle in dorsum of left hand valves of endotracheal tube, and double cassette tunnel ready for venography Arms are fixed with elastic adhesive strapping and in this figure left hand is supported on small pillow

We have therefore adopted the hornpipe position f many operations as well as those for portal hypertension o for exploration of the biliary passages and for operatio on the pancreas, liver, spleen, cardiac end of the stomac oesophageal hiatus of the diaphragm, and lower end o the oesophagus In operations which are certainly goi to be restricted to one side of the body it is not alwa necessary to have both arms elevated, but it may be a advantage if the X-ray cassette tunnel opens on t opposite side of the patient to the surgeon

Sometimes, after the preliminary investigations of patient with an obliterated portal tree, it has been decid that proximal gastric resection through a left thorac incision is the correct approach In these circumstanc additional rotation of the patient's chest towards th right has been easily effected with the minimum o disturbance by pulling on the left arm and fixing it or on a rest

Summary

Fixation of the patient on the operating-table in position akin to that adopted at the start of the hornpip dance (fig 2) is of great value in operations for port hypertension, &c

Our thanks are due to Dr Ronald Bowen who has giv most of the anæsthetics, to Miss K D Bartlett and th theatre sisters who have helped us with these operation Miss M Rutherford, Miss A F Mallett, Miss J B Chri and Miss E A V Jenkins, and to Mr Henry Dowsett o senior theatre orderly, who has always been of the great help to us Fig 2 is based on a figure which appeared in a article by G H du Boulay and B Green (*Brit J Radi* 1954, 27, 423)

WEIGHT LOSS AND PERNICIOUS ANÆMIA*

A E Read
M D Lond, M R C P
REGISTRAR

Richard Asher
M D Lond, F R C P
PHYSICIAN

CENTRAL MIDDLESEX HOSPITAL, LONDON

Addison (1855), when describing the clinical picture o pernicious anæmia, wrote "The bulkiness of the genera frame and the obesity often present a most strikin contrast to the failure and exhaustion observable in ever other respect The general frame becomes flabb rather than wasted"

Most clinicians and textbooks concur and do no mention loss of flesh as prominent in addisonian anæmi Students are taught that most patients with the dis are well covered or obese—indeed many are How ever it is not uncommon to find a history of lo weight, and clinical examination often confirms th I some cases of pernicious anæmia this weight loss may b quite alarming and may lead the clinician to make anothe diagnosis, usually malignant disease

Jones (1938) described 76 patients with pernicio anæmia 42 of these had lost weight when admitted this loss ranging from 2 to 12% of their usual weight Further, he showed that a gain in weight followed treatment (in those days liver by intramuscular injectio in 28 of these 42 patients

It is our purpose to re-emphasise the importance o these observations and to stress that weight lo i addisonian anæmia is common As it will be seen—th weight loss misled the clinician on several occasions a

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* Read at a meeting of the Middlesex County Medical S at the Central Middlesex Hospital on Dec 9, 1955

Such an introduction must be very carefully planned It does not aim at and must not result in a hazy picture of the whole—vague principles and half-facts What is learnt must be understood, and be definite

I would not at this stage include elaborate schemes to increase the student's awareness that man is a social animal, a member of a family and of a society Such schemes are used in American schools, but I doubt whether they have real value at this stage The difference in age of students and ways of life in the two countries have also to be remembered Nevertheless, it is very important that the student should begin to consider the social aspect of medicine To this end it would perhaps be worth setting him certain tasks—such as making a survey of local industry or health services

This first stage would require, perhaps, one year divided into three terms as now—or two longer terms

Study of the Abnormal

Study of the causes and effect of variation from normal would be based on the departments of bacteriology, morbid anatomy, psychiatry, and pharmacology Clinical problems should be used as illustrations, and the natural link between infectious disease and bacteriology be exploited

Again teaching would be integrated and experience systematised Special pathology would not be included I think one term would be enough

Introduction to Clinical Method

Here I have in mind the present clinical introductory course in a modified form, lasting one term—i e, slightly shorter than at present Six weeks of applied anatomy and physiology would be devoted to learning the technique of clinical observation, the student being concerned only with the methods of obtaining evidence In this he would be instructed, and his instructors would not attempt to teach him to interpret evidence, but only how to elicit it In the next four weeks he would be introduced to interpretation by systematised demonstrations combining medicine and pathology In this period, which would prepare him for work in the wards, he would require teaching, as opposed to instruction He must be helped to bring his own reason to bear on the problems presented

Practice of Clinical Method

After this instruction in clinical method, the student should have the opportunity to practise it under supervision—i e, by an inpatient clerkship and dressership totalling six months This is the place in the plan where a combined surgical and medical firm could be attempted I am not certain that it is practicable, but it should be tried

Stage of Consolidation

At the end of this six-month period of unsystematic exposure to clinical experience, during which much knowledge would have been gained, I would present the student with a "survey of human disease" combining the study of "special pathology," social pathology, and the systematic study of medicine

General Experience

I would then send him into the wards for six months for further general experience He should have responsibility for clinical laboratory investigation, and his work should be closely integrated with that of the firm, so that he may learn the team work of medicine by being a member of the team Though I should prefer his medical firm to be as general as possible, I would let him join any surgical department that he wished I would not worry him with lectures in this period, and I would like him to live in or near the hospital

Special Experience

The student would now be in his fourth year at medical school—for holidays must be added to the times I have stated In this year he should hold an appointment in midwifery and pædiatrics (with further teaching from the department of anatomy) and an appointment in the outpatient department Together these would cover ten months In this year and in the last there would be a free period of two months in which the student could be attached to two special departments of his choice, one in each year He would attend the outpatient clinics of other departments

Practice under Supervision

In this five-year plan there are now six months unallocated, and these should be for the student a stage of practice under supervision—three months in hospital and three months outside The hospital appointment I envisage would be to a general medical outpatient clinic, served by students and supervised by teachers I believe it would be of inestimable educational value and perfectly feasible It would be complementary to the outside appointment, which would be in a university health centre, such as that in Edinburgh, but with more provision for student service In this way the student would, under the supervision of his own school, learn something of practice in both fields of medicine—that in hospital and that outside—and of the links between the two He would learn by participation and not by observing This would be of incomparably greater value than any number of weeks spent "seeing and hearing" what a general practitioner does By this means, too, the school could test his practical ability—a form of assessment we now lack

The Tutorial System

At all stages teaching should be integrated by a tutorial system The duty of the tutor is to inspire and guide the student to bring his own intelligence, previous education, industry, and character to bear on rewarding work He need not necessarily be the student's philosopher and friend, but he must be his guide, and he can only guide him well if he really knows him

The tutorial system is the solution to the problem of the large teaching staff and the groups of unknown students It should enable us to re-create apprenticeship, but an apprenticeship suited to modern medicine —not concerned with passing on the "tricks of the trade" but contriving to make the student understand by his own efforts, and thus acquire both lasting knowledge and the ability to go on learning

The tutor can guide the student in three main ways

(1) In his reading, especially from original work

(2) In his writing Few students can learn to think if they do not regularly transmit their thoughts to paper

(3) In his follow-up of selected patients This is now essential, and the most effective method is for the tutor to select patients from those encountered in early clinical appointments

The work of tutoring should not be arduous, for it is done more by thinking than by talking It can be done well only by those who are sincerely interested in the education of students, who are able to give it the time required, and who have professional experience and ability

Methods of Assessment

An educational plan, such as I have outlined, must include a system of assessment, and this must be integrated with the curriculum itself Examinations are at present the most powerful of all the incentives determining the student's method of learning, and under present conditions their influence is unhealthy Though they are indispensable as one form of assessment, they must be related at all stages to the educational plan Furthermore, other forms of assessment, based on continuous observation of the student's progress, are more reliable and provide a better stimulus to proper habits of learning But under our present system, no form of progressive assessment is possible if barium meals are to be done in patients misdiagnosed as having malignant disease these are much better tolerated after, than before, the appropriate therapy

It is interesting to speculate as to the cause of weight loss in these patients Vitamin B_{12} has been shown experimentally to act as a "growth factor" It has also been used with success by some workers (Larcomb et al 1954) in the treatment of underweight schoolchildren Thus one might expect the depletion of vitamin B_{12} in pernicious anæmia to cause loss of weight, and it is difficult to see why this is not more common and more severe

We do not pretend to have produced anything new or unusual in this paper, but we believe that the recognition of weight loss as a complication of pernicious anæmia is both of interest and of importance

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A SHORT SMALL INTESTINE ASSOCIATED WITH FIBROSIS OF THE LIVER

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THERE is considerable experimental and clinical evidence that dietary deficiency or imbalance may either cause liver disease or influence unfavourably the progress of non-nutritional liver disease

Himsworth and Glynn (1944) showed that both massive hepatic necrosis and diffuse hepatic fibrosis (portal cirrhosis) could be produced experimentally in laboratory animals by an abnormal diet, massive necrosis by methionine or cystine deficiency and diffuse fibrosis by a high fat diet with a moderate amount of protein Diffuse fibrosis follows severe fatty change in the liver cells, it develops around the portal tracts and central veins and is essentially a replacement fibrosis The fibrosis of congestive heart-failure develops in a similar manner (Day and Armstrong 1940) from the portal tracts and from the region of the central vein

Dietetic liver disease in laboratory animals is most easily produced in young males (Farber et al 1951) and may be enhanced by the administration of thyroid gland (Beveridge 1954) retarded by giving antibiotics (Gyorgy et al 1951), and even prevented by rearing the animals in strictly aseptic conditions from the moment of birth (Gyorgy 1954)

In man the tropical and subtropical syndromes of dietetic liver disease are probably closely related to the diffuse fibrosis following fatty degeneration seen in the rat, but in temperate climates nutritional liver disease is probably nearly always due to protein deficiency caused by the effects of extrahepatic disease or of alcoholism the latter a more complex situation in which toxic and nutritional factors combine

Hepatic fatty change followed by fibrosis is stated to be often associated with ulcerative colitis Kimmelstiel et al (1952) put the frequency at 40% The contributory factors in this disease are dietary restriction, impaired intestinal absorption, blood loss and possibly bacteræmia

A similar situation might well arise after extensive resection of small intestine, but it seems clear that the intestine is more than adequate in area considera lengths may be removed with impunity, and if surge are alert to the possibility of intestinal insufficie after very extensive operation the diet will reinforced

Hypoplasia of the intestine has not been mention and for that reason the following cases are descri The measurements taken were from the duodenoje flexure to the cæcum

Case-reports

Case 1 —A woman, aged 72, was admitted in coma had complained of headaches and had not been quite h several years About a year previously she had been tr for generalised œdema and given digoxin and mersaly for the last few weeks she had had vomiting swelling of legs, and enlarging abdomen She died three days a admission, deepening coma, ascites, œdema and albumi were the only positive findings

Necropsy Findings —A wasted and œdematous woman w bilateral pleural adhesions and severe œdema of the lu The liver weighed 28 oz and was shrunken and fibrous w regeneration nodules throughout The spleen was firm of normal size The peritoneal cavity had been tapped contained only two pints of fluid The jejunum and il *together measured 11 ft but appeared otherwise normal* organs and tissues were œdematous

Histology —The liver showed severe fibrosis with prolif tion of bile ducts and an abundance of chronic inflamma cells in the portal tracts There were changes due to po obstruction in the spleen, and the jejunum and ileum contai a few areas of neutrophil leucocytic infiltration in the muc

Case 2 —A woman, aged 62, complained of lassitu weakness, and diarrhœa of about two months duration had been vaguely unwell for five years, and four ye previously she had been investigated because of attack diarrhœa, and her blood pressure had been found to 230/130 mm Hg, her liver had been palpable She *presented with severe anæmia (Hb 44%) and ascites* condition rapidly deteriorated and she died

Necropsy Findings —A pallid and wasted woman jaundice Venules on the nose and prolapsed hæmorrho 6 pints of fluid in the peritoneum The liver weighed 32 and showed diffuse fibrosis There were scanty regenerati nodules about 0 5 cm in diameter The spleen weighed 10 The other organs showed changes due to anæmia The sm *intestine measured 6 ft and was otherwise normal*

Histology —Fibrosis of the liver with regeneration of li cells and bile ducts and infiltration of the fibrous ti inflammatory cells The spleen showed a myeloid reacti in addition to changes due to portal obstruction Sections the intestine were normal but for slight œdema

Case 3 —A woman, aged 59, complained of stead increasing lassitude, loss of appetite, loss of weight a occasional diarrhœa for more than a year Four siblings a four children were perfectly healthy Her liver and sp were impalpable, but she had severe ascites distension abdominal veins moderate œdema, and severe seconda anæmia (Hb 34%) She died within two days of admission

Necropsy Findings —A sallow wasted woman with œde of the legs and distended abdomen Ascites of 12 pi The liver weighed 32 oz, its capsule was wrinkled and secti showed diffuse fibrosis, the pattern being distinctly coar the right lobe The spleen was firm and weighed 6 oz T other organs showed changes due to anæmia and œdema a *there was terminal bronchopneumonia* The small intesti measured 4½ ft jejunum 3 ft, and ileum 1½ ft Th was no evidence of any disease to account for this extraordi appearance The marrow of the vertebræ showed a regeneration

Histology —The liver showed diffuse portal fibrosis a centrilobular necrosis, with some regeneration of bile du and scattered inflammatory cells but there was practicall no regeneration of liver cells The spleen showed the due to portal obstruction and a slight myeloid reaction T jejunum and ileum showed subacute inflammation confi to the mucosa, and there was chronic inflammation of t mucosa of the colon Active hæmopoiesis in bone marr of vertebræ

Case 4 —A woman, aged 80, was admitted in a confu state and incontinent after a short period of coma are many others which require careful study and positive action if the selective clinical experience so essential to education is to be realised. At some hospitals population changes have adversely affected the clientele. The establishment of well equipped and well staffed regional-board hospitals has led to the diversion of acute emergencies, and of patients with common and easily treated ailments, away from the teaching hospitals. The number of children needing hospital treatment has fallen dramatically in all areas, and the numbers of the aged and chronic sick have increased. To maintain adequate turnover of patients at teaching hospitals the arrangements under which they can be discharged or transferred require further attention. In future the trend of hospital activities is likely to be towards increasing outpatient diagnosis and treatment and diminishing inpatient care—the latter being predominantly surgical. The possibility of much of the teaching hospital's work being diverted to health centres must be envisaged, together with an increase in domiciliary medical care. All these factors must be taken into account in working out the educational plan. Our greatest need is for a teaching hospital to be based on the community, and where the community health services lead, the teaching must to a large extent follow. Only if we have our educational objectives firmly established and our plan clearly conceived can we lay down and preserve the foundation which we need.

Method of Reform

Obviously we cannot present a clear cut alternative to our present system of medical education, in the shape of a well defined, universally applicable curriculum which any and every medical school can adopt without difficulty.

I have said that any medical school in the country could at once take steps to work out its own curriculum on the basis of an educational plan. It should do so, and plan, as an integral part of it, the examinations and other forms of assessment required. It should define and choose the teaching team it would use. It should go further and devise means for the improvement in student-teacher contacts that is vital to the success of medical education. It should integrate the provisional-registration appointments with the rest of the curriculum. Lastly, it should set out to evaluate the results; for only by evaluation can adjustment be made, efficiency maintained, and progress secured.

All this can and must be done by the medical school. It cannot be done for it by any other body. And it can be done effectively only by democratic method—a representative planning committee. For even the best curriculum will become largely ineffectual unless the teachers not only picture it clearly in its entirety but are also aware of why it differs from the ideal plan.

Democratic methods are slow. The planning committee of a medical school could not make progress by occasional meetings. Hard work and much time are required. But the task is urgent and necessary because medical education can no longer safely be a by-product of other medical work.

No school will devote the time and concerted effort that are required unless it is given a strong stimulus to do so. And the stimulus is unlikely to act without the knowledge that the responsibility for making, and continuing to make, improvements rests upon the school itself.

Today the existence of minimal requirements which, though "recommended" by the General Medical Council have come to be accepted as regulations, together with rigid examinations, stand as a bar to those who wish to make changes. To many they are a disincentive to question what change is required, and by the remainder they can be used as an excuse.

"At this juncture," I quote from a recent memorandum of the Royal College of Physicians, "no detailed guidance by the General Medical Council could do so much good as a relaxation of their 'control by prescription,' which would encourage—even oblige—teaching authorities to consider their curricula afresh."

The Medical Act of 1950 gave the General Medical Council for the first time the power to inspect medical schools. Thus a new way of meeting their statutory obligations—that of inspection of the medical school (its curriculum and examination system being seen as a whole)—is now open to the council.

Freedom to experiment, and greater freedom to make improvements, could therefore be given to universities and licensing bodies if the council were now to lay down the broad aim of medical education but place on those authorities the responsibility for planning a satisfactory curriculum and giving a satisfactory education. Since nearly half the medical schools of the country are within one university, it is clearly essential that London University should not only set up a planning committee at the highest level but also should transmit the same freedom and stimulus to its twelve medical schools.

This, I am certain, is the first step which has to be taken in the reform of medical education. When it has been taken, however, we shall—more even than now—come up against the hard reality that facilities for teaching urgently need to be improved and new ones provided. I am quite sure that no medical school can meet these needs by its own unaided efforts. If it were possible to do so, much more would already have been done.

As I have shown, there are three main requirements—accommodation, teachers, and clinical facilities. The first demands that the highest priority must be given by the teaching hospitals of the National Health Service to providing the physical conditions necessary for medical education. The second demands arrangements between the Ministry of Health and the universities by which some at least of the clinical teachers can devote more time to teaching and research in the teaching hospitals, so that their work, for the health service and in private practice, is centred on the place where they are teaching. (If long term research is to continue and the needs of education be met, the universities must also increase the number of senior full time teachers.) The third requirement—the most serious of all—demands action by the Ministry of Health to promote the formation, especially in London, of teaching hospital groups, with the simultaneous establishment of regional consultant hospital centres. The teaching-hospital group must be such that it can give patients care of the highest standard (which involves specialisation), can undertake research, and can admit patients with acute and common conditions from the community around it. Its size and cohesion must be such that the influence of the non-clinical departments of the university can permeate the whole.

These requirements can be met only if there is, in all regions, an authoritative medical advisory committee, which will secure collaboration between teaching and regional board hospitals. The establishment of university health centres, with staff holding university appointments, is a new (but in my opinion essential) requirement, in which again the universities and the Ministry of Health must combine.

Freedom of medical schools to experiment is the first step in the reform of medical education, and provision of proper facilities is the second. It is not, however, the last. For medical education must never again be allowed to fall behind and lose touch with the advance of medicine and change in practice. Not only must it keep up to date; it must anticipate events, and not be the frustrated victim of their effects. Indeed, medical education must initiate trends. It alone can really ensure that the prevention of disease becomes increasingly the aim and results were rather surprising both patients felt better, the signs of myxœdema diminished, and the blood-cholesterol level fell, but the basal metabolic rate (B M R) remained unchanged at a low level These observations suggested that triac might differ qualitatively in its physiological effects from thyroxine and triiodothyronine However, experience with another case of myxœdema (Trotter 1955) showed that oral triac could raise the B M R in addition to relieving the symptoms of myxœdema and depressing the blood cholesterol level But subsequently it was found that, when this patient was treated with thyroxine, his blood-cholesterol level remained not much below its original level in spite of a greater increase in B M R than had been obtained with triac (fig 1) This again raised the possibility that the action of triac might differ from that of thyroxine, though it was clear that the difference could not be absolute But it remained possible that triac could have a relatively greater action on the blood cholesterol level than on the B M R, compared with thyroxine This possibility would not only be of theoretical interest but might also afford a means of lowering the blood cholesterol levels of euthyroid people without causing side effects

Some further results are now reported In 2 other cases of myxœdema an attempt was made to compare the effects of triac and of triiodothyronine on the B M R and the blood cholesterol levels Triac was also given to 3 euthyroid people to discover whether the blood-cholesterol level can be lowered without an increase in the B M R In addition, the short-term effect of triac on the blood cholesterol level was investigated in 15 other euthyroid people, but without estimation of the B M R, and 12 other comparable patients were similarly treated with triiodothyronine

Methods

A standard apparatus of Benedict-Roth type was used for B M R determinations, using Aub-Dubois standards The patients spent the previous night in hospital in all cases

The plasma cholesterol level was estimated by a modification of the method of Sackett (1925) The patients were fasting when the blood was taken Triac, triiodothyronine, and thyroxine were administered orally as tablets in twice daily doses

Material

Cases of Myxœdema

Case 1 has been described previously (Trotter 1955)

Case 2 —A man, aged 53, had noticed during the past two years increasing fatigue and slowness He had become sensitive to cold, and his voice had become hoarse and his skin rough On examination he showed much puffiness round his eyes and his skin was dry and thickened His thyroid gland was impalpable The uptake of radio iodine was 18% in twenty four hours and the initial B M R −31%

Case 3 —A woman aged 73 had been diagnosed, ten years previously as having pernicious anæmia, which responded well to liver injections and at the time of admission was well controlled by fortnightly injections of vitamin B_{12} Her hæmoglobin was 94% During the past two years she had become increasingly sensitive to cold and her hair was coming out Her voice was hoarse and her skin rough and dry Her thyroid gland was impalpable The uptake of radio iodine was 8% in twenty four hours and the initial B M R −32%

Case 4 —A woman aged 63 complained of swelling of the face and increased sensitivity to cold for the past six weeks Her hair had been coming out for the last few years Her face was bloated and her skin dry She had severe hypertension (blood pressure 210/150 mm Hg) and radiographs of her chest showed enlargement of the left ventricle Electrocardiography showed right bundle branch block The uptake of radio iodine was 7 5% of the dose at twenty four hours The plasma cholesterol level (determined before admission) was 406 mg per 100 ml and the initial B M R −30%

Euthyroid Patients

Case 5 —A man, aged 72, had had thyrotoxicosis in 19 This was treated by subtotal thyroidectomy There was subsequent recurrence of symptoms the thyroid gland was impalpable, and there was no clinical evidence of myxœdema In 1950 he started to get precordial pain on exertion and in 1953 he also developed typical intermittent claudication In 1951 his plasma cholesterol level was 360 mg per 100 ml Thyroxine up to 0 5 mg daily had no clinical effect and did not produce any definite change in the plasma cholesterol level In 1953 his plasma cholesterol level was 495 mg per 100 ml, he was not having any treatment at this time Before triac was started he could walk only slowly, being limited both by intermittent claudication and by anginal pain He was somewhat obese, though otherwise normal in appearance Radiography showed that his heart was normal in size Electrocardiography showed much depression of the ST segment in lead V_5 The uptake of radio iodine was 28% in twenty four hours and the initial B M R +7% and −6%

Case 6 —A man aged 57, had had coronary thrombosis in 1947 and in 1950, with electrocardiographic changes on both occasions In 1953 he was readmitted because of a sudden attack of precordial pain, but electrocardiography did not suggest that a further infarct had developed Since his first thrombosis he had been subject to precordial pain, both at rest and on exertion, but the description did not sound typical of anginal attacks There were no abnormal findings on physical examination, except that the blood pressure was 164/100 mm Hg Before the start of triac therapy the uptake of radio iodine was 10% and 11% in twenty four hours (measured on separate occasions) The low uptake could not be explained by any drugs he was taking He did not appear at all myxœdematous and the B M R before the start of treatment was −6%, −5%, and +1% (readings on separate days) and the plasma cholesterol level 269 mg per 100 ml

Case 7 —A man, aged 56 had been admitted fifteen months previously with a typical attack of coronary thrombosis and electrocardiographic changes characteristic of a recent anterior infarction Before triac was started his only symptom was mild breathlessness on exertion There were no abnormal physical findings Electrocardiography showed deeply inverted T waves in lead V_3 The uptake of radio iodine was 41% in twenty four hours and the initial B M R −10% and −12% The initial plasma cholesterol level was high (365 mg per 100 ml), but the absence of clinical signs and the normal uptake of radio iodine were considered to exclude myxœdema

The remaining euthyroid patients were all women with slight to moderate goitres without evidence of either thyrotoxicosis or myxœdema

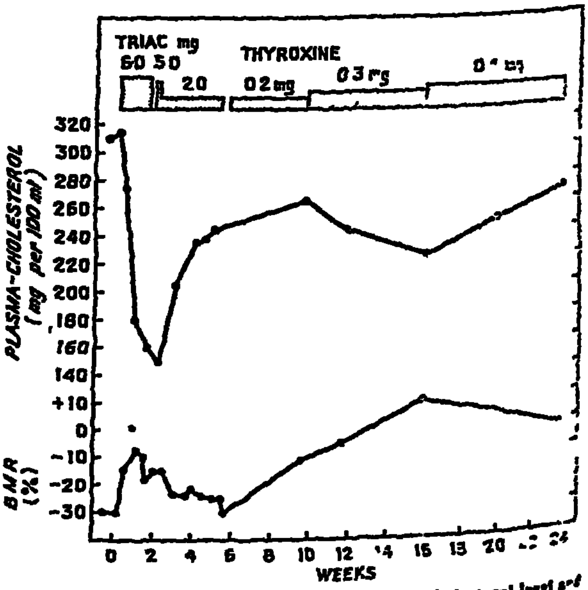

Fig 1—Effect of triac and of thyroxine on blood-cholesterol level and B M R in myxœdema

Method

The patients studied had either advanced pneumoconiosis or bronchitis and emphysema, and breathlessness prevented them from walking more than a few yards Some were inpatients at the time of the investigation The remainder were identified as having breathlessness grade 4 or 5 (Fletcher 1952) from the records of patients previously discharged from our ward, and they were invited to come in again for this investigation Some of the patients were found to benefit from chemotherapy, antispasmodics, postural drainage, or diuretics before investigation This reduced factors other than oxygen which might influence walking performance and improved the repeatability of the results If oxygen proved to be beneficial under these conditions it would be likely to be more rather than less effective under the conditions in which these patients normally exist

Exercise performance was assessed on a treadmill, the speed and slope of the belt being adjusted so that, breathing air, the man could walk for two minutes before stopping because of breathlessness A constant time, rather than a constant work load, was selected because the degree of activity producing breathlessness varied from one patient to another The period was chosen to reproduce conditions where a patient is repeatedly obliged to pause for breath on exertion In addition, the effect of oxygen in increasing the duration of maximal exercise in healthy people is not apparent unless the exercise is at least of this duration (Christensen et al 1934)

Once these conditions had been established, the walking time while the patient was breathing air and oxygen was determined, the gases (of composition unknown to the patient) being delivered through a humidifier to either a mask or a mouthpiece through a demand system operating at a low suction Each walk was continued until the patient chose to "take a spell" because of breathlessness, or for five minutes, whichever was the shorter time Five minutes was chosen because a man who can walk for this time without incapacitating breathlessness is likely to be able to continue longer, and his time of stopping may then be more influenced by fatigue or other factors

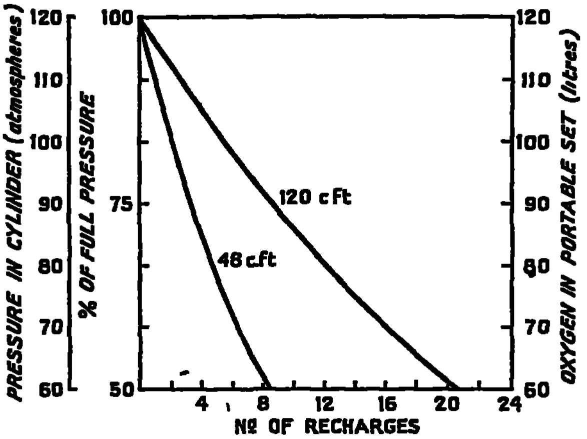

Fig 3—Relationship between number of recharges and pressure in charging cylinder

In some cases the arterial oxygen saturation was recorded with an ear oximeter previously calibrated against samples of arterial blood collected simultaneously The ventilation was measured on a low resistance gas-meter The portable oxygen sets were tested by some of the patients in hospital, and in a few cases they were lent for trial at home Visits were made to each patient's home at intervals of not longer than four weeks, in addition to weekly visits by their practitioners

Results

Effect of Oxygen in Increasing Exercise Ability

29 patients in clinical grades 4 or 5 were studied, 28 of them had been coalminers, and 18 had pneumoconiosis X ray category 2 or above on the International Classification (1950) (Cochrane et al 1951, Fletcher 1955) All these patients gave a history of chronic bronchitis and had emphysema and cor pulmonale 17 of them were admitted for treatment of acute exacerbations of their

TABLE I—MATERIAL AND RESULTS

Case no	Age (yr)	Diagnosis	Receiving oxygen at home	Walking ability (yd) between attacks (patient's estimate)	Admitted for series	Requiring treatment	M V V litres per min	Exercise ability: Treadmill setting: Speed (m p h)	Exercise ability: Treadmill setting: Slope (%)	Exercise ability: Walking time (sec): Air	Exercise ability: Walking time (sec): 100% oxygen
1	69	CB E	Yes	Nil	Yes	Yes		5/8	0	105	>300
2	65	CB F		Nil	Yes	Yes	16	1/2	0	105	130
3	55	CB Pnc (–/B 4/4)		25	Yes	Yes	22	1/4	0	100	105
4	64	CB Pnc (2/A 3/1)		40	Yes	No		1 3/8	10	128	283
5	49	CB Pnc (–/D 4/5)		100	No	Yes		1 1/2	5	105	285
6	64	CB Pnc (–/D 3/2)	Yes	25	Yes	No	14	1 1/	10	160	215
7	58	CB E Pnc (–/C 4/4)		Nil	No	Yes	27	5/8	0	148	>300
8	60	CB E Pnc (2/A 2/–)	Yes	12	No	Yes	32	1 1/	10	114	>300
9	62	CB Pnc (–/D 5/5)		3	No	Yes	33	1	10	132	>300
10	36	E	Yes	Nil	No	Yes	10	5/8	0	80	>300
11	55	CB		20	Yes	Yes	18	1/4	0	45	85
12	63	CB Pnc (–/D 4/3)	Yes	Nil	No	Yes	10	5/8	0	157	294
13	56	CB Pnc (3/B 1)	Yes	18	Yes	Yes	24	5/8	0	102	>300
14	66	CB E	Yes	About house	Yes	Yes		1 1/4	10	153	290
15	60	CB E Pnc (–/C 4/4)		50	Yes	No		1	7	107	>300
16	61	CB E		100	No	Yes		1 1/	10	105	250
17	70	CB		200	Yes	Yes	38	1/	0	165	170
18	53	CB Pnc (–/D 5/4)	Yes	?	No	Yes	14	3/4	5	120	138
19	64	CB		20	No	Yes	20	1/2	0	90	110
20	71	CB Pnc (–/D 4/6)	Yes	Few	No	Yes		1/4	0	100	195
21	50	CB Pnc (–/C 5/4)	Yes	Few	No	Yes	20	3/4	5	113	277
22	64	CB Pnc (3/B 5/2)	Yes	20	No	Yes	16	1 1/4	10	90	260
23	63	CB Pnc (–/D 3/3)	Yes	30	No	Yes	16	3/4	5	140	140
24	35	CB Pul fib A	Yes	25	No	Yes	14	1	2 1/2	110	>300
25	54	CB	Yes	500	Yes	Yes	12	1 1/2	7	85	270
26	66	CB	Yes	Nil	No	Yes		1 1/8	10	116	>300
27	66	CB	Yes	1760	Yes	Yes	19	2	10	125	245*
28	62	CB E	Yes	Nil	No	Yes	25	1/2	0	78	160
29	53	CB Pnc (3/D 5/3)		100	No	Yes	38	1	7	105	>300

* 30% oxygen
M V V maximum voluntary ventilation
CB, chronic bronchitis
E advanced emphysema
Pnc pneumoconiosis (X ray category in parentheses)
Pul fib pulmonary fibrosis
A infective asthma

TABLE I—EFFECT OF ADMINISTRATION OF THREE DRUGS IN DAILY DOSES FOR TWO WEEKS ON UPTAKE OF RADIO IODINE, MEASURED BY NECK/THIGH RATIO TWO HOURS AFTER TRACER DOSE

Drug	Dose (mg daily)	No. of patients	Initial neck/thigh ratio (mean ± S.E.)	Final neck/thigh ratio (mean ± S.E.)
Thyroxine	0·4	13	7·0 ± 1·02	2·7 ± 0·42
Triiodothyronine	0·04	4	8·2 ± 1·51	2·7 ± 0·45
Triiodothyronine	0·08	4	7·6 ± 2·42	2·4 ± 0·84
Triac	2·0	7	8·1 ± 1·89	1·5 ± 0·18
Triac	3·0	4	5·1 ± 0·83	2·3 ± 0·73
Triac	4·0	4	8·7 ± 1·76	1·7 ± 0·18
Controls (dummy tablets)		3	6·3 ± 2·07	6·1 ± 1·17

It seems therefore that in these 2 cases of myxœdema triac has about a seventy-fifth of the activity of triiodothyronine, as regards both elevation of the B.M.R. and depression of the blood-cholesterol level. Further comparisons of triac, triiodothyronine, and also thyroxine are being made in both these patients.

Euthyroid Patients

In the 3 euthyroid subjects whose B.M.R. were also measured the dose of triac was initially 1 mg daily and was raised gradually to 3 or 4 mg daily. This was done because it was anticipated that triac would inhibit the production of thyroid stimulating hormone by the pituitary gland. The patient's own thyroid would then cease to secrete and he would require larger doses of exogenous hormone to produce effects after the stores of endogenous hormone had been exhausted. In case 4 the initial radio iodine uptake of 28% was reduced to 3% after three weeks' treatment with triac (1 mg daily for a week followed by 2 mg daily for two weeks). In case 6 the initial uptake of 41% was reduced to 4% after six weeks' treatment (1 mg daily for four weeks followed by 2 mg daily for two weeks). In 15 cases of non-toxic goitre treated with triac for two weeks measurements of the ratio of neck count to thigh count at two hours after a tracer dose of radio iodine were available ("neck/thigh ratio"). These figures were comparable to those found by Morgans et al. (1952) in cases of non-toxic goitre treated with 0·4 mg of L-thyroxine for two weeks. In table I the two series have been compared, together with some results in comparable cases treated with two different dosages of triiodothyronine. It will be seen that the degree of inhibition obtained with 2–4 mg of triac daily is at least as large as with 0·40 mg of thyroxine or 0·04–0·08 mg of triiodothyronine. This suggests at first sight that triac is much more potent (relative to triiodothyronine) than appeared from the effects of the two drugs on the blood-cholesterol level and the B.M.R. in the 2 cases of myxœdema; but in interpreting these figures one must take account of the possibility that much of the iodine contained in triac may be released sooner or later as iodide. Although the amount of iodide released by 0·4 mg of thyroxine is insufficient to affect the radio iodine uptake (Morgans et al. 1952), the amount released by 2 mg of triac might well depress the uptake to some extent. Nevertheless it seems reasonable to assume that at least part of the decrease in uptake is attributable to the inhibition of production of thyroid stimulating hormone because such inhibition has been shown in animals (Pitt-Rivers 1953). If this is so, it would be expected that the effects of a constant dose of triac on the blood cholesterol level and metabolism would be greatest when administration is first started, and would decrease progressively as the patient's own contribution of thyroid hormone declines. This view is supported by observations on the blood cholesterol levels of 3 patients with non-toxic goitre, treated for up to ten weeks with a constant dose of 2 mg of triac daily (fig. 6). The blood cholesterol levels were initially depressed but gradually reverted towards their original levels.

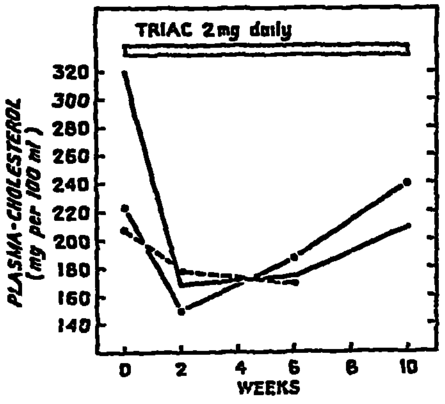

Fig. 6—Effect of constant dose of triac 1 mg twice daily on blood-cholesterol levels in 3 euthyroid patients.

The results obtained by a gradual increase in triac dosage are shown in figs. 7–9 (cases 5–7). In all 3 cases the blood cholesterol level fell gradually over months. In case 5 (fig. 7) the B.M.R. rose slightly when the dose was raised from 2 to 3 mg daily but it subsided after a few weeks without a change of dose. This minor rise of the B.M.R. (maximum +8%) did not appear to inconvenience the patient although he has severe angina of effort. Electrocardiography on six occasions while he was taking triac showed no significant change. The small fluctuations in the B.M.R. observed with cases 6 and 7 were not considered to be significant and were not associated with any change in symptoms. Pulse-rate and blood pressure did not alter significantly in any of the 3 patients. Their body weights fell by 2–5 lb. over the period indicated in the charts.

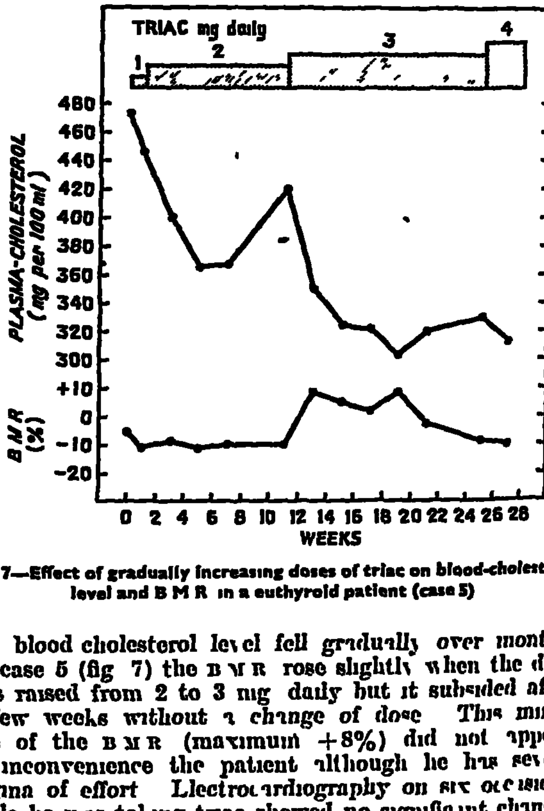

Fig. 7—Effect of gradually increasing doses of triac on blood-cholesterol level and B.M.R. in a euthyroid patient (case 5).

Triac was also given for two weeks to 15 women with small non-toxic goitres. The plasma cholesterol level was estimated in the fasting state at the beginning and end of the two weeks. 12 similar patients were treated for the same length of time with triiodothyronine in doses of 0·04 and 0·08 mg daily. In addition, 4 similar patients were given dummy tablets for two weeks. The results are shown in table II. It will be seen that doses of 2, 3, or 4 mg of triac daily depressed the plasma cholesterol level by about 26%. All 15 patients treated those of the first experiment in suggesting that the breathing of 30% oxygen instead of air significantly increases exercise performance. With higher oxygen concentrations there was a further increase, but, since the patients were then often able to walk until stopped at the end of five minutes (or five and a half minutes in case 7 *), the relative value of 50% and 100% oxygen could not be inferred directly. However, the exercise ventilations while breathing these two concentrations of oxygen were almost identical (mean 22.3 and 21.9 litres a minute), which suggested that the two gases were equally effective.

Increasing the oxygen flow from 2 to 4 litres a minute when an oxygen mask was used also increased exercise performance. However, the walking distance of the 1st patient, breathing 2 litres of oxygen a minute through a mask of the B.L.B. type, was apparently less, and that of the second 2 patients, breathing 3 litres of oxygen a minute through a mouthpiece adjusted to have the volume and flow characteristics of a mask, was significantly less, than that achieved while breathing 30% oxygen. The calculated average inspired oxygen concentrations were similar, and oximeter readings indicated that the blood was as effectively oxygenated. We thought that the difference was caused by the respiratory embarrassment produced by the accumulation of carbon dioxide in the rebreathing bag. Support for this view was obtained by inserting a valve in the neck of the bag. This reduced the ventilation on average by 4 litres a minute in both healthy people and patients with chronic lung disease at rest and during exercise (Cotes and Merrick 1956).

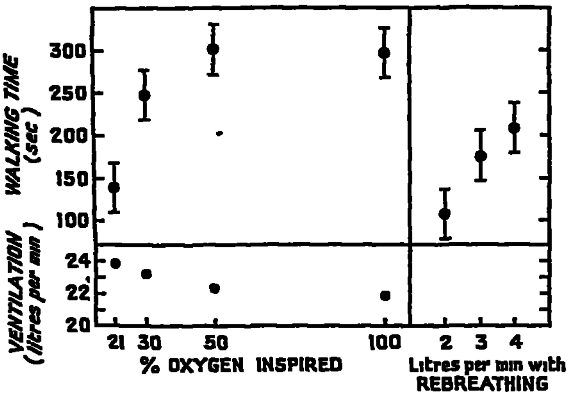

Fig 5—Effect of oxygen on walking time (cases 4 and 7)

The relative effectiveness of air, 30% and 50% oxygen in nitrogen, and of 3 litres a minute fed into a modified mouthpiece with and without rebreathing was assessed in 3 patients (cases 8, 12, and 26). The results have been combined in fig 6. They confirm that these patients can walk further breathing 30% oxygen than breathing air. 30% oxygen was, however, significantly less effective than 50% oxygen in increasing exercise ability, and the exercise ventilation was in every case higher when the patient was breathing the lower oxygen concentration. 3 litres of oxygen a minute through a mask with a check valve in the neck of the bag enabled the patients to walk significantly further than under the same conditions but without the valve; however, even after this modification, oxygen delivered to a mask proved rather less effective than the corresponding oxygen mixture.

We conclude that the substitution of 30% oxygen for inspired air much increases exercise ability in some patients. With 50% oxygen there is a further increase but small in proportion to the increased amount of oxygen required. The effect of 30% oxygen can be reproduced by 4 litres of oxygen a minute delivered to a well fitting oxygen mask with an oxygen reservoir bag and check valve to prevent rebreathing. This combination is the optimum for a portable oxygen supply for use in these circumstances.

TABLE III—ESTIMATED COST OF MAINTAINING THE ALVEOLAR OXYGEN CONCENTRATION AT 35% FOR A WEEK

—	Oxygen flow (litres/min.)	Cost per week		
		Equipment (pence)	Oxygen (pence)	Total (£)
Nasal spectacles	4.5	5.3	821	3.4
Oxygen mask	2.0	6.3	365	1.5
Disposable mask	2.5	15.0	456	2.0
Oxygen tent (hired)	6.0 *	1260.0	1095	9.8
Domiciliary set (N.H.S.)	2.5	136.0	1692	7.6

* Including an allowance for flushing

Portable oxygen Therapy

Exercise ability was much increased by breathing oxygen in 22 of the 29 patients in the series, and we think that, if temperament and other factors are taken into account, about half might benefit by portable oxygen therapy. 4 patients (cases 8, 12, 21, and 26) have been fitted with oxygen masks incorporating a non-return valve to prevent rebreathing and have been provided with oxygen sets adjusted to deliver 4 litres of oxygen a minute. In each case a daily charge of oxygen has enabled a man, previously virtually immobilised by breathlessness, to move about the house and to walk out to sit in the garden. No adverse effects have so far been observed. These preliminary trials are continuing. An extended trial of portable oxygen equipment might be worth while when the improved equipment with detachable oxygen bottles becomes available.

Domiciliary Oxygen Therapy

More oxygen is supplied for home use than is probably generally realised. During 1955 a third of all chemists in Wales and Monmouthshire (population 2,600,000) were asked for oxygen or oxygen equipment, which was supplied on prescription to 860 patients. The consumption in April that year amounted to 750 of the 48 c.ft. cylinders. On April 30, 134 patients were using oxygen, of whom 83 had done so for more than three months and 10 for more than three years.

The quantity of oxygen used at home is small in comparison with that supplied to hospitals, however, litre for litre, domiciliary oxygen is at present four times as expensive (table III) and contributes appreciably towards the total oxygen cost. The expense of distributing domiciliary oxygen might be reduced by the substi-

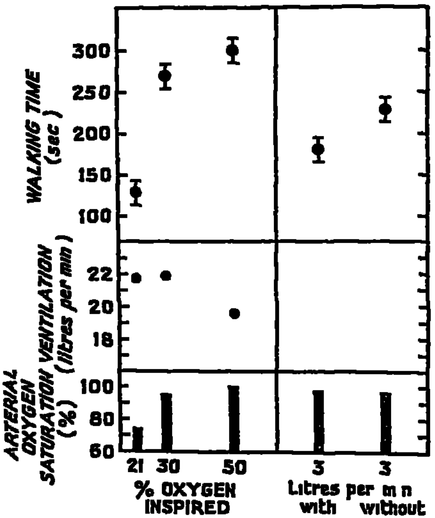

Fig 6—Effect of oxygen on walking time (cases 8, 12, and 26)

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* The statistical analysis is somewhat impaired by this deviation from procedure, but the conclusions are unlikely to be invalidated.

THE PHYSIOLOGICAL ACTIVITY OF TETRAIODOTHYROACETIC ACID

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THE acetic acid analogues of thyroxine and triiodothyronine differ from the circulating thyroid hormones in that the alanine side chain is replaced by acetic acid. The synthesis of tetraiodothyroacetic acid (tetrac) was described by Harington and Pitt-Rivers (1952). Pitt-Rivers (1953) compared the activity of tetrac and triac (triiodothyroacetic acid) in the prevention of thiouracil induced goitres in rats and found that both possessed about a tenth of the activity of L-triiodothyronine. Thibault and Pitt-Rivers (1955) found that the acetic acid analogues of both thyroxine and triiodothyronine were effective in raising the oxygen consumption of rat-kidney slices in vitro without a preincubation period, and that a single dose of tetrac raised the basal metabolic rate (B M R) of thyroidectomised rats within two hours, the effect wearing off after four hours. Lerman and Pitt Rivers (1955) described the effect in myxœdema of triac given daily by intravenous injection. Clinical improvement was accompanied by reduction in weight and plasma-cholesterol levels but no significant change in B M R. Trotter (1955) investigated the effect of triac in myxœdema and observed a clinical remission, with return of the B M R and plasma-cholesterol to normal values on a daily oral dose of 6 mg.

It was therefore of interest to determine the potency of tetrac in myxœdema, with particular emphasis on its effect on the plasma cholesterol level. A patient with primary untreated myxœdema was selected as a suitable subject for a therapeutic trial. A euthyroid volunteer was given tetrac in about the same dosage as the patient.

Methods

Both the patient and the control were given tetrac orally as an aqueous solution or in a capsule (figs 1 and 2). The solution was prepared by dissolving tetrac in sodium hydroxide (375 mg per ml of N NaOH), water being added to a final concentration of 4 mg per 30 ml. The solution was kept refrigerated. The 2 mg gelatin capsules were made up with a carbohydrate base. The B M R was measured with a Benedict-Roth apparatus, the results being expressed as a percentage of average normal values according to Robertson and Reid (1952) standards. Serum cholesterol was estimated by a modification of the method of Zlatkis et al (1953). The therapeutic effect in myxœdema was assessed by clinical observation, the daily weight record, the plasma cholesterol level, and the B M R.

Case-report

A woman, aged 62, was admitted to hospital, after a street accident, with mild concussion and fractures of both forearms. After a month in hospital she was discharged to a convalescent home. During convalescence it was noted that she was myxœdematous, and she was admitted to hospital for investigation and treatment. She gave a history of rheumatic fever at the age of 19 and had been admitted to hospital in 1948 with mild congestive failure, which responded to the usual measures. Aortic stenosis and incompetence due to rheumatic carditis were then diagnosed. After the accident she developed intolerance of cold, lethargy, postural vertigo, constipation, dryness of the skin, muscular cramps, impairment of memory, and inability to concentrate. Her daughter noticed an alteration in her voice and mental retardation. She may have been hypothyroid for some time but it appeared that her condition had deteriorated considerably since the accident.

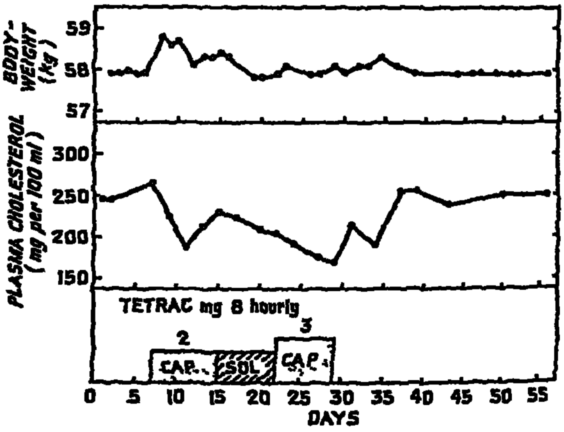

Fig 2—Effect of tetrac on weight and plasma cholesterol level in a euthyroid subject.

On admission she was lethargic and had a pale waxy complexion, thin hair, obvious puffiness of the eyelids, a deep voice, and dry scaly skin. Her thyroid gland was impalpable. There was evidence of aortic stenosis and incompetence but no sign of congestive failure except slight œdema of the ankles.

Investigations.—Chest radiography showed no cardiac enlargement. The initial B M R was −17%. The serum cholesterol level was 510 mg per 100 ml. Electrocardiography showed ischæmic changes but no evidence of myxœdema. Radio-iodine studies of thyroid function showed no appreciable thyroid uptake at 48 hours, 90% of the dose being excreted in the first 48 hours. No protein-bound radio-iodine was detected in the plasma. Serum electrolytes were within normal limits. The urinary excretion of 17-ketosteroids was 17 mg per 24 hours. The amount of follicle-stimulating hormone was greater than 48 mouse-units in 48 hours.

Response to Treatment.—Treatment with tetrac was started in a dosage of 1 mg 8-hourly (fig 1). No appreciable change was detected after 48 hours, when the dose was increased to 2 mg 8-hourly. After 2-3 days on the larger dosage there was obvious improvement, which was maintained for 2 weeks, by which

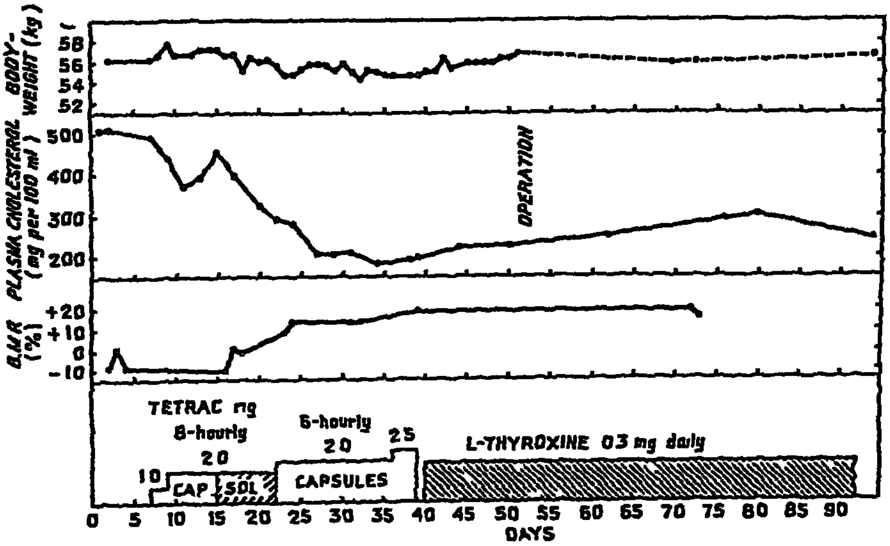

Fig 1—Effect of tetrac on weight, plasma-cholesterol level, and B M R in myxœdema

Selection of Patients

Since 1951 records have been kept by the joint consultative clinic of the Brompton Hospital and the Royal Marsden Hospital of all patients with a bronchial carcinoma attending the two hospitals, whether or not they were treated. The initial selection of patients for radiotherapy, once surgical treatment had been excluded, was made by the physicians and surgeons of the hospitals. The selected patients were, with few exceptions, referred to the clinic, where the final decision on treatment was made. Selection has therefore not been according to a single uniform policy. Radiotherapy was usually advised to alleviate symptoms rather than to prolong life. But many factors that cannot satisfactorily be recorded influence a decision on treatment, and some patients with few or no symptoms were treated, whereas others with symptoms were not. Although it is inevitable that the group of treated patients should contain fewer in a less advanced stage of the disease than the untreated group, the methods of selection at these hospitals have perhaps tended to reduce the difference between the groups.

Three-quarters of the treated patients in the present investigation were treated at the Royal Marsden Hospital. The length of treatment and the dose of irradiation were largely governed by the patient's general condition and the symptomatic response. It seems likely that in the whole series the more robust tended to get larger doses of irradiation.

Construction of Groups

The patients were selected from the 996 with bronchial carcinoma seen at the two hospitals in 1951–53, 221 of these were treated surgically, 321 were treated by radiotherapy, and 454 received no treatment likely materially to prolong life.

Exclusions

Patients with extrathoracic metastases at the time of diagnosis live for shorter periods than those without. Since so few such patients were treated by radiotherapy, their inclusion in the series would, of course, heavily prejudice the untreated groups. All with evidence of extrathoracic metastases at the time their treatment was decided have therefore been excluded. A patient must live for at least a month after first attending hospital if he is to receive a dose of radiotherapy sufficiently large materially to alter the course of the disease, for it is unlikely that the necessary investigations and arrangements can be made and the treatment given in a shorter time than this. To include among the untreated patients those who died within a month would bias the group, and these also have been excluded.

The groups for comparison were therefore taken from those patients without evidence of extrathoracic metastases when the treatment was decided, who lived for at least a month after first attending hospital, and in whom the time of the first appearance of symptoms was known. 213 patients treated by radiotherapy with an estimated dose delivered at the site of the primary tumour greater than 1000r fulfilled these requirements, as did 251 who received neither surgical treatment nor radiotherapy.

The after-history of 9 of these 464 is unknown. The remaining 455 were followed for two years from first attending hospital or until earlier death. To simplify the comparisons the few incompletely followed up have been excluded. This is thought to be justified because including them as dead at the time they were last heard of does in fact alter the survival experience of the groups very little, and the conclusions drawn from the comparisons are unchanged. There are therefore 207 treated by radiotherapy to be compared with 248 untreated.

TABLE I—THE TREATED AND UNTREATED GROUPS

—	Number of patients		
	No mediastinal metastases	Mediastinal metastases	Total
1000–3900r	49	65	114
Untreated	148	100	248
4000r or more	54	39	93
Untreated *	126	89	215

* 33 of the 248 untreated patients died within 2 months of first attending hospital, they have been excluded from the untreated group for comparison with treated patients having 4000r or more.

To receive a tumour dose of more than 4000r the patients must be under treatment for about four to six weeks. No patient who dies within two months of coming to hospital is likely, therefore, to have been able to receive such a dose of irradiation. 33 of the 248 untreated patients died within this period, 215 living for more than two months. The survival of the patients who received 4000r or more has therefore been compared with the survival of these 215.

Subgroups

The 207 patients in the radiotherapy group have been divided into two subgroups. 114 patients who received an estimated tumour dose of 1000–3900r, and 93 patients who received a dose of 4000r or more.

One group of patients might live longer than another because it contains fewer with regional node metastases and not because the treatment is different. The groups were therefore further divided into those with and those without evidence of mediastinal metastases at the time of diagnosis.

There are therefore four pairs of treated and untreated groups to be compared (table I).

Comparison of Groups

The groups were compared as regards the known distribution of histological types, the ages of the patients, and the durations of illness before diagnosis.

Only small and clearly unimportant differences were found in the distribution of histological types of tumour and ages of the patients between the groups receiving 1000–3900r and the corresponding untreated groups. The survival of a group containing a large proportion of patients with a duration of symptoms of about six months before diagnosis is likely to be shorter than that of a group with fewer such patients (Bignall 1955).

There were only slight and unimportant differences in the distribution of the durations of symptoms, and the proportions with symptoms for three to eleven months were almost identical in treated and untreated. In the untreated group there were, however, more in whom the diagnosis might be doubted. For instance, there was neither histological, thoracotomy, or necropsy confirmation of cancer nor knowledge of metastases throughout the illness in 66 (45%) of the untreated compared with only 11 (22%) of the corresponding radiotherapy groups. 2 of the 66 and 1 of the 11 patients were still alive when last heard of.

A comparison of those treated with 4000r or more with the corresponding untreated groups also shows only minor differences. There was neither histological thoracotomy, or necropsy confirmation nor knowledge of metastases in 54 (43%) of the untreated and 11 (20%) of the treated. 2 of the 54 and 3 of the 11 patients were still alive when last heard of.

In these selected groups there were therefore no important differences in the distribution of factors known to influence survival. In spite of this the untreated

CARDIAC PAIN FROM ŒSOPHAGEAL LESIONS

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In his St Cyres lecture Dr William Evans drew attention to the association between œsophageal contraction of an abnormal type and cardiac pain (Evans 1952) He found that pain suggesting coronary disease was present in 332 patients, all of whom had a normal electrocardiogram They were contrasted with an adequate control series He found that in some cases the pain could mimic that of angina of effort and in others that of myocardial infarction Two of his points, particularly worthy of clinical comment, were

(1) The frequency with which such patients summoned medical aid, and the corresponding frequency of the diagnosis of coronary thrombosis, for which morphine was given

(2) That in 83 cases there were long intervals of freedom from pain—in 34 cases lasting up to two years, and in 49 for more than two years

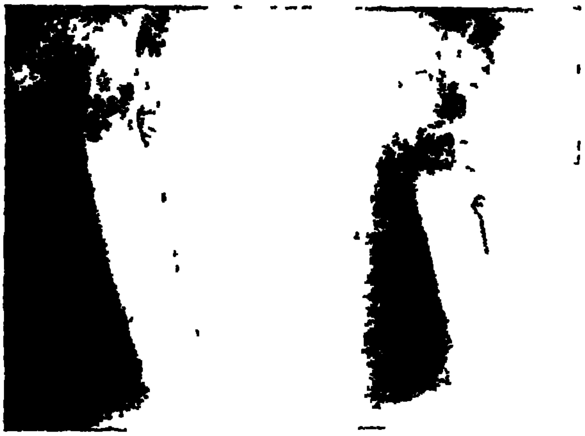

Fig 1—Case 1 diverticulum in middle third of œsophagus

Other observers have described cases in which pain suggesting coronary disease was present, the apparent cause being an abnormality of the œsophagus

Moersch and Camp (1934) found pain characteristic of angina pectoris in 2 patients with œsophageal spasm

Wolferth and Edeiken (1942) believed that many of the seizures thought to be due to angina pectoris were really caused by œsophageal spasm

Harrison (1945) reported 35 cases of œsophageal disease in which the pain resembled that of coronary disease, but in these patients he did not notice a relation between physical exercise and pain

Many other observers have stated that hiatus hernia can produce chest pain similar to that of coronary disease (Jackson and Jackson 1936, Jones 1941, Jones and Chapman 1942 Herman and Singer 1946)

The following is an account of two patients with organic œsophageal abnormalities who suffered from pain In one the pain resembled that of myocardial infarction, in the other it resembled angina of effort

Case-reports

Case 1 —A man aged 54 was admitted to St Bartholomew's Hospital after having a sudden attack of pain in the chest at the level of the upper part of the sternum whence it radiated down the left arm and up into the neck

On admission he was given morphine which relieved the pain He was not shocked His blood pressure was 120 80 mm Hg There was no evidence of increased venous pressure in the neck The heart sounds were normal and nothing abnormal was found in the abdominal organs, limbs, and nervous system

Treatment and Progress —Later in the day he had another exactly similar, attack, and two days later he had several more All were relieved by morphine His white cell count three days after the first attack was 5500 per c mm and erythrocyte sedimentation rate (E S R) 25 mm in the first hour (Westergren) The electrocardiogram was normal except for slight changes in the Q R S in lead VL only but such changes were thought to be possibly within normal postural limits He was discharged and returned to his work, and he remained perfectly well for two years

Readmission —He was then admitted as an emergency case, having again developed severe gripping retrosternal pain radiating to the left side of the thorax He was perspiring nauseated, and shocked Again no noteworthy abnormality was found in the heart or elsewhere The blood pressure was 110/95 The E S R was 16 mm in one hour and remained raised for two weeks

Treatment and Course —During this second admission he had seven further attacks in eight days, all of them requiring relief with amidone They lasted an hour or more—considerably longer than the average attack of anginal pain The electrocardiogram still remained within normal limits except for the very minor changes previously noted in lead VL it showed no evidence of myocardial infarction in the standard leads, the unipolar limb leads, or the unipolar precordial leads V_1, V_3, V_5, V_7

Diagnosis —Although on his first admission the diagnosis had been coronary thrombosis, suspicion was aroused during the second admission by the normal electrocardiogram and by the normal size and shape of the heart—which was, indeed small for his physique The transverse diameters of the heart and thorax respectively on the 6 foot X ray film were 10 5 cm and 25 5 cm

In view of these facts, and because it had been noticed that from time to time he swallowed air, the œsophagus became suspect On radiography a diverticulum of its middle third was found (fig 1) The stomach and duodenum were normal

The family history and the past history contained no point which appeared to be of importance

Case 2 —A man, aged 67, had for three or four years suffered from pain in the chest, radiating to both sides but not to the arms or to the neck It was induced by hurrying and by climbing hills or stairs and it was not associated with shortness of breath It lasted two or three minutes and was generally more severe in the morning Clinically it was strongly suggestive of typical angina of effort due to myocardial ischæmia from coronary disease

On examination his heart rate was 86, the rhythm being regular, and his blood pressure was 184/100 The heart lungs, and abdominal organs were clinically normal Radiologically the heart was small (10 4 cm in diameter) and vertical, the lung fields suggested emphysema The electrocardiogram, after considerable exercise, remained normal in the standard leads, the unipolar limb leads, and the unipolar precordial leads V_1, V_3, V_5, V_7

On radiography the œsophagus showed a sliding hiatus hernia (fig 2) but with very little gastro œsophageal reflux

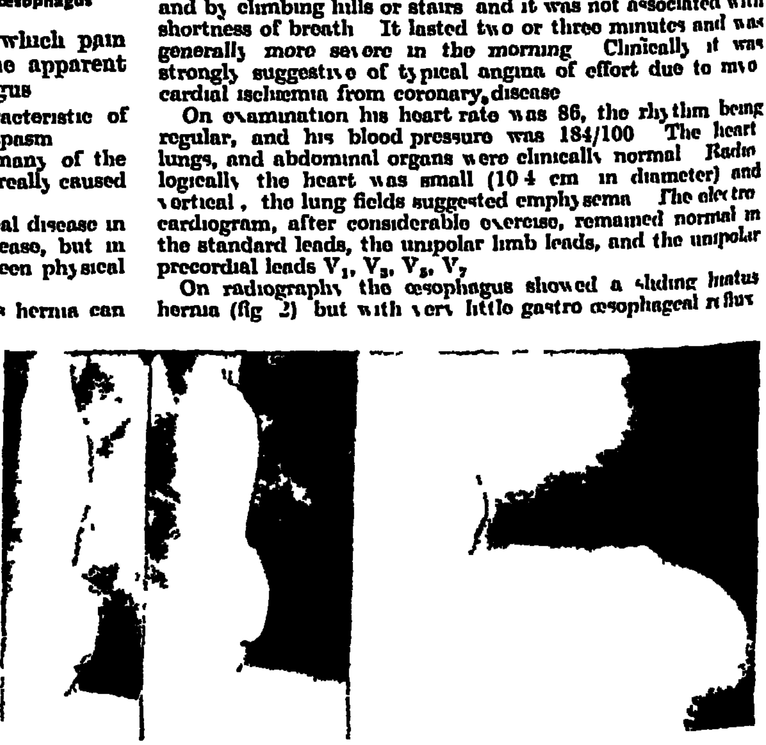

Fig 2—Case 2 hiatus hernia

futile to make direct comparisons Bloch and Bogardus (1940), on the other hand treated 88 patients and found that duration of life from the first symptom was the same as in untreated patients, and Graham et al (1935) stated that radiotherapy does not prolong life

Craver (1940) recorded longer survival in those treated with the larger dose of irradiation Brown (1952) found that 6 of 39 patients treated with 2000–3000r survived nine months, compared with 39 of 92 treated with 4000–5000r, and concluded that the survival-rate was definitely improved when doses of over 4000r were given But Adelman (1952), who also noted increasing mean survival with increasing dose of irradiation, pointed out that patients receiving high doses are generally in a less advanced stage of cancer and would be expected to live longer without any treatment

There is, it appears, no conclusive evidence that radiotherapy prolongs life or that large doses have a greater effect on survival than small doses

The differences observed in the present investigation may have been due to chance sampling variations differences in the composition of the groups, or the effect of radiotherapy The treated and untreated groups were undoubtedly dissimilar In spite of the attempt to select groups as near as possible alike, the untreated groups probably contained more patients in an advanced stage of the disease For instance, in the case of those without metastases who received 4000r or more, only 6 (11%) had been judged to be in too poor general condition to withstand lung resection, but in the untreated group with which they were compared there were 34 (27%) such patients However, if these more ill patients are excluded from both groups, the differences in survival are little changed, 38% of the 48 remaining in the treated group lived a year and 17% two years, compared with 27% and 6% of the 92 untreated

The differences between treated and untreated might have been partly due to there being more patients in the untreated group likely to die in a short time There would then be more untreated patients dying within six months of first attending hospital This was indeed found But there was a large excess, and it is doubtful whether it was entirely due to selection For instance, in the group in which the difference was greatest—those without metastases treated with 4000r or more—as much as 30% of the 126 untreated patients must be assumed to have been too advanced for inclusion in the group to bring the pattern of survival close to that of the treated patients On the other hand, such an explanation of the differences is certainly possible, because, if 38 (30%) are excluded from the number who died in the first six months, the proportions of the remaining 88 dying in the four six-month periods up to two years would be 24%, 47%, 19%, and 7%—proportions remarkably similar to those observed in the corresponding treated patients 22%, 43%, 15%, and 4%

The observed differences between treated and untreated groups could have been due entirely to the dissimilarity of the groups and random sampling variations, without radiotherapy having had any effect, beneficial or deleterious, but it seems improbable The differences between treated and untreated in the patterns of survival are greater in those without mediastinal metastases than in those with them In the groups treated with small doses of irradiation the patterns were indeed almost identical in those with metastases, although there were noticeable differences in those without But there seems to be no reason to believe that more patients with advanced disease were selected for treatment from those with metastases than from those without Selection probably operated to about the same extent in both groups Some of the differences observed might therefore have been due to the treatment, and it seems reasonable to suppose that, if the course of the disease is changed at all, it will be altered least in patients who already have intrathoracic metastases

There seems to be suggestive but by no means conclusive evidence that radiotherapy prolonged the life of some patients in this series, but, even if life were prolonged, it is highly unlikely that the larger doses of radiotherapy given to the most favourable patients—those without manifest mediastinal metastases—caused an increase of as much as 10% in the proportion surviving a year after first attending hospital or 5% in those living for two years

This report is not concerned with whether a probable increase of the order suggested justifies greater or less use of radiotherapy in bronchial carcinoma, nor with the effects of treatment on the patient's symptoms or his peace of mind

Summary

The course of the disease has been studied in 455 patients with bronchial carcinoma 207 were treated by radiotherapy, 114 receiving an estimated tumour dose of 1000–3900r and 93 4000r or more Their survival is compared with that of 248 who received no treatment likely to prolong life

The groups were selected to be as far as possible alike in the factors known to influence survival No patient was known to have extrathoracic metastases when the decision on treatment was made

The greatest difference between treated and untreated in the duration of life from first attending hospital was found in those without mediastinal metastases treated with 4000r or more 35% lived a year and 15% two years, compared with 24% and 6% of the untreated

In the patients with mediastinal metastases the differences were less, and the pattern of survival of those treated with 1000–3900r was almost identical with that of the corresponding untreated group

There is suggestive evidence that the differences were not due entirely to selection and random-sampling variations but were contributed to by the radiotherapy

In this series of patients it is unlikely that radiotherapy caused an increase of as much as 10% in the proportion surviving a year after diagnosis or 5% in those living two years, even in the most favourable cases treated with higher doses

I am indebted to the medical committees of the Brompton Hospital and the Royal Marsden Hospital for permission to publish this report which records part of the work of the joint consultative clinic of the two hospitals The keeping of records and tracing of patients was largely done by Mrs I Appleby of the secretarial staff of the Institute of Diseases of the Chest I am grateful to Mr P M Payne statistician to the Royal Marsden Hospital for his advice

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easy access to a clinic should refer to one of the original papers, which are listed in the book or can be found from Dr Fraser's paper This caution applies particularly in one or two instances where Dr Reed has used a method of arriving at the risks which is of doubtful validity, and has led him to quote too high a risk—for example, for harelip In this instance a better estimate is given in the appendix But in general the book is stimulating and should well fulfil its purpose of indicating when advice on genetic risks can be helpful to parents

Medical History of the Second World War

Royal Air Force Medical Services Vol II Commands Edited by Squadron Leader S C Rexford-Welch, M R C S R A F H M Stationery Office 1955 Pp 703 75s

THIS volume describes clearly, and at times dramatically, how wide was the range of duty which fell to the medical branch of the R A F The estimation of flying stress and its relation to courage, the choice of rations for crews on long flights or in escape dinghies, the supervision of the early parachute troops, the industrial hazards of some of the maintenance work—these were some of the problems thrust on doctors as an addition to routine public health and care of the sick The story is extremely well set out, with detail enough to present a tale worth reading, and it does not shirk the difficult matter of the relationship of the medical officer with the executive officer

Planning had to be, and was, adjusted to unforeseen changes in the pattern of warfare The accounts of the expeditions to the Azores and to Iceland are both fully elaborated both contain lessons of general application to any military exploit, whatever the weapons used Though the book is long, it is hard to see how it could have been made much shorter without losing its value as a textbook and guide for doctors who choose or are called on to undertake medical duties in a fighting service

The Cornea

CHARLES I THOMAS, M D, associate clinical professor of ophthalmology, department of surgery, Western Reserve University School of Medicine Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1955 Pp 1318 £10 16s

MUCH industry ingenuity and thought have gone into this comprehensive book It is an admirable achievement to correlate, as far as is at present possible, such a large mass of scientific and clinical data There must be little in the enormous literature on the subject of the cornea which has escaped attention

For the scientist there is particular interest in the chapters dealing with embryology, anatomy, physiology, and pathology of the cornea, and for the clinician there is valuable instruction in the chapters on diseases of the cornea The difficult subject of corneal dystrophies is especially well treated

The author has not made clear Paufique's technique for dealing with a broad synechia before a corneal transplant The reader is left with the impression that this is done at the same time as the keratoplasty and by using an 8-9 mm trephine, which is not the case Not all surgeons would agree with the use of ointment in the conjunctival sac at the end of a penetrating corneal transplant operation and many surgeons would prepare the donor material before the recipient site Most of the illustrations photographs artist's drawings, and diagrams are excellent, but a few photographs are indistinct

This is a book to which all ophthalmologists and those interested in the basic sciences of ophthalmology will wish to refer

Heaven and Hell

ALDOUS HUXLEY London Chatto & Windus 1956 Pp 88 7s 6d

TWO years ago in *The Doors of Perception*, Aldous Huxley described his subjective experiences after taking a dose of mescaline He was an experimental subject who was exceptionally well qualified to communicate the nuances of this peculiar intoxication, which is of medical interest because of its relationship with other forms of hallucinosis He was, if anything, too eloquent His insistence on the transcendent qualities of his perceptions became in the end reminiscent of a neurotic patient's exaggeration of his symptoms Finally, it seemed that it was not the effects of mescaline but rather the exquisite sensibilities of the author that were being demonstrated to the reader

In this sequel to that essay, he offers his reflections upon the psychological implications of the mescaline experience It is soon made plain that his temperament is antipathetic to any scientific assessment of the phenomena Instead, speculation and metaphor are interwoven with fragments of physiological data in order to construct a plausible fiction, in a manner reminiscent of D H Lawrence's *Fantasia of the Unconscious* Systematic observation and verification are alien to this approach, and yet he does throw out perceptive insights such as "Colour turns out to be a kind of touchstone of reality"

As a contribution to the phenomenological study of the *fantastica*, this essay must itself be regarded as a potent stimulant—to be taken with a pinch of nicotinic acid

Progress in Clinical Obstetrics and Gynæcology

T L T LEWIS F R C S, M R C O G, obstetric surgeon, Guy's Hospital, surgeon, Queen Charlotte's Maternity Hospital London J & A Churchill 1956 Pp 594 55s

WRITTEN for the specialist who has not been able to keep up with the vast literature, and for the postgraduate student who is reading for the M R C O G examination, this book tackles many difficult and debatable matters

For example, there are chapters on congenital malformation and rubella, postmaturity, postpartum hæmorrhage and the management of the third stage, and of afibrinogenæmia and amniotic fluid embolism In the gynæcological section Mr Lewis deals among other things, with stress incontinence, venous thrombosis and pulmonary embolism, cytology in uterine cancer, and pelvic exenteration The subjects have been well chosen, and each is thoroughly discussed

The author says he has "tried to present the evidence without prejudice before drawing conclusions," and he has succeeded admirably His book is well written and contains much wisdom

Final Contributions to the Problems and Methods of Psycho-analysis

SANDOR FERENCZI M D Editor MICHAEL BALINT, M D, PH D, M SC Translators ERIC MOSBACHER and others London Hogarth Press and the Institute of Psycho Analysis 1955 Pp 447 30s

PSYCHO-ANALYSTS are tireless in their bibliographical labours they gather, and if necessary translate, the whole corpus of published writings by the notable pioneers This is the third volume of Ferenczi's literary remains There is a hint in the preface that his scientific diary and the correspondence between him and Freud over a period of 25 years are also to be issued in due course The papers here presented include those written between 1926 and his death in 1933, and various notes, fragments and minor articles The most interesting are those written after 1927 in which he put forward his heterodox proposals about relaxation and indulgence (*Nachgebigkeit*) in therapeutic technique There are throughout the volume and especially in the fragmentary notes, intimations of Ferenczi's intuitive, fertile and sometimes startling approach to the problems that he saw in psycho analysis The book also contains a complete bibliography of those of his papers that have been translated into English and an elaborate index for which the explanatory notes alone take up a page

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Bacterial Anatomy (London Cambridge University Press 1956 Pp 360 30s)—The fifteen papers which were discussed at the sixth symposium of the Society for Microbiology were published shortly before the meeting last April, so that members might consider them in advance Under the editorship of Prof E T C Spooner and Dr B A D Stocker and supplemented by some excellent plates they make a handsome volume which will also be an informative consolation prize to non attenders

Discussion

We fully recognise that the number of cases treated in this way is very small and that therefore the figures are not of statistical value but they suggest that the results of radiotherapy may eventually bear comparison with those of surgery. One must also bear in mind that with improved apparatus and greater skill, the results of radiotherapy may reasonably be expected to improve.

In 4 cases reported by Brooks et al. (1951), which were treated by X rays alone and came to necropsy, there was no macroscopical evidence of the original growth in the lung. This suggests that the growth, in some cases, can be adequately treated by radiotherapy provided there is no secondary deposit elsewhere.

There are three other factors which may influence the results of treatment.

(1) There is no immediate mortality after radiotherapy whereas the operative mortality-rate in the series of Bignall and Moon (1955) was about 10%.

(2) Clinical evidence of cerebral metastases seems to be more common after surgical intervention than after radiotherapy. 10 of 25 patients who died after surgery in a series described by Bignall (1955) showed clinical evidence of secondary cerebral deposits, whereas only 2 of 18 patients had cerebral deposits after treatment by radiotherapy.

(3) 24 of 81 cases thought to be operable were found at operation to be inoperable (Bignall 1955). This mistake may well have occurred in our own selection of cases; hence we also may have been including cases more advanced than was evident.

Conclusion

Although this is an extremely small series, the results suggest that radiotherapy in selected cases may be an adequate alternative to surgery.

We are indebted to Dr K. F. W. Hinson, pathologist at the London Chest Hospital, for examining the biopsy sections and sputum for carcinoma cells; Mr. P. Armitage, honorary statistician to the Institute of Diseases of the Chest, for his advice with regard to our figures and for estimating the standard error; and Dr. L. Capel for help in preparing the tables.

Appendix

A more detailed analysis of these results is shown in table I and compared with the results of Bignall and Moon (1955) in table II. The survival-rate is calculated by the life-table method, which enables those patients followed up over a shorter period to be assessed. Bignall and Moon made similar calculations for their larger series. It will be seen that, in the series treated by radiotherapy, a two-year survival-rate is 55·6%. From statistical considerations the standard error is estimated at 9·3%; hence the true figure lies between 37% and 74% with a 95% chance that this is correct.

The two-year survival rate for surgically treated cases is 45%. At least 10% of the patients treated surgically died within two months of operation and were excluded from the series. This would reduce the two-year survival rate for surgically treated cases to 42%. This figure lies well within the range of our findings. If a reasonable allowance is made of a standard error of 2½% in the surgical list, it may be calculated that the probability of getting by chance so big a difference in the two-year survival rate (55·6% for radiotherapy and 42% for surgical resection) is between 0·1 and 0·2.

TABLE I—SURVIVAL RATES OF PATIENTS AT 3 MONTH INTERVALS AFTER RADIOTHERAPY

Interval (completed mos. from bronchoscopy)	At risk at start of interval	Survival-rate (%)
0–2	33	100·00
3–5	32	100·00
6–8	30	96·83
9–11	29	96·83
12–14	23	76·80
15–17	22	73·46
18–20	20	70·04
21–23	18	63·04
24–26	14	55·63
27–29	10	43·27
30–32	7	38·46
33–35	7	38·46
36–38	6	38·46
39–41	5	32·05
42–44	5	32·05
45–47	5	32·05
48–62	4	32·05

TABLE II—SURVIVAL-RATES OF PATIENTS LIVING LONGER THAN 2 MOS. AFTER OPERATION *

Interval (completed mos. from operation)	At risk at start of interval	Survival rate (%)
0–2	453	94
3–5	423	82
6–8	367	73
9–11	326	63
12–14	282·5	58
15–17	259·5	54
18–20	237	51
21–23	222	47
24–26	204·5	45
27–29	188	43
30–32	174	41
33–35	162	39
36–47	133	35
48–59	85	33

* Taken from Bignall and Moon (1955).

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THE HORNPIPE POSITION

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SURGEON

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OPERATIONS for portal hypertension require careful planning. The patients need to be fixed on the operating-table in such a position that it is possible to alter the tactical approach in the light of discoveries made on exploration. We had to be prepared, for example, to change from a right lateral approach to the portal vein (through an oblique incision extending from the umbilicus

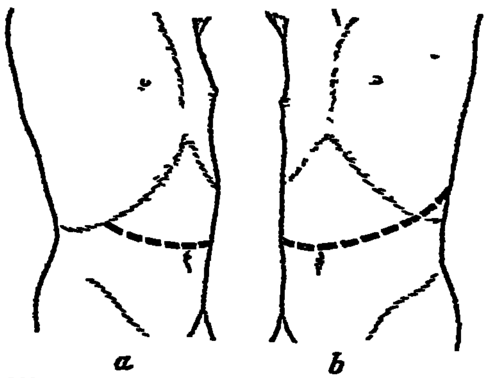
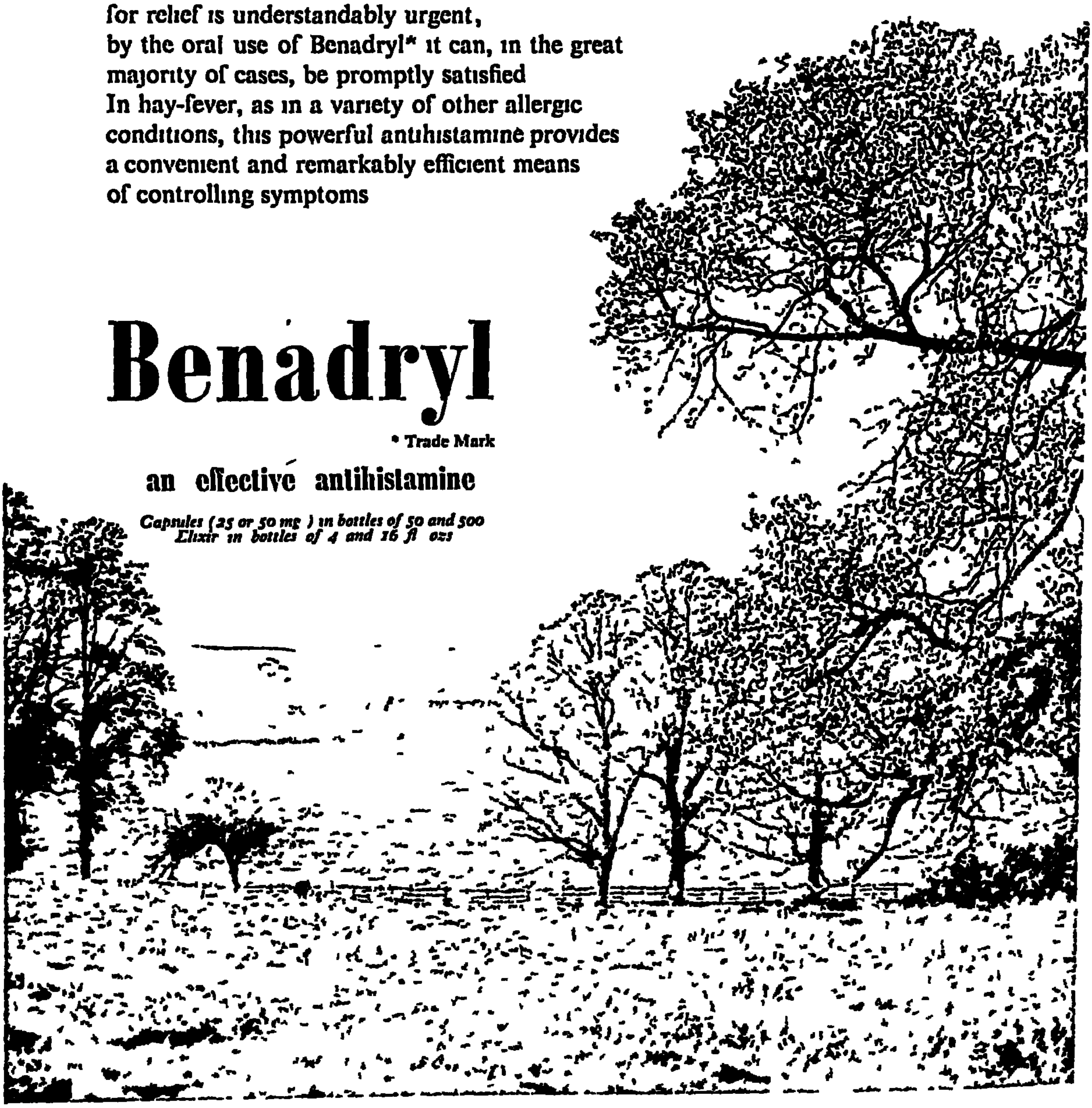


Fig. 1—Oblique abdominal incision (a) for exploration of portal vein before intended portacaval anastomosis. Vein was found unsuitable; so incision was extended (b) to left and up through bed of left 10th rib for lienorenal anastomosis.

Nothing so active is as that which least seems so

Francis Thompson

A peaceful countryside scene but an active source of intense discomfort for all those susceptible to hay-fever, for now is the time of the year when invisible air-borne pollens begin to take their toll Incapacitated by continual weeping, sneezing and nasal congestion, the hay-fever patient's desire for relief is understandably urgent, by the oral use of Benadryl* it can, in the great majority of cases, be promptly satisfied In hay-fever, as in a variety of other allergic conditions, this powerful antihistamine provides a convenient and remarkably efficient means of controlling symptoms



Benadryl

* Trade Mark

an effective antihistamine

Capsules (25 or 50 mg) in bottles of 50 and 500
Elixir in bottles of 4 and 16 fl ozs

PARKE, DAVIS & COMPANY, LIMITED (Inc U S A) HOUNSLOW, MIDDLESEX Tel Houn[illegible] had a profound effect on the outcome of the disease in 2 cases

Material

50 "new" cases of pernicious anæmia attending hospital were reviewed and their weight losses (if any) were measured After treatment the patients were weighed regularly for at least eighteen months

Of our 50 cases it was found that 14 (28%) admitted to losing at least 1 st in weight in the months preceding admission The largest weight loss was 3 st 4 lb, and it is interesting that 4 (28%) of these 14 cases were first diagnosed as carcinoma of the stomach

2 other cases were similarly diagnosed because of weight loss which was described as "gross" in 1 case and justifying the label "cachectic" in the other The amount of weight lost was not recorded in the notes in these cases, so they are not included in the above 14

Anorexia was commonly associated with weight loss and 12 of the 16 patients who lost weight had this symptom The anorexia was often accompanied by nausea, upper abdominal pain, and sometimes diarrhœa, and it seems that cases with weight loss commonly have alimentary symptoms Following our cases after treatment we were able to confirm that weight loss seems to be regained fully after vitamin-B_{12} therapy, often rapidly but sometimes not for twelve to eighteen months

An example of gross weight loss in pernicious anæmia and of a resulting mistaken diagnosis is given below.

Case 1—A man, aged 65, was seen as an outpatient complaining of severe anorexia and gross loss of weight—3 st in four months This was accompanied by central epigastric pain and vomiting There was clinical anæmia, wasting, and slight jaundice but no other abnormal physical signs Because of these signs the diagnosis on admission was malignant disease of the "alimentary tract or pancreas"

Investigations—Weight 13 st 12 lb Blood count Hb 5 6 g per 100 ml (38%) red cells 1,200,000 per c.mm mean corpuscular volume 133 c μ, mean corpuscular hæmoglobin concentration 35%, white cells normal Bone marrow biopsy extreme cellularity with megaloblastic erythropoiesis Barium meal normal. Fractional test meal histamine fast achlorhydria

Progress—After vitamin B_{12} therapy there was a reticulocytosis reaching 25% on the seventh day, with subsequent improvement in the hæmoglobin level Most dramatic of all was the rapid return of well being with a voracious appetite and a quite remarkable increase in weight He put on 1½ st in the fourteen days after the first injection, is now very well and symptomless with a normal blood count, and in six months has regained 2½ st of his lost weight

Though the severe weight loss in this case temporarily misled the clinician and caused the patient to have an unnecessary barium meal, the outcome was most gratifying

However, there are cases in which such a fortunate outcome is not obtained, and failure to recognise that weight loss is fairly common with pernicious anæmia may have disastrous results as in the following case

Case 2—A woman aged 67, was admitted with a history of pallor, shortness of breath anorexia, and considerable loss of flesh in the past year Four months before admission she had been seen by a specialist who because of the anorexia, slight icterus, cachexia, and hepatomegaly, diagnosed carcinomatosis from a gastric primary neoplasm. Unfortunately, because of her age and feebleness he did not investigate her further

On admission she was grossly anæmic and wasted There was slight icterus and some epigastric tenderness, but no other abnormality

Investigations—Hb 17% Red cells 630,000 per c mm, red cell diameter 8 4 μ Blood film showed pronounced anisocytosis and poikilocytosis

Course—Despite intensive treatment with intramuscular injections of liver extracts, as was usual at this time, and slow administration of a blood transfusion, she died three days after admission, without responding to treatment

Necropsy revealed the classical changes of pernicious anæmia in the bone marrow and gastric mucosa

Fortunately such errors in diagnosis are not common, but there is little doubt that this illness, if detected earlier, would not have been fatal The simulation of malignant disease was here so close as to lead to a confident diagnosis of carcinomatosis There is, therefore, a risk that patients with pernicious anæmia will be dismissed as having untreatable cancer, particularly when weight loss is severe

This danger, though small is much greater when pernicious anæmia develops in patients who have already been treated for malignant disease, because when loss of weight, pallor jaundice, and hepatomegaly develop, and they complain of anorexia and general ill health it is easy to assume that metastases have arisen from their original neoplasm Hence the symptoms and signs of pernicious anæmia may be mistaken for those of widespread neoplasia, particularly if the surgeon concerned is not used to recognising and treating pernicious anæmia The next case illustrates this danger

Case 3—A man, aged 77 was operated on in 1943 for a rectal neoplasm The growth was excised and a colostomy performed He remained well until 1952 when he began to complain of anorexia, loss of weight, and general debility The surgeon attending him noticed that he was anæmic and jaundiced and that his liver was palpable Carcinomatosis was diagnosed, so no investigations were done till a year later when he was admitted moribund

On admission he was obese, anæmic and slightly icteric The liver was firm smooth and enlarged three finger breadths below the right costal margin Apart from a normally functioning colostomy there were no other abnormal physical signs

Investigations—Hb 4 9 g per 100 ml (33%) Blood film showed pronounced macrocytosis, anisocytosis, and poikilocytosis Bone marrow biopsy changes of classical megaloblastic erythropoiesis

Course—Vitamin-B_{12} therapy induced a reticulocytosis of 10% but the patient contracted bronchopneumonia a week after the start of treatment and this, together with his anæmia, resulted in his death

Necropsy revealed the changes of pernicious anæmia There was no evidence of any recurrence of the rectal neoplasm

Discussion

In about a third of all cases of pernicious anæmia weight loss usually associated with anorexia, is an important feature This loss may be masked by (1) patients being stout despite their loss of flesh, and (2) elderly patients being uncertain of their usual weight

We have shown that in pernicious anæmia severe weight loss may result in a mistaken diagnosis and an occasional tragedy The simulation of malignant disease is in some cases very close and may be misleading

In dealing with patients who complain of loss of weight, pernicious anæmia should be remembered as a possible cause Usually severe weight loss in such cases is accompanied by correspondingly severe anæmia, but we have seen cases where weight loss of a stone or more has been present with a hæmoglobin of 70% or higher It is, therefore, important to examine blood-films and bone-marrow where weight loss has occurred Of course clinical evidence of anæmia accompanying weight loss and other alimentary symptoms may well be due to a malignant neoplasm of the alimentary tract, but it is always worth while fully investigating the anæmia before sending patients for radiographic studies of the alimentary tract When pernicious anæmia has been diagnosed and treatment instituted, the return of appetite, weight and well-being will usually dispel all thoughts of neoplasia

It has been shown that carcinoma of the stomach is commoner in patients with pernicious anæmia than in other members of the community (Videbæck and Mosbech 1954), and an incomplete response to vitamin-B_{12} and persistence of alimentary symptoms may occasionally lead to the discovery of a gastric neoplasm However, other nutrients, such as pyridoxine pantothenic acid, biotin, and folic acid whose full importance may not yet be apparent If we did not know that very small nutritional deficiencies (conditioned or otherwise) can have very great effects, and if we were quite sure that none of the current disorders of civilised man can possibly have a nutritional origin, we might be happier about the panel's implication that what is unproven can be (fairly) safely ignored Admittedly it reaches its conclusions after the proper hesitations —' the history of nutrition reveals many instances where the refinement or over-purification of food has led to ill-health and there is no reason to believe that this chapter of knowledge is closed '—but this does not lessen our doubts about the conclusions themselves When the panel says that a lowering of the extraction-rate from 80% to 70% *is very unlikely* to lead to any nutritional disturbance from lack of pyridoxine, pantothenic acid, biotin, and folic acid, and that there is no ascertainable difference between National flour and fortified flour which would *significantly* affect the health of the population " in any foreseeable circumstances," it is making guesses that embody risks, and these are risks that are going to be multiplied by 50 million Even in the more limited " present circumstance " to which the Minister of Agriculture confines his own statement,[2] bread is probably becoming perforce an increasingly prominent part of the diet of many people in this country, and their number may rapidly increase We share the view of the M R C conference that, though the new policy may not lead to an increase in recognisable illness, it carries a risk that can be avoided

As things stand there is every prospect of the nation returning to the familiar situation in which people receive what it suits the millers to give them

Thyroid Hormones and Coronary Disease

NOT long ago, coronary-artery disease was regarded as an inevitable accompaniment of the process of growing old, which there was no prospect of averting In recent years a remarkable change has come over our attitude to this condition, and many people now regard it as something which could be corrected if enough was known about its cause We have lately referred to some of the reasons for this change of attitude[3] If further investigation shows that high blood-cholesterol levels do in fact predispose to thrombosis with or without atheroma various means of avoiding excessive cholesteræmia may prove practicable One would be to lower the total fat content of the diet, or the proportion of different kinds of fats Another which has been proposed is the administration of sitosterol, a plant steroid which interferes with the absorption of cholesterol[4] though only when taken in inconveniently large quantities Another possible line of attack is hormonal It is well established that coronary artery disease is less prevalent in women than in men, particularly at the younger ages, and administration of œstrogens lowers the blood cholesterol[5] Similarly TURNER and STEINER[6] showed that thyroid extract lowered the blood cholesterol level of euthyroid subjects, though it also raised the basal metabolic rate (B M R) by an average of 20% GILDEA et al[7] made similar observations in patients with hypometabolism but no signs of myxœdema, again, a fall in blood-cholesterol was accompanied by a rise in B M R They noted, however, that larger doses of thyroid extract were needed to lower the blood cholesterol of euthyroid subjects than was the case in patients with myxœdema STRISOWER, GOFMAN and others[8] [9] have recently shown that large doses of thyroid extract given to schizophrenics lowered not only the total blood-cholesterol but also the lipoprotein fractions which they regard as particularly associated with atheroma The patients' B M R s were not measured, but they lost weight Thyroid extract clearly changes the blood-lipoprotein pattern in the right direction, but only at the expense of an increase in general metabolism This increased metabolism is a disadvantage, in that it is likely to make the patient uncomfortable, and it might also be dangerous in a person whose coronary arteries are already narrowed, for it must necessarily increase the work of the heart, and therefore the amount of blood which must be carried by the coronaries

The hormone secreted by the thyroid is thought to consist mainly of thyroxine, in addition, triiodothyronine is also either made by the gland or formed elsewhere from thyroxine These two substances are supposed to have similar physiological actions, though triiodothyronine is the more powerful Numerous synthetic variants of these two substances are also known, many of which are physiologically active in varying degrees It has been presumed that the difference in the physiological activity of these substances were purely quantitative But now it is suggested, in papers by Dr TROTTER and Dr GOOLDEN in this issue, that there may be qualitative differences between the various chemical versions of the thyroid hormone Just as changes in the chemical structure of the adrenal cortical hormones increase the relative effects on either glucose or mineral metabolism, so alterations in the thyroxine molecule may emphasise either the cholesterol depressing or the metabolic effects of the thyroid hormone As it happens, both Dr TROTTER and Dr GOOLDEN deal with the same modification of the molecule whereby the tyrosine side-chain is replaced by acetic acid Dr GOOLDEN'S substance is the acetic-acid analogue of thyroxine (tetrac), while Dr TROTTER'S is the acetic acid analogue of triiodothyronine (triac) Both substances originated in Mrs PITT RIVERS's laboratory at the National Institute for Medical Research where their physiological properties are being closely studied

It is evident that in their action in man the new compounds do not differ radically from their parent substances Both will relieve the symptoms of myxœdema, at the same time restoring B M R and blood cholesterol to normal The action of both substances is more rapid than that of thyroxine, though not necessarily more rapid than that of triiodothyronine The main point of interest is that both Dr TROTTER and Dr GOOLDEN suggest, though only tentatively that the acetic acid analogues may history could be obtained other than that of repeated hæmatemesis during the previous three months She died forty eight hours later after a hæmatemesis

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Necropsy Findings—Of senile physique, wasted and slightly jaundiced Hæmorrhage from œsophageal varices, and much blood in stomach and intestines Œdema of lungs, brown atrophy of myocardium, ischæmic scarring of the kidneys Liver shrunken, with prominent regeneration nodules Spleen enlarged and firm Moderate ascites Length of small intestine 12 ft 6 in.

Histology—Chronic inflammation of the mucosa of the jejunum, with focal subacute inflammation The ileum and colon were normal The liver showed coarse fibrosis, with fatty degeneration of the residual cells and regeneration of bile ducts.

Case 5—A man, aged 52 complained of vomiting blood at intervals for a year He had always been regarded as an invalid and until the age of 20 had epileptic fits He had lost weight recently, fluid was present in his abdomen, his ankles were swollen, and his superficial abdominal veins were distended. He died after a severe hæmatemesis

Necropsy Findings—A thin, œdematous, and lightly jaundiced male with venules on nose and prominent abdominal veins Bilateral pleural effusions, each of about 2 pints, and severe pulmonary œdema Ascites of 4 pints Œsophageal varices present but not ruptured Hæmorrhage from multiple acute erosions of stomach and colon The liver weighed 90 oz and showed diffuse portal fibrosis, small regeneration nodules being more prominent in the left lobe than in the right The spleen showed changes due to portal obstruction and weighed 15 oz The small intestine measured 14 ft

Histology—Portal fibrosis of liver with regeneration of liver cells and bile ducts Section of intestine showed slight terminal inflammation of mucosa

Discussion

There is very little accurate information about the length of the small intestine, 18–23 ft being the usual estimate, but Underhill (1955) has found the following measurements (including the duodenum)

	No of cases	*Minimum ft*	*Average ft in*	*Maximum ft in*
Male	65	16	20 11	25 9
Female	35	11	19 5	23 6

There is still no guide to the normal range, and it would be interesting to know the causes of death of patients with a short intestine and whether any had hepatic fibrosis

There are four possible causes of a short small intestine (1) surgical interference (which can be excluded in the present cases), (2) intestinal disease or disease elsewhere, (3) hypoplasia, and (4) simple atrophy (for which there is no evidence)

It is theoretically possible that a severe inflammation of the mesentery and serosal surface of the intestine—e g, tuberculosis—in an adolescent might limit the normal growth of the intestine, and so might internal inflammation, but this would more likely cause local deformity and a disturbance of the jejunum/ileum ratio

Disease in other sites may also influence the intestine

A woman, aged 47, who died of bronchopneumonia, had a most severe angular deformity of the lower cervical spine and a remarkable kyphoscoliosis, the result of spinal tuberculosis during adolescence Her lungs were small her liver depressed, and her small intestine 13 ft. long The growth of her intestine was probably limited by the bodily distortions; In precisely the same way one malformation in utero may induce other malformations in surrounding organs (Raeburn 1951)

In the present cases, however, nothing suggested antecedent disease as a cause of intestinal hypoplasia

Hypoplasia remains, and in the complete absence of any local disease this, we suggest, is the true explanation Whether this is entirely a failure of natural postnatal growth, or whether congenital or familial factors operate, is unknown

In cases 1–4 the length of the small intestine was only 25–66% of the average and was well below the accepted minimal normal length of 14 ft Even thus deficiency would not necessarily produce any detectable impairment of intestinal absorption, but, if there were any severe intestinal disturbance, such a person would be liable to liver damage because of the small reserve of function

There is no direct evidence that a short intestine contributes to hepatic fibrosis, but it is not a common condition and is therefore worthy of record Of the 5 present cases 4 were in females Hepatic fibrosis is stated to be twice as common in males as in females (Anderson 1953)

We have since observed 2 other cases of portal fibrosis, both in males, 1 of them being associated with hæmochromatosis In these 2 cases and in numerous instances of "cardiac fibrosis" the intestine was of normal length

Summary

5 cases of short small intestine associated with hepatic fibrosis are described

Perhaps measurement of the alimentary tract should be a routine post-mortem procedure

In none of the present cases was there any history of acute hepatitis

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EFFECT OF TRIIODOTHYROACETIC ACID ON BLOOD-CHOLESTEROL LEVELS

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D M Oxfd, M R C P

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THE acetic acid analogue of thyroxine was synthesised by Harington and Pitt-Rivers (1952) and the acetic-acid analogue of triiodothyronine by Pitt-Rivers (1953) These compounds were named tetraiodothyroacetic acid and triiodothyroacetic acid respectively, and the name of the latter compound has been still further abbreviated to triac (Trotter 1955)

Both compounds were assayed physiologically by Pitt Rivers (1953) using the goitre-prevention test in rats Both had about a tenth of the activity of triiodothyronine, and it was shown that triac, given by daily injections, raised the oxygen consumption of intact rats

Thibault and Pitt-Rivers (1955) have shown that, unlike thyroxine and triiodothyronine, triac appears to have an immediate effect on the oxygen consumption of kidney slices in vitro, and the same workers described an increase in the oxygen consumption of thyroidectomised rats only two hours after a single injection Roche et al (1955) have identified triac in kidney slices incubated with ^{131}I-labelled triiodothyronine It is therefore possible that triac is normally formed from triiodothyronine in the body, and that the oxidative deamination and decarboxylation of triiodothyronine to triac are an essential step in the process by which the thyroid hormones exert their action on the tissues

Triac is therefore a substance of considerable physiological interest, and it became desirable to know something of its action in man It was first administered to man by Lerman and Pitt-Rivers (1955) They gave repeated injections to 2 patients with myxœdema The undernutrition and unemployment. For example, Barbados which has fully developed its agricultural resources and can hardly increase its income or food-supply any further, had a 1953 population of 221,000 in its 166 square miles. Since 1921, there has been negligible change in its birth-rate but the annual death-rate has fallen from 33 per 1000 population to 14 per 1000 in 1953, resulting in an annual rate of population increase which rose from 0·2% to 1·9% over those years and which is still rising proportionately.[3] And things are much the same in most of the other West Indian islands. If medicine upsets so rudely a stable natural balance, it must join in the efforts to restore a new balance, and the doctor must share the social responsibility in this change with pioneers in other fields. What is now needed is a corresponding success in the bigger and more difficult task of combating the disabling diseases, where malnutrition and psychiatric ills, both intricately linked with social problems, play a very important part.

The Caribbean is sparsely doctored. In Jamaica, for example, there is *only* 1 qualified doctor to every 4000 people.[4] The University College of the West Indies can remedy this in the course of time, but only if local schools provide an adequate input of capable students. It is right that when there are suitably qualified West Indians available they should run the medical services, teaching, and research; but it is equally wrong to court a danger of parochialism. A free exchange of medical men and women between this country and the West Indies is to be encouraged by every means. In research, the Medical Research Council and the Colonial Office are already following the admirable policy they started in Africa, whereby activities and funds are to be coordinated through a local medical research committee. Above all else there is need for continued unity of purpose in these widely separated but closely linked lands: if the recent conference heralds this for medicine, it may well have been an historic occasion.

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Annotations

DEADLY SWEETS

A RECENT inquest[1] on a child who died of ferrous sulphate poisoning is another reminder of the disturbing number of accidental deaths caused by drugs. Iron, barbiturates, and antihistamines, three of the most dangerous groups of drugs,[2] are among those which appear as attractively coloured sugar-coated tablets. Elliot[3] has lately discussed this sinister modern tendency to make drugs look like sweets. When the drugs are intended primarily for adults such methods of presentation are indefensible.

In recent years a wide range of drugs has been introduced solely for children; and sedatives, analgesics, sulphonamides, and antibiotics are among those now appearing as attractively coloured and flavoured suspensions or tablets designed to appeal to the childish palate. If these preparations enable children to be effectively treated at home rather than in hospital, or eliminate the psychological trauma of repeated injections, they are welcome. But their potential danger must be thoroughly appreciated.

The problem of accidental poisoning will not be solved by reproaching the manufacturer. Indeed Fraser[4] has suggested that the attractive appearance of drugs may not in fact be as decisive as is generally supposed; and this view is supported by the interesting work of Craig[5] on the type of child who swallows poisons. He points out that those children who are very keen on putting things in their mouth are likely to poison themselves indiscriminately, although an attractive tablet or medicine is an added temptation. Some infants will eat the most unpleasant things, and often do so whenever they are allowed access to them. The insecurely guarded family medicine chest with its assortment of harmless placebos and potent drugs—legacies of long forgotten ills—is a menace. The garden shed and the cleaning drawer contain dangerous chemicals, and in a doctor's household there is the collection of unopened samples. Secure screw-topped bottles, locked cupboards, and the disposal of unused drugs provide some safeguard; but the final remedy must lie in wider education of both parents and doctors. Parents must be repeatedly reminded that the exploring toddler is at great risk and that it is not only drugs labelled "Poison" that are dangerous.

Reports of success with heroic measures in the treatment of poisoning by ferrous sulphate[6] and barbiturate[7] among others, suggest that lives might be saved if action was swifter and surer. In some cities in the United States, "poison centres" have been set up where immediate information can be had about the toxic ingredients of drugs and household preparations and the best treatment. These centres can collect valuable statistics, and could be a source of authoritative propaganda to doctors, clinics, and the press.

But such measures will not immediately improve a situation for which the inaction of doctors is at least partly to blame. The replacement of all attractively coloured and flavoured drugs of potential danger by something less deceptively decorated is long overdue, and is the most effective single step we can take towards preventing these tragedies.

THIOPENTONE IN OBSTETRIC ANÆSTHESIA

FOR many years most obstetricians and anæsthetists have accepted the view that drugs given to the mother take several minutes to achieve an equal concentration in the fœtus. Thus, the use of intravenous thiopentone for operative obstetrics has usually been an indication for a speedy delivery to avoid the risk of the drug's depressant action affecting the child. Indeed, much of this opinion has been based on theory rather than proven fact, though there is some evidence in its favour.[8] Most experienced anæsthetists and obstetricians would probably agree, however, that a small dose of thiopentone, used only for the induction of anæsthesia, does little to a healthy child no matter how long after the injection the baby is delivered.

Crawford[9] has lately recorded the results of an investigation of maternal and fœtal serum thiopentone levels in 41 cases during delivery. (Dr. Crawford's contribution to the correspondence on anæsthesia in obstetrics appears on p. 913.) He found that the fœtal serum

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Results

Myxœdema

Before attempting to compare the effects of triac on the blood-cholesterol level and B.M.R. it was necessary to get some idea of the speed and duration of its action. If, as experiments on animals suggest, its action is both more rapid and more transient than that of the other thyroid hormones, the time interval between the administration of triac and estimation of the B.M.R. might be critical. I have suggested above that the observations of Lerman and Pitt-Rivers (1955) may indicate a greater effect of triac on the blood-cholesterol level than on the B.M.R., but since in their cases the triac was given in the afternoon and the B.M.R. was not measured until the following morning, it might equally well be argued that a sharp but transient rise in the B.M.R. may have taken place undetected in the interval. The same objection might be brought against the present observations, although in this instance triac was given twice daily and the patients were instructed to take the evening dose between supper and bedtime (at the time of estimation of the B.M.R. they were routinely asked whether they had in fact taken the previous evening's dose at the usual time). This criticism would not apply to case 1 while he was receiving 6 mg. of triac daily, because during that time the triac was being given four-hourly day and night, and the maximum effect of triac on the B.M.R. certainly persists longer than four hours. As a matter of fact, it was shown for this patient (Trotter 1955) that, when he received triac 2 mg. daily as a single dose, the time-interval between its administration and the estimation of the B.M.R. could be varied between one and twenty-three hours without affecting the result.

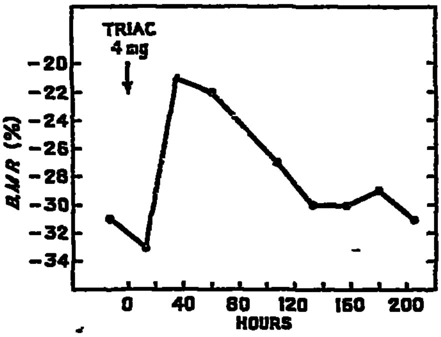

Fig. 2—Effect of single oral dose of triac 4 mg. on B.M.R. in myxœdema (case 2).

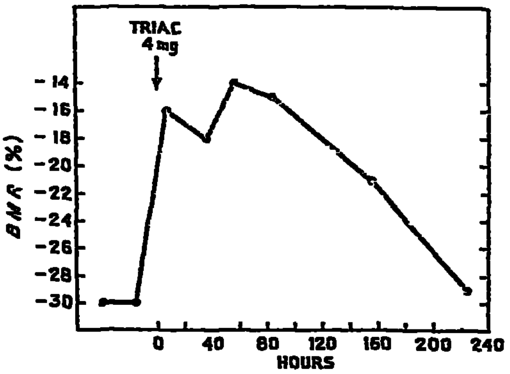

Fig. 3—Effect of single oral dose of triac 4 mg. on B.M.R. in myxœdema (case 4).

The effect of single oral 4 mg. doses of triac on cases 2 and 4 before the patients had received any treatment is shown in figs. 2 and 3. In both patients there was a slight but significant rise in the B.M.R. In case 4 this was already present nine hours after the dose, but in case 2 it was not apparent until thirty-six hours. The B.M.R. remained raised in case 2 for two days and in case 4 for four days. If these patients are representative, it seems certain that, when triac is given at twelve-hour intervals, its effects should be fairly assessed by B.M.R. estimations done from twelve to fifteen hours after the last dose.

Fig. 1 shows the effect of continued administration of triac and of thyroxine in case 1. Both drugs increased the B.M.R. and lowered the blood cholesterol level. With triac 6 mg. daily the blood cholesterol level fell to 150 mg. per 100 ml., yet the highest B.M.R. was only -8%. With thyroxine, on the other hand, the lowest blood-cholesterol level observed on any dose was 225 mg. per 100 ml., but the B.M.R. at the time was +10%. It will be seen that with both drugs the blood-cholesterol level and the B.M.R. varied reciprocally, but in the case of triac a given increase in the B.M.R. was associated with a larger fall in the blood-cholesterol level. It is, however, possible that the comparison of the two drugs is to some extent invalidated because the subject was an inpatient while receiving triac, and an outpatient while receiving thyroxine.

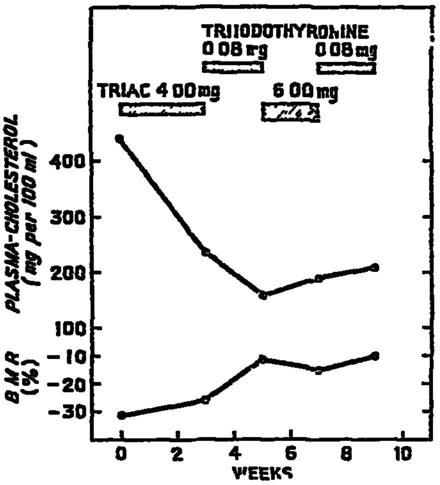

Fig. 4—Effect of triac and of triiodothyronine on blood-cholesterol level and B.M.R. in myxœdema (case 2).

Figs. 4 and 5 show the effects of triac and of triiodothyronine in cases 2 and 3. In case 2 treatment was started with triac 4 mg. daily. This practically reproduced the results of Lerman and Pitt-Rivers (1955), in that there was a substantial fall in the blood-cholesterol level with almost no change in B.M.R. In case 3, however, even 2 mg. of triac daily caused an appreciable rise in B.M.R. as well as a large drop in the blood-cholesterol level. After the initial response had been obtained triac and triiodothyronine were given alternately for two to four weeks at a time. In both cases the relative effect of the two drugs on the B.M.R. and the blood-cholesterol level appeared to be much the same. In case 2, the effect of 6 mg. of triac was similar to the effect of 0·08 mg. of triiodothyronine, as regards both B.M.R. and cholesterol. In case 3, 3 mg. of triac would appear to be roughly equivalent to 0·04 mg. triiodothyronine

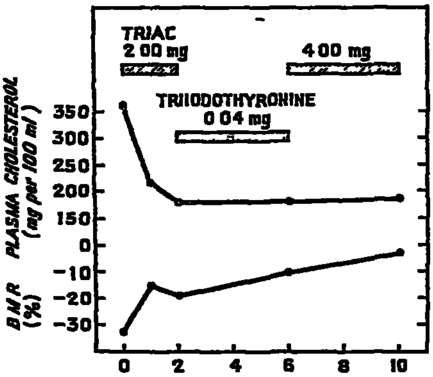

Fig. 5—Effect of triac and of triiodothyronine on blood-cholesterol level and B.M.R. in myxœdema (case 3).

which could profitably be expanded, and which could ensure that when the patient benefits from the operation, his relations and friends do so too

STREPTOCOCCI AND RHEUMATIC RELAPSES

THE antistreptococcal antibody levels in the blood during the first few weeks of an acute attack of rheumatic fever support the view that group A streptococcal infections are a cause of this condition Thus, it is well known that in about 80% of cases the serum antistreptolysin-o titre is raised or rising, and if more than one antistreptococcal antibody is looked for (if, for instance, anti-streptokinase and antihyaluronidase levels are also measured), then the antistreptococcal antibody titre is raised in nearly every case of acute rheumatism[1] In chronic or polycyclic rheumatic fever, the behaviour of the various antistreptococcal antibodies is less well established The strikingly successful prophylactic use of penicillin or sulphadiazine against rheumatic relapses[2] is strong evidence that streptococcal infection is no less important in reactivating than in initiating the rheumatic process yet serological proof of this has often been lacking Some recent studies of Professor Stollerman and his colleagues[3] have related the immune response to streptococcal infection to three clinical manifestations of rheumatic fever—the acute attack, the chronic activity, and the rheumatic relapse

In acute "monocyclic" cases (in which all clinical and laboratory evidence of rheumatic activity had subsided within six months of onset), Stollerman et al found, initially, the expected high incidence of raised antistreptococcal antibody titres In these patients (all of whom were receiving prophylactic antibiotics) they also measured the rate of fall of antibody levels during the twelve months after the acute episode This rate of fall was determined solely by the absence of new streptococcal infection, and not by the course of the disease When a comparison was made between these acute cases and those showing chronic activity in which clinical symptoms had persisted for more than six months, the rate of fall of antibody levels was found to be no different This seems to rule out renewed streptococcal infection as a cause of chronic activity In the third group—the rheumatic relapses—two types of case were differentiated on clinical grounds and they were also distinguishable by antibody tests The first type included the ones which relapsed after withdrawal of aspirin or cortisone therapy All relapsed within two months and 95% within one month of stopping treatment, and none showed increased antibody levels The second type relapsed more than two months after previous activity had subsided, they had all had no prophylaxis and the antistreptococcal antibody titres were newly raised It is clear that it is only in this type of case that reinfection with group A hæmolytic streptococci is primarily responsible for renewal of the disease

Taranta and Stollerman[4] have investigated cases of Sydenham's chorea along the same lines It is known that when chorea is associated with other rheumatic manifestations it usually follows them after a variable period of weeks or months Taranta and Stollerman found, however, the same lag period even when the rate of fall of antibody levels and continuous antibiotic prophylaxis could be said to rule out the possibility of intercurrent reinfection with streptococci In patients in whom the only clinical manifestation was chorea ("pure" chorea) the incidence of raised streptococcal antibody titres was 73% in those studied within one month of onset and 15% in those studied later (one to five months after on While these figures would be low for rheumatic fever a similar intervals after onset, they may, Stollerman suggests, reflect the existence of a long latent period between streptococcal infection and the onset of chorea—a period measurable perhaps in months In America [illegible] points out the peak incidence of chorea in fact follows the peak incidence of rheumatic fever at an interval of one to three months[5]

Although it is hard to determine the precise time of onset of chorea, and to dissociate pure chorea from rheumatic fever with certainty, the evidence suggests that the relation of streptococcal infections to rheumatic fever is close throughout the natural history of the disease Stollerman's work emphasises once more the importance of defence against streptococci at all stages of rheumatic fever

BIRTHDAY HONOURS

THE peerage conferred on Sir Henry Cohen is decorative but also functional Reformed or not, the House of Lords will remain a useful place for explanation and discussion by the expert, and its new member can speak to it with authority on a remarkably large number of medical issues His knowledge of the National Health Service has been gained diversely as physician, professor of medicine at Liverpool, member of the General Medical Council, president of the British Medical Association vice chairman of the Central Health Services Council and adviser to all the Ministers of Health since the service started So great have been the demands made upon him that nowadays no explorer of this part of medicine can go far without finding the tracks of some pioneer Cohen committee in the sand With Sir Henry's immense capability go other qualities that make his friends glad that this new honour should be paid him In his union of quietness with brilliance, of delicacy with endurance, he resembles intellectually the good silver from which, with other kinds of art, he gets so much enjoyment

A second former president of the B M A appearing in the list is Mr Tudor Thomas, whose tour of the association's branches in the Middle and Far East was a notable contribution to its work But it is for his large part in making corneal grafting into a practicable operation that the name of Tudor Thomas is most widely known, and many have reason to be grateful for the surgical research he has pursued so skilfully since the 1920s Another of the new knights, Professor Bedson has had an even longer career of fruitful investigation happily continuing since his academic retirement But whereas his virus studies, particularly of psittacosis earned him the fellowship of the Royal Society, his new distinction chiefly recognises what he has done so much for the organisation of pathology in this country—during the war as a sector pathologist, and since 1949 in succession to the late Sir Philip Panton as chairman of the Central Committee of Pathology at the Ministry of Health Dr Arthur Massey, chief medical officer of the Ministry of Pensions and National Insurance was, like Dr Bedson a combatant officer in the first world war and he first gained a national reputation by his outstanding work for Coventry, where he was M O H for sixteen years including the time of the bomb damage Formerly chairman of the Central Council for Health Education, he is himself a writer and lecturer, and is welcomed as a friend even when he comes as an examiner The last of the four knights, Dr Harkness is less generally known in this country for he reached his present post in the West Indies through appointments in Palestine and in Africa including the directorship of medical services of the Gold Coast and Nigeria With many other colleagues abroad as well as at home whose names appear on p 907, he has our congratulations

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[4] Taranta, A, Stollerman, G H Ibid p 170

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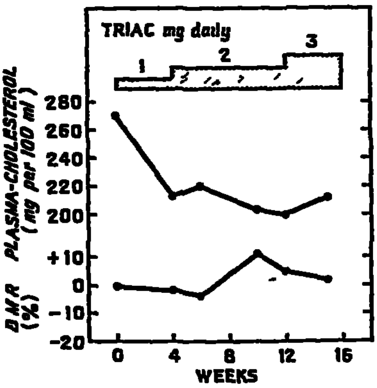

Fig 8—Effect of gradually increasing doses of triac on blood-cholesterol level and B.M.R. in a euthyroid patient (case 6)

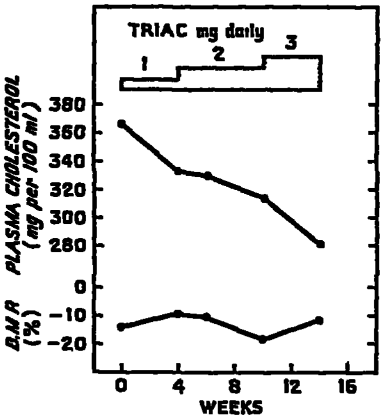

Fig 9—Effect of gradually increasing doses of triac on blood-cholesterol level and B.M.R. in a euthyroid patient (case 7)

with triac showed a fall in the blood cholesterol level. The mean drop in the blood cholesterol level differed significantly from zero at the 1% level in the 2, 3 and 4 mg groups. Analysis of variance showed that the degree of depression by the three different doses was not significantly different. The degree of depression produced by 0·08 mg daily of triiodothyronine was not significantly different from that produced by triac. The present observations have therefore not shown any clear difference between the effect of triac and of triiodothyronine on the plasma-cholesterol level, though they do not exclude the possibility that such a difference would appear in more extensive trials.

Of the 15 patients given triac for two weeks only 1 complained of symptoms suggesting hyperthyroidism. This was a woman treated with 4 mg daily. She noticed palpitations and was found to have lost weight and to have tachycardia. None of the 12 patients treated with triiodothyronine had any symptoms attributable to the drug. The mean weight loss in the triac group amounted to 2 lb., the patients on the small dose of triiodothyronine lost 1 lb. and those on the large dose 4 lb.

DISCUSSION

In 2 cases of myxœdema the relative effect of triac and triiodothyronine on the blood-cholesterol level and the B.M.R. appeared to be similar. In a single case of myxœdema triac appeared to have a greater effect on the blood-cholesterol level relative to the B.M.R., than did thyroxine. It is, however, possible that the results in this case may have been influenced by a change of diet or some other factor, since the patient was in hospital while taking triac, and at home while taking thyroxine. These preliminary trials have therefore not shown any unequivocal difference between the action of triac and of the other two hormones, except that triac is a great deal less potent.

TABLE II—EFFECT OF TWO WEEKS' TREATMENT ON BLOOD CHOLESTEROL LEVEL OF EUTHYROID PATIENTS

Drug	Dose (mg.)	No. of patients	Mean initial blood cholesterol level (mg. per 100 ml.) and S.E.	Mean fall in blood-cholesterol level (mg. per 100 ml.) and S.E.	% change
Triac	2	5	247·8 ± 20·1	83·6 ± 20·7	34
Triac	3	5	222·4 ± 21·8	44·6 ± 9·3	20
Triac	4	5	214·0 ± 13·3	49·2 ± 7·5	23
Triiodothyronine	0·04	7	245·1 ± 18·3	28·4 ± 10·0	12
Triiodothyronine	0·08	5	234·0 ± 14·6	49·8 ± 10·6	21
Controls (dummy tablets)		4	189·3 ± 34·5	0·3 ± 8·5	

In 3 euthyroid subjects with coronary artery disease it appeared to be possible to lower the blood-cholesterol level without materially changing the B.M.R. These results were obtained by giving triac, but the evidence at present available does not exclude the possibility that equally striking effects might have been achieved with the other thyroid hormones in carefully graded doses. It is also possible that the fall in blood-cholesterol level was coincidental, since the trials have not as yet been controlled by observing the effect of discontinuing the drug. Other possibilities are that the fall in blood-cholesterol level is merely a temporary change, or that the initial values for the B.M.R. were erroneously high thus masking a subsequent rise. In any case the small number of patients studied does not permit any generalisations to be made. For these reasons it cannot be claimed at present that triac has any properties not shared by the other thyroid hormones or that it is likely to be particularly useful in lowering the blood-cholesterol level of euthyroid patients. Nevertheless these preliminary trials suggest that a detailed comparison of the effects of thyronine derivatives on blood lipids and on the B.M.R. would be worth undertaking.

Summary

Triiodothyroacetic acid (triac) was given to 3 patients with myxœdema and 18 euthyroid patients.

Its relative effects in lowering the blood-cholesterol level and in raising the B.M.R. have been compared with those of thyroxine in 1 case of myxœdema. Triac appeared to have a relatively greater effect than thyroxine on the blood-cholesterol level.

A similar comparison with triiodothyronine was made in 2 other cases of myxœdema. In these cases the action of the two drugs appeared to be similar, but triiodothyronine was about seventy-five times more effective than triac as regards both depression of the blood-cholesterol level and elevation of B.M.R.

In euthyroid patients triac 2–4 mg daily lowered the blood-cholesterol level by about a quarter. Triiodothyronine 0·08 mg daily had a similar effect. In 3 patients whose dose of triac was increased gradually up to 3 or 4 mg daily, there was no obvious rise in the B.M.R., although the plasma cholesterol level appeared to fall.

Triac reduced the uptake of radioactive iodine in euthyroid patients, the dose required being about twenty-five times greater than the triiodothyronine. This observation is difficult to interpret quantitatively, owing to the relatively large amount of iodine which may be released during the breakdown of triac in the body.

I am deeply indebted to Dr. R. Pitt Rivers for supplying both triac and triiodothyronine, Prof. M. Maizels and his staff for estimations of plasma-cholesterol, and the Sir Halley Stewart Trust for a personal grant.

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TABLE II*—PERCENTAGE CONTRIBUTION OF BREAD AND FLOUR TO SOME ELEMENTS OF THE DIETS OF HOUSEHOLDS IN 1954

Element	Households with 1 male and 1 female and					
	Children only				Adolescents only	Children and adolescents
	1	2	3	4 or more		
Calories	25	25	27	29	27	30
Total protein	29	29	31	34	31	35
Iron	25	25	26	29	26	29
Vitamin B_1	31	31	33	35	33	36
Riboflavine	7	7	8	8	5	8
Nicotinic acid	26	26	28	30	26	30

* The figures in this table are derived from the National Food Survey and are provisional only. During 1954 bread made from flour of 70–72% extraction was available in addition to bread made from flour of 80% or higher extraction. Almost all the bread consumed, however, was made from National flour which was required under the Flour Order 1953 to be of 80% extraction or its equivalent.

and iron (table III), but also of a number of other nutrients which are present in wheat but about which less is known. No figures are available to show the extent of the fall of these less well-known nutrients between 80% and 70% extraction flours, but table IV, which gives the levels for white "top patent" flours, indicates that there might be a considerable fall. Those who advocate a policy of fortification in this country do not propose to restore to bread all the nutrients that have been lost by milling to a low rate of extraction. The proposal is to add only iron, vitamin B_1 and nicotinic acid, the implication being that the restoration to flour of other substances is not necessary, under present conditions in this country, even though some of these substances are known to be essential for animal nutrition in planned laboratory experiments. In the opinion of the conference, present knowledge provides no basis *for an assumption such as this*, and past experience should make one cautious of accepting it.

In 1936, when the suggestion was first made that bread in this country should be fortified, the only constituent which it was proposed to restore was vitamin B_1. Ten years later the Conference on the Post-War Loaf [4] recommended minimum values not only for vitamin B_1 but also for iron and nicotinic acid, and the official medical and scientific members held that these values should be attained not by restoration but by retaining the substances during the milling process, so as to include along with them, as far as possible, all the other nutritional factors which might be present in the original wheat. Recent experience with pyridoxine has shown that it would be unwise to neglect the possible nutritional importance of lesser-known or unknown nutrients. When the Conference on the Post-War Loaf met, the nutritional importance of pyridoxine was known only from animal experiments; it has now been shown to be essential to human nutrition, for pyridoxine deficiency has been found to give rise, under special conditions, to recognisable disease in man. In the opinion of the conference it cannot be assumed that this process of discovery is at an end.

The Widdowson/McCance Studies of the Effect of Variations on the Extraction rate

The most recent investigations of the effects of variations in the extraction rate of flour are those of Dr E. M. Widdowson and Prof R. A. McCance.[5]

Their investigations were carried out after the war on children in two German orphanages. For the purposes of the trial, each child continued to receive his full German ration with the exception of the German bread, which was replaced by unlimited amounts of bread made from one of five types of flour specially milled in England: (1) 100% extraction, (2) 85%, (3) 70%, (4) 70% with iron, vitamin B_1, nicotinic acid, and riboflavine restored to the 85% level, *and (5)* 70% with iron, vitamin B_1, nicotinic acid, and riboflavine restored to the 100% level. All contained added calcium. The children obtained up to three quarters of their calories in the form of flour products; the rest of their food consisted chiefly of vegetables and contained very little milk or other animal protein.

TABLE IV*—MEAN CONTENTS OF CERTAIN NUTRIENTS IN FLOUR OF 80% EXTRACTION AND 'TOP PATENT' FLOURS

—	Mean content (mg per 100 g)	
	80% extraction flour (straight run)	Whitest ('top patent' mill streams)†
Iron	1.7	0.9
Vitamin B_1	0.21	0.01
Riboflavine	0.062	0.01
Nicotinic acid	1.7	0.9
Biotin (× 10^{-3})	23	5
Pyridoxine	0.29	0.11
Folic acid	0.026	0.012
Pantothenic acid	0.37	0.33

* Figures supplied by the Ministry of Agriculture, Fisheries and Food.

† No figures are available for flour of 70–72% extraction. The flours in the 'top patent' mill streams varied from 30% to 60% extraction.

Before the investigation began the children had been receiving an inadequate diet and they were in consequence of less than normal height and weight. During the year for which the trial continued, their health improved and their gains in height and weight considerably exceeded those accepted as normal for American children of the same age and sex. This was equally true whichever bread was included in their diets.

In interpreting these results it is important to recognise that nutrients were provided at levels comparable with those of the B.M.A. recommendations ‡ by all the diets irrespective of the type of flour used. It is therefore understandable, although surprising at the time in view of what was thought about the importance of animal

TABLE III—COMPOSITION OF FLOURS NORMALLY USED IN THE U.K. COMPARED WITH THAT OF FLOURS USED IN THE FEEDING TRIALS IN GERMANY

Element	U.K. flours* (mg per 100 g)								Flours used† in investigation in Germany (mg per 100 g)	
	100% extraction		85% extraction		80% extraction		70–72% extraction*		85% extraction	70% extraction [illegible]
	Mean	Range	Mean	Range	Mean	Range	Mean	Range		
Vitamin B_1	0.37	0.[illegible]–0.46	0.29	0.2[illegible]–0.[illegible]	0.21	0.1[illegible]–0.39	0.08	0.06–0.10	0.31	0.1
Riboflavine	0.12	0.09–0.1[illegible]	0.07	0.0[illegible]–0.0[illegible]	0.06	0.0[illegible]–0.07[illegible]	0.0[illegible]	0.03–0.06	0.05	0.[illegible]
Nicotinic acid	[illegible]	4.2–7.2	2.00	1.[illegible]–2.[illegible]	1.60	1.2–2.0	0.80	0.60–1.0	2.[illegible]	1.[illegible]
Iron	[illegible]		2.1		1.65		1.[illegible]		[illegible]	1.70

* Figures supplied by the Ministry of Agriculture, Fisheries and Food. The figures for flour of 70–72% extraction are from analyses made before the war.

† Figures derived from the report on the feeding trials in Germany (*Spec Rep Ser med Res Coun Lond* 1954 no 287).

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[4] Ministry of Food. Report of the Conference on the Post-War Loaf. Cmd 6701 H.M. Stationery Office 1945.

[5] Widdowson, E. M., McCance, R. A. Studies on the Nutritive Value of Bread and on the Effect of Variations in the Extraction Rate of Flour on the Growth of Undernourished Children. *Spec Rep Ser med Res Coun Lond* 1954 no 287.

‡ Riboflavine was an exception.

EFFECT OF TETRAC ON PLASMA CHOLESTEROL LEVEL OF A EUTHYROID SUBJECT

Tetrac therapy	Date (1955)	Plasma cholesterol (mg per 100 ml)
	Oct 19	245
	„ 20	245
6 mg daily	„ 25	265
	„ 27	225
	„ 29	188
	31	212
	Nov 2	230
	„ 4	224
	6	208
	8	205
9 mg daily	9	
	„ 10	192
	„ 13	176
Stopped	15	170
	„ 17	215
	20	191
	23	255
	25	255
	29	238
	Dec 6	250
	12	250

time the B M R and the serum cholesterol level had returned to normal values, although the patient was not yet clinically euthyroid The dosage was increased to 2 mg 6 hourly, further improvement took place within 48 hours, and the patient became clinically euthyroid after two weeks on this dosage The dosage was increased to 2 5 mg 6 hourly for 4 days, with slight further subjective improvement At this stage L thyroxine 0 3 mg daily was substituted for tetrac A bone graft for an ununited fracture of the ulna was performed before she was finally discharged from hospital six weeks after the start of L thyroxine therapy Although she showed only a slight tendency to relapse when tetrac was discontinued, there was a delay of two months before the full therapeutic response to thyroxine was obtained The operation may have been partly responsible for the delayed response

Effect of Tetrac in Euthyroid Subject

Tetrac was given in a dosage of 2 mg 8 hourly for 16 days, after which the dose was increased to 3 mg 8-hourly for a further 6 days A sensation of warmth was experienced about half an hour after the dose, except when it was given in a capsule There was no change in the peripheral circulation, and no other symptoms except intermittent headaches were noted The body-weight remained constant throughout the period of observation except for a transient increase during the initial 48 hours, and no change in pulse-rate or blood-pressure was noted The withdrawal of tetrac gave rise to general malaise, which lasted about a week, and persistent headaches The plasma-cholesterol level was significantly depressed from an initial mean value of 250 mg per 100 ml to 170 mg per 100 ml and returned to its original value a week after tetrac was stopped The values are given in the accompanying table

Discussion

A patient with myxœdema was given tetrac in gradually increasing doses and became euthyroid on a dose of 8 mg daily No attempt to assess the effect of a single intravenous dose was made, because of the previous history of cardiac failure and the unknown potency of this substance It was to be expected that tetrac would have a rapid metabolic action in myxœdema because a single dose raised the metabolic rate of thyroidectomised rats within two hours (Thibault and Pitt-Rivers 1955) A therapeutic response after each increment in the dose was observed within about 48 hours It is unlikely that any sudden change in thyroid status would have been detected with thyroxine given in comparable dosage The absence of a latent period of action implies a rapid rate of degradation, and preliminary observations with ^{131}I-labelled tetrac indicate that the disappearance-rate from plasma may exceed that of triiodothyronine If these observations are confirmed, it may be assumed that equilibrium would soon be reached in response to any alteration in the administered dose, and on the basis of the results obtained in this patient 8–10 mg of tetrac is equivalent to 0 3 mg of L-thyroxine The potency of tetrac in myxœdema is therefore about a thirtieth of that of L-thyroxine

The effect of tetrac on the plasma-cholesterol level of a euthyroid subject is of some interest Strisower et al (1954) have investigated the depression of the plasma-cholesterol level in response to the administration of thyroid hormone They found a significant fall in the plasma cholesterol level of four healthy people given gr 3 of thyroid extract (*U S P*) daily for 2–3 weeks It is surprising that the plasma cholesterol level fell on a dose of tetrac which appears to be less than that required for replacement therapy

It was thought worthwhile to observe whether another quick-acting thyroxine analogue affected the plasma cholesterol level of euthyroid people in a similar way There was no apparent alteration in two such people given triiodothyronine 0 06 mg daily for 10 days, and, when the dosage was increased to 0 12 mg daily for a further week, no significant depression of the plasma cholesterol level was found, although toxic symptoms developed at this level (I J L Goldberg, and A W G Goolden, unpublished) The effect of tetrac on the plasma-cholesterol level in other conditions associated with hypercholesterolæmia is being further investigated

Summary

A patient with myxœdema was given tetrac orally in gradually increasing doses The plasma-cholesterol level and the B M R reverted to normal, and a clinical remission was obtained on a dose of 8 mg daily The latent period of action appeared to be short On the results obtained in this patient it is estimated that the potency of tetrac is about a thirtieth of that of L-thyroxine

A euthyroid subject was given tetrac in about the same dosage as the patient A significant fall of the plasma-cholesterol took place on a dosage less than that required for replacement therapy

I am indebted to Dr R Pitt Rivers, F R S, of the National Institute of Medical Research, for the supply of tetrac, and to Dr I G Gilliland, of the Postgraduate Medical School of London, for permission to treat his patient I wish to thank the personnel of the 7520 U S A F Clinical Laboratory for plasma cholesterol estimations, and Miss Judith Chambers for B M R estimations

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" It is interesting to consider how much warmer a family environment the working class baby enjoys in this country, compared with an infant in a better class home The one lives in the centre of the kitchen, which is the centre of family life, and is rarely left alone, in nine cases out of ten he spends the interval from the 6 p m to 10 p m feeds, being nursed and played with, handed round the family circle If mother is ill, or expecting another infant, father frequently takes a week off work and looks after the family In the better class home, 6 p m is a sacred hour at which the infants must be placed in their cots upstairs, after a day spent lying in the garden contemplating the trees, with a brief play-time after tea Father rarely sees his infant for his hours are long and his work responsible he expects to be free to spend his evenings in cultural pursuits beyond the scope of the young If mother is ill, help has to be hired or acquired in some way, as it never even occurs to the father to put his duty to his family before his duty to the community"—Dr BEATRICE WATTS, *College of General Practitioners Research Newsletter* no 11 May, 1956

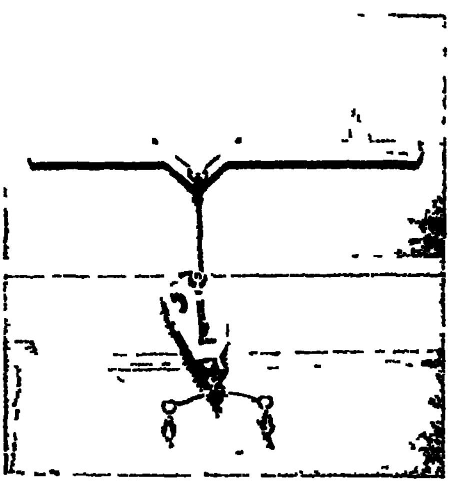

Fig 3—Traverse beam, geared chain hoist, and coat hanger bar

The 'Beem' bed, designed by an American physician, is a more ambitious and expensive piece of furniture (*Nursing Mirror* 1955). It has appropriately been called the "push-button" bed. Tests made in the U S A suggest that there is a saving of 46% of the nurses' time during a *twenty-four-*hour spell of its use. It comprises a self-contained stretcher, a flush toilet, two cabinets for linen, and push-button control within reach of the patient's hand.

Allen (1954) has patented for incontinent patients a simpler bed incorporating a movable centrepiece over a compartment containing a bedpan.

Turner (1954) describes a more elaborate suspended plaster bed frame used at Doncaster Gate Hospital, Rotherham, Yorks. Frames of this type have been specially designed for spinal cases, and the aim has been to make the whole unit mobile and so arranged that the patient can use the various movements at will.

The Standard Sales Co Ltd, Maidstone Building, 74/76, Borough High Street, London, S E 1, manufacture an exceptionally light and mobile hoist (fig 1) operated hydraulically and provided with a safety slow-release valve. The hoisting arm is hinged to the main pillar and the trolley wheels are mounted on a tubular base whose arms can be closed to a minimum of 26 inches, so that the machine can pass through the doorways of a private house. These tubular arms can be spread apart to admit the widest type of invalid wheel chair. Various accessories include canvas or nylon slings for use in a bath or with an aperture for toilet purposes, and an elaborate chair with rests for legs, back, and arms (fig 2). By a simple drill described by the maker a single attendant can prepare a patient, lift him from the bed and lower him into a chair in not more than 5-7 minutes.

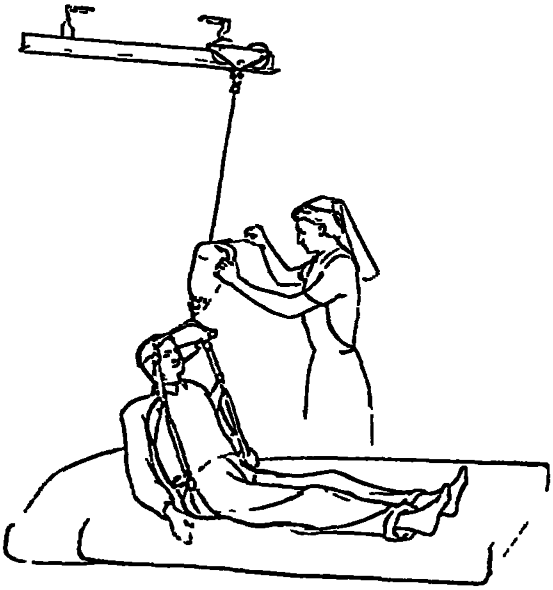

Fig 4—Adjustment of harness

Recently Prior (1956) has described a bed crane specially designed by Mr James Genet, senior orthopaedic technician at Wellington Hospital, for a patient who for six years could not lift herself out of bed or on a bedpan without help. The machine incorporates an ordinary *motor-car hydraulic jack, and the patient* by working the handle can lift herself off the bed or wheel chair and lower herself as necessary. The cost to make it is about £23. The design is not covered by patents of any kind and is available for any hospital to copy.

A New Device

We owe these machines to the efforts of those in attendance on the helpless. A recent device however is of special interest in that it is the invention of a patient, M Watson, a victim of severe poliomyelitis causing extensive paralysis of the muscles of the trunk, almost all the muscles of the arms, and all those of the legs, has devised, with the help of a builder, a machine which enables a single attendant to move him with ease and comfort for every general and special purpose connected with nursing and with no more effort than is necessary to wind an easily worked handle.

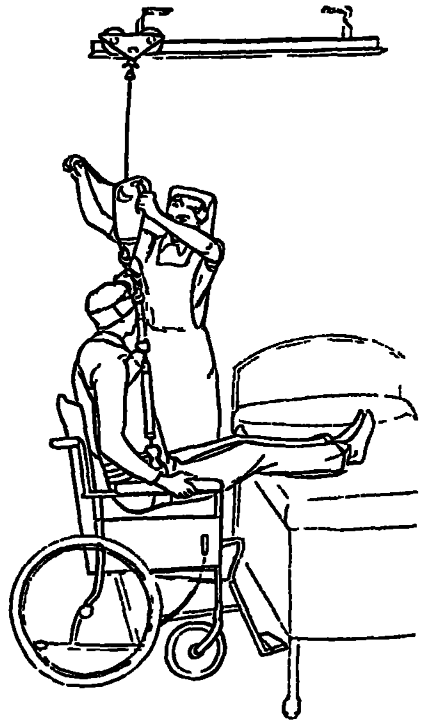

Fig 5—Transference from bed to chair

The webbing harness for attachment to the patient resembles in its general pattern that of most such appliances, but the special features which make it unique in its efficiency and handiness are the use of a traverse beam attached to the ceiling and a geared chain hoist. The beam allows easy lateral movement not only from bed to chair, commode or bath and back, but also, when the patient is in a general ward, transport with minimal assistance from one bed to another limited only by the length of the beam. Indeed if the beam is extended sufficiently the hoist could be used for transport along a corridor to a bath without much difficulty. The geared chain hoist is an adaptation of that used in garage and workshops for raising motor engines.

Fig 3 shows clearly the simplicity and clean line of the appliance unencumbered by vertical upright or a multiplicity of pulleys and ropes which hinder access to the patient for nursing or feeding. Figs 4 and 5 show, in two stages, the procedure of 'bridging the gap' from bed to chair by a helpless patient with the aid of only one attendant. Many other applications of the apparatus easily suggest themselves including lifting for attention to the back, use of a bedpan, insertion of an air pillow, remaking the bed for a helpless

There was also some irregularity of function of his stomach, probably due to the hiatus hernia

The past history and the family history were both negative

Comments

These two cases are put on record to draw attention to the necessity for a full investigation of the œsophagus when pain, which clinically appears attributable to coronary disease, is not associated with any other abnormality, whether clinical, electrocardiographic, or radiological

The proof that in these two cases the pain was œsophageal and not coronary in origin is wanting On the other hand, proof that the pain was coronary is equally wanting Definite knowledge could be obtained only by necropsy, and if the symptoms were in fact due to the œsophageal lesions, it is likely to be unobtainable for many years What is certain is that in each case there was an organic œsophageal abnormality , and we know that " anginal " pain can be a manifestation of œsophageal disorder

The œsophageal condition should be treated by advice about the proper mastication of food, by a low-residue diet, by prescribing aluminium hydroxide or bismuth before meals, and belladonna in full doses, and by raising the head of the bed on nine inch blocks The complete disappearance of symptoms after such treatment would argue for an œsophageal rather than a coronary origin

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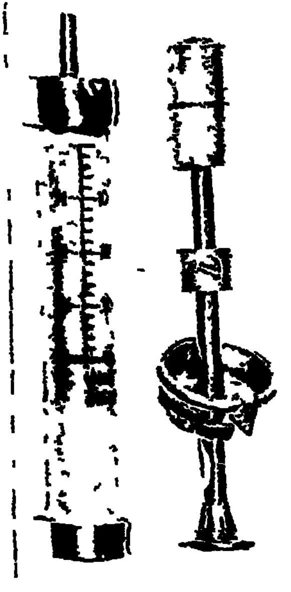
New Inventions

A CHEAP SYRINGE STOP



THERE has long been a need for a cheap and convenient syringe which can be used safely by those with poor eyesight and others who are incapable of drawing accurately up a solution into a syringe

The adjustable syringe stop illustrated appears to meet these requirements It consists of a plated brass collar with a grub-screw The collar can be slipped on to the plunger of any glass-metal syringe and fixed in a chosen position with a screwdriver

Its advantages are that the collar cannot be moved accidentally but is nevertheless easily adjustable by the simple expedient of loosening the grub-screw A syringe fitted with such a collar is cheaper than any other stopped syringe on the market, the collar can be made for a few pence and, if the syringe breaks, can be transferred to any other glass-metal syringe

The collar was made for me and is obtainable from Messrs Whitelaws, 44 Great North Road, Newcastle upon Tyne I am very grateful to Dr C C Ungley and Dr R E Irvine for their help and encouragement

Royal Victoria Infirmary,
Newcastle upon Tyne

P W R M ALBERTI
Medical student

Reviews of Books

The Practice of Medicine

JOHN S RICHARDSON, M V O, M D, F R C P, physician, St Thomas's Hospital, London London J & A Churchill 1956 Pp 1076 40s

MANY students, if asked what they seek most in a textbook of medicine, would probably say, clarity and brevity and they might add that if the writing could have interest as well, so much the better One virtue which students seldom seem to call for, and perhaps rarely feel the need for until they have qualified, is attention to detail and the avoidance of vague generalisations Unfortunately examiners sometimes have a tiresome habit of asking meticulous questions which require exact answers, and the new text which Dr Richardson has edited will arm students against such questions, besides appealing to them on other grounds as well

It is written by fourteen contributors, of whom half are teachers at St Thomas's Hospital, and all may fairly be regarded as belonging to the younger school The writing throughout is clear and up to date There is no padding and for the most part the teaching is firm and authoritative indeed, in places, it may be too brief, and of necessity some subjects receive rather scant mention

It is perhaps significant of our times that psychiatry occupies some 150 pages, while dermatology is omitted as a special subject and the alimentary tract receives only 15 pages—which have a rather defeatist and "passed to you" attitude towards such mainly surgical conditions as carcinoma of the œsophagus and colon The constructive and even optimistic 10 pages and 8 illustrations on occupational diseases of the lungs are remarkably well done There is an excellent short chapter on tropical diseases, and the up to date sections on allergy, collagen diseases, and venereal diseases are also prominent

The index is good and there are useful appendices on, for example, diets, and normal laboratory values It is a notable achievement to produce a book of this size at this price

The authors have not hesitated to express themselves forcibly and it is refreshing to find almost throughout a brisk and practical attitude, with here and there a spark of humour, and a refusal to offer those unconvincing explanations which tend to get perpetuated from textbook to textbook This is a book which undergraduates will find much to their liking

Counseling in Medical Genetics

SHELDON C REED, director, Dight Institute for Human Genetics, University of Minnesota Philadelphia and London W B Saunders 1955 Pp 268 28s

THE Dight Institute of the University of Minnesota was one of the earliest departments to establish a clinic for advising would-be parents on the risks to their children Like some other American genetic counsellors, Dr Reed was trained as a geneticist and is not himself medically qualified Over the course of years, however, he has accumulated considerable clinical experience of the medical conditions in which genetic factors are important, and he has the help of a clinical colleague

In this book he aims to show doctors and the lay public something of the scope of genetic counselling There is an excellent chapter on the philosophy of counselling In common with those doing similar work in America and this country, Dr Reed's practice is never to make decisions for his patients, but to advise them as precisely as possible on the risks and at the same time to put the matter into perspective for them The actual conditions he considers in detail are all common ones, for which in his experience parents often seek advice—mental defect, psychosis, and some of the congenital malformations Some illustrative case histories are given at the end of each chapter Information on the rarer conditions is given in an appendix, which is taken from a recent paper by Dr F C Fraser, of Montreal

This is not intended to be a textbook and anyone wanting information on a particular condition, with no

The council considered in camera the question of the admission to examinations held by licensing bodies of practitioners whose names have been erased from the Medical Register

On resumption in public, Dr J P HEDLEY, the senior treasurer, presented the report of the finance committee In 1955 total expenditure was £7948 greater than in the previous year, income exceeded expenditure by £3926 The increased expenditure was almost wholly attributable to a special allocation of £5000 towards the heavy expenditure which was at present being incurred on the visitation and inspection of examinations and the visitation of medical schools, and an increase of about £2745 in fees and allowances paid to members in accordance with revised arrangements approved by the Treasury

Dr H GUY DAIN presented the report of the pharmacopœia committee He said that the British Pharmacopœia Commission was preparing lists of drugs to be added to or omitted from the *British Pharmacopœia* in the 1958 edition The omission of a drug from the *Pharmacopœia* did not preclude its inclusion in the *Codex*, and some drugs left out last time were to be included this time, indicating that ideas of usefulness might change even in five years

Medical Disciplinary Committee

The committee began its session on May 30, under the chairmanship of the President There is to be an additional session in July

APPLICATION FOR RESTORATION

William Arthur Chanmugan Nason made application for the restoration of his name to the Register The application was rejected

FURTHER POSTPONEMENT

William Frank Cruickshank, registered as of c/o Milne, Brown Cottage, Westmuir, Brechin, Angus, M B Glasg (1935), did not appear for an adjourned judgment and was not represented In May, 1954, he had been found to have been convicted of being drunk and disorderly and to have been guilty of failing to visit or treat patients neglecting over a considerable period his duties as a medical practitioner under the National Health Service, and disregarding his personal responsibilities to patients Judgment was then postponed for a year, but last May the committee found that the evidence so far received concerning his habits and conduct would not warrant it in discharging the case and judgment was further postponed until the present session

Mr G J K Widgery solicitor to the council read a letter in which Dr Cruickshank stated that he was unable to attend Since judgment had been postponed last May, Mr Widgery said there had been a further conviction, when Dr Cruickshank was fined £15 and ordered to pay costs for being under the influence of alcohol to such an extent as to be incapable of being in charge of a car

In order to give Dr Cruickshank a further opportunity of being present, the committee postponed the case until its meeting in July "In his own interest he should be present on that occasion," added the chairman

CONVICTION FOR ASSAULT

Convictions for assaulting Isabella Gourlay Nicol or Whitelaw and conducting himself in a disorderly manner and committing a breach of the peace were admitted by *James Watson Richmond*, registered as of Rosskeen Kelty, Fife M B Glasg (1929) He had been fined at the Sheriff Court of Fife and Kinross at Dunfermline £12 on the first charge and £4 on the second with the alternative of 40 days and 20 days imprisonment to run consecutively

Mr Widgery recalled that Dr Richmond was convicted of similar offences in 1952 relating to three young women who were patients At the same Sheriff Court he was fined £25 He appeared before the committee in November, 1952, when he said that he was having treatment Judgment was postponed for a year and then the case was dismissed

The Chairman announced that the committee took the gravest view of a conviction of this sort and this was the greater because of the earlier convictions of a similar nature but in order to give him one further opportunity of reconsidering his habits and conduct it had postponed judgment for two years, until May, 1958 He would be required to appear in May, 1957, and before that date he would be asked to furnish the names of colleagues and other persons of standing to whom the committee could apply for testimony as to his habits and conduct

ADULTERY

Ernest Benjamin Dawe, registered as of 235, Downham Way, Bromley, Kent, M R C S (1941), was charged with an improper association with a patient, which had led to his being found guilty of adultery in the Divorce Court The Chairman announced that the committee found Dr Dawe guilty of infamous conduct in a professional respect and ordered his name to be erased from the register This is subject to appeal within 28 days

John William Pooley, registered as of Nunswell House Boney Hay, Walsall, Staffs, M B Birm (1939), appeared on a charge of infamous conduct in a professional respect

Mr John Hobson, instructed by the council's solicitors, read a letter from Dr Pooley admitting that he had had intercourse with a young woman who was on his list and that he was the family doctor of her father, but denying that he stood in professional relationship to the young woman and stating that it was untrue that he gave her medical treatment Intimacy arose solely from her being a domestic servant in his house, the fact that she was on his list was wholly irrelevant

At the close of the case for the complainant Mr N Leigh Taylor, solicitor of Messrs Hempsons, submitted that there was insufficient evidence of which the committee could find Dr Pooley guilty, and that the facts were not such as to constitute infamous conduct in a professional respect Was it possible to say that merely because a person was on a doctor's list there was then a professional relationship? Suppose a person went on a list and had all his treatment privately Mr Hobson had referred to Dr Pooley's obligations under the regulation to treat the young woman as a patient, but that liability only arose if she asked for treatment, and there was no evidence that she did so

The committee found Dr Pooley not guilty of infamous conduct in a professional respect

Frank Stanley Mellows, registered as of 63, Hatherley Road Cheltenham, M B Camb (1948), admitted committing adultery with a patient The committee found him guilty of infamous conduct and ordered his name to be erased He has 28 days in which to appeal

DRUG OFFENCES

John Millar Matthew, registered as of 176 Farley Road, Selsdon, Surrey, M B Camb (1932), was charged with a conviction in 1948 of failing to keep records of dangerous drugs, when he was fined a total of £300, with convictions in 1954 of unlawfully prescribing, supplying and possessing dangerous drugs when he was bound over in the sum of £5 for three years, and with a conviction in February, 1956 at the Stevenage Magistrate's Court of driving a motor car when under the influence of drink or drugs, when he was fined £20 ordered to pay £27 1s costs, and disqualified from driving for five years

In order to give Dr Matthew an opportunity to overcome the tendency which led to the convictions, the committee postponed judgment for a year

NAME NOT ERASED

In view of the satisfactory information concerning his habits and conduct which the committee was gratified to receive it did not direct the erasure of the name of *Ralph Martin Ca*, registered as of 71, Gillott Road Edgbaston, Birmingham, M B Birm (1934) Judgment had been postponed for a year to give him one further opportunity of overcoming his tendency to abuse of dangerous drugs following a conviction for procuring dangerous drugs in 1953

MOTORING OFFENCES

William James registered as of Parc y Ddol College Road Carmarthen M R C S (1912) had had judgment postponed for a year He had been convicted in 1953 and 1955 of being in charge of a motor vehicle while under the influence of drink When judgment was postponed last year the chairman said that Dr James should make every effort to be present when his case was again considered

The Registrar was not directed to erase Dr James's name

DANGEROUS DRUG CONVICTIONS

Joseph Hirschmann registered as of Upper House Clunbury Craven Arms Salop, M B Dubl (1920) had had judgment

Her Pride and Joy

And a great deal of the credit belongs to YOU!

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The food of choice? Breast milk, of course Failing this, a Milk Food of the highest quality

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Surgeon Lieut Commander **John Stuart Pepys Rawlins**, B M Oxfd, R N

M B E (Civil)

James Kenneth Craig, M D Dubl
Provincial medical officer, Central Province, Kenya

Rosina Gwen Dabb, M B Edin
Medical officer in charge of Church of Scotland Mission Hospital, Blantyre, Nyasaland

Albert Benjamin Foo, L R C P E
Maternity and infant welfare officer, Municipal Infant Welfare Centre, Georgetown, British Guiana

Joan Inman Franklin Adams, M B Lond
For services in Jordan under the Save The Children Fund

William Scott, M B Glasg
Admiralty surgeon and agent and medical officer, Royal *Navy Torpedo Factory, Alexandria*, Dunbartonshire

William Alexander Sloss, M B Edin, F R C S E
Member of the committee of management of the Ballarat and District Base Hospital, State of Victoria, for public services

Public Health

HEALTH VISITING

Working Party's Report

The working party which has been inquiring into health visiting has now issued its report[1] The working party was set up under the chairmanship of Sir Wilson Jameson in 1953 by the Ministers of Health and Education and the Secretary of State for Scotland * Its terms of reference were "to advise on the proper field of work, the recruitment and training of health visitors in the National Health Service and School Health Service" Its report is part of a review of the work, recruitment, and training of domiciliary visitors in the field of health and welfare An inquiry into the work, recruitment, and training of social workers in this field is now proceeding, under the chairmanship of Miss Eileen Younghusband

FUTURE WORK OF HEALTH VISITORS

The working party concluded that work with mothers and young children, with school-children, and with the tuberculous will continue to be important but that the emphasis will change More attention should be paid by health visitors to the mental-health aspects of maternal and child care and more help given with the problems of handicapped and maladjusted school-children On the other hand, inessential duties must be avoided and time concentrated on essentials The same health visitor should be responsible both for the young child at home and the child at school

The health visitor must be closely associated with the work of the general practitioner not only in her traditional fields but in relation to care and aftercare generally She could come to be useful in any part of a family doctor's practice, in the exercise of her proper functions The working party note with approval the wide support for a domiciliary team of which the family doctor would be the clinical leader, and they believe that the health visitor should play a central part in such teams

In all her work, the health visitor should have regard to the psychological aspects of what she is doing, and especially in her work with mothers and young children she can make an important contribution to mental health It is unlikely that the *problems of established* mental illness will be in her competence

It follows from her association with general practice that the health visitor may be in touch with a vastly wider range of families than hitherto While the working party reject the possibility of an omnicompetent family visitor, they feel that the future health visitor can serve a general purpose in her family visiting She would act as a common point of reference and source of standard information, a common adviser on health teaching, a "common factor" in family welfare—and to that extent a general-purpose family visitor

THE PRIMARY AIM

Primarily, the report says, the health visitor's functions are those of health education and giving such social advice as will enable the family to benefit from her advice on health She will carry out her other functions of cooperation with other workers incidentally to her main purposes She is not to be described as a social worker nor, in general, to practise as a nurse or midwife, and a recognition of her proper status will be important if her work with family doctors is to be fully effective Again, because of the new link with general practice the health visitor will increasingly be concerned with families where some form of social action is needed She should be trained, however, to recognise the limitations of her skills in this direction, to see that the appropriate worker is put in touch with the case, and to cooperate in any way required

TRAINING

The working party regard as undesirable, but for some *time inevitable*, the *present three-part training in* nursing, midwifery, and public health Midwifery training could be replaced by a special three-month course Nurse-training is open to criticism as a preparation for health visiting, but it is still the most convenient means of gaining the essential medical background, and the objections are not insuperable On the other hand, the total length of training—four years or four years and three months—is likely to deter school-leavers and others who, the working party hope, will be eventually the main source of recruits They therefore hope that training for health visiting will prove a fruitful source of experiments designed to reduce the length of nurse-training—the main stumbling-block They *strongly support* the institution of integrated training courses embodying all the elements of the three trainings essential to health visiting, and designed for health visiting as a career

The public-health element in the training should take between nine months and a year or the equivalent It should aim not at covering the whole possible field and producing a finished worker but at introducing the future health visitor to the principles and including as much practice in their *application as possible* Special attention should be paid to the mental-health aspects of her work with families, to the *problems of* cooperation with other workers, and to the techniques of health education

Arrangements will be necessary for providing further training and retraining of existing staff for their new rôle If the report's suggestion of a "group adviser" grade for health visitors of exceptional ability is accepted, diploma courses will be needed for future group advisers

Organisation of Training

The working party recommend the establishment of new central training bodies—possibly based on the organisations of the present examining bodies The new bodies would prescribe the syllabus and arrange examinations, constitute training centre committees to run courses of training, and approve their arrangements Some 25 to 35 courses would be needed *each year, more than one* being run by one committee if necessary An important function of committees should be the final selection of students

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[1] An Inquiry into Health Visiting Report of a working party on the field of work, training and recruitment of health visitors H M Stationery Office Pp 183 6*s* 6*d*

* The other members were Dr A Beauchamp, vice chairman, Birmingham Executive Council, Alderman Mrs K Chambers, chairman, Bradford Health Committee and Bradford Executive Council, Miss E W Himsworth, county nursing officer, Midlothian and Peebles, Miss E Stephenson, chief nursing officer Newcastle upon Tyne, Dr J F Warin, medical officer of health and principal school medical officer, Oxford

THE LANCET
LONDON SATURDAY, JUNE 9 1956

The Millers Decide

"In this country," said the Medical Research Council conference, "bread is the largest and most important single item of the diet, providing between one-fifth and one-third of the calories and protein and a high proportion of other essential nutrients ' As a protective food, bread is particularly valuable to people who cannot afford a good mixed diet, and therefore to children of large families Hence a reduction in the nutritional value of bread may have consequences which, though not readily perceptible, are none the less grave, and in authorising such a reduction the Government risk damage to the public health The decision by which they are now abandoning 80%-extraction National flour in favour of "enriched ' or "fortified " flours of a lower extraction has the backing of a highly expert panel,[1] but it is contrary to the opinion of their own medical advisers and of the M R C conference whose evidence we publish on p 901 Moreover, the scientific weight to be attached to the panel's conclusions is lessened because these seem to be based on administrative rather than purely nutritional considerations—on what the panel thinks practicable rather than what it thinks desirable The report was in fact written in the knowledge that the flour-millers are determined that bread shall be white, and have already abolished National flour by quietly altering the composition of what is sold under that name The extraction-rate of National flour has already come down generally from the 80% (or its equivalent) specified under the Flour Order 1953 to about 74%, for enforcement of the order has been prevented by the need to allow a wide range of variation in the vitamin content of high-extraction flour—which makes it very hard to prove that a particular batch is at fault In face of the "continuing fall" in the vitamin-B_1 and nicotinic-acid content of National flour since decontrol, which it attributes primarily to "deliberate disregard of the intention of the Flour Order," the panel evidently feels that we should cease to bother about extraction-rates (which only the millers can control) and should make sure, by enforceable regulation, that they enrich their white flour with at any rate the three "token nutrients '—iron, nicotinic acid, and vitamin B_1 The national policy of high extraction—adopted on grounds both of economy and health—is to be replaced by a weaker policy of fortification The millers have virtually settled the matter for themselves—though it must be pleasant for them to have the Government's approval

The degree of freedom that ought to be allowed to the man who processes and distributes food is going to need further thought On the one hand, the public often has to thank him for making his product convenient, cheap, and readily transportable, but on the other hand there is no doubt that these qualities assume a higher place in his calculations than the damage he may be doing to the nutritional value of the food The flour-millers, for example, have earned respect by their enterprise and many of their services to the nation, but from the standpoint of the nutritionist their treatment of bread has been irresponsible To nutritionist and layman alike, it seems obvious that before someone, for reasons of convenience, alters the character of a staple food, the onus lies on him to show that the change at least does no harm but it sometimes seems as though the modern food-processor thinks himself entitled to do what he likes with his product—after which the onus lies on someone else to prove his process dangerous or damaging At the time when the flour-millers first produced their chemically treated low-extraction white flour, they were not alone in the illusion that this was a genuinely superior product but it is harder to forgive the tenacity with which they have stuck to their original mistake, and have resisted efforts to make their flour safer and more nutritious The onus rested chiefly on Sir **Edward Mellanby**, they felt, to show good cause why they should not continue to use a flour-improver, agene, which causes fits in dogs, and though he won at last a posthumous victory, and the use of agene was forbidden, we do not know how confidently we can rely on the substitutes now in use In the late 1930s, after the worst period of unemployment, it had become clear that impoverishment of the flour had harmfully reduced its content of vitamin B_1, and its enrichment with this particular vitamin was proposed As a further concession, it later had to be admitted that people relying on the 72%-extraction flour which was current before the war might be missing some of the iron or nicotinic acid they needed from their bread so these have now been added And no doubt, as knowledge grows, and the millers are gradually shifted from their positions, we shall be allowed further instalments of the nutrients which they have removed

The expert panel's report sets out the arguments very ably and burkes none of the issues Why then should it come down on the side of supplying the public, henceforward, with fortified white bread? First, perhaps, because the panel was too ready to believe that the public (as well as the bakers and the millers) are eager for low-extraction flour Secondly, because the panel thought the industry possibly right in saying that if people can obtain only bread made from 80%-*extraction* flour they will eat less bread and more of other manufactured foods which may be less nourishing Thirdly, because, with *fortification*, we know just where we are a true 80%-extraction flour may give a more widely spread insurance against possible, but as yet unproved, deficiency in the diet, but the 70%-*extraction enriched flour* "gives a more *certain* cover against possible deficiency of the three ' token ' nutrients with well recognised deficiency states" These are substantial reasons, and so is the fact that the millers have virtually ignored the Flour Order and cannot easily be made to obey it Yet with all respect we say that the panel has given the wrong advice As a result of that advice, bread is to be slightly more reliable as a source of iron, vitamin B_1, and nicotinic acid, but it will contain less of certain in a subacute form, or (c) clinical recovery with the later development of cirrhosis of the liver The ætiology has not been finally established but the evidence points to certain bush teas, particularly those made from *Crotalaria retusa* and senecio as being important factors Cooperation with the veterinarians has proved profitable

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[1] Report of the Panel on Composition and Nutritive Value of Flour Cmd 9757 H.M Stationery Office 1956 See *Lancet* May 26, 1956 p 800 The members of the panel were Sir Henry Cohen F R C P (chairman) Prof A C Chibnall, F R S Prof J H Gaddum M R C S F R S, Prof R A Morton F R S, and Prof L J Witts F R C P

The pathological and histological features were presented by Dr G **Bras** The essential change, which he was *the first to describe*, is occlusion of the small hepatic veins by intimal swelling, with resultant centrilobular *congestion and death of the liver cells* Injection of the hepatic veins with radio-opaque material has demonstrated and confirmed the site of the obstruction very beautifully The vascular change is not found elsewhere in the body In the chronic stage the cirrhosis which develops is non-portal in type, as distinct from Laennec cirrhosis

VOMITING SICKNESS

The pharmacological and biochemical aspects of vomiting sickness and its relationship to ackee poisoning[2] were presented by Dr P **Feng** and Dr S J **Patrick** This condition develops acutely, mainly in young children Vomiting is not a striking feature but clouding of consciousness always occurs and may proceed to coma Severe hypoglycæmia is a constant feature Two polypeptides, hypoglycin A and B, have been isolated from the ackee, and they produce severe hypoglycæmia in animals In these animals the outstanding clinical features are vomiting, drowsiness, coma, and death Rats fed on a low-protein high-carbohydrate diet ("a Jamaican type diet") are more sensitive to hypoglycin A than rats fed on a normal diet In the rat, hypoglycin A reduces the total carbohydrate stores of the body Liver glycogen falls almost to zero, but muscle glycogen is not greatly affected Synthesis of glycogen by the liver is impaired The ackee-poisoned rat converts very little radioactive glucose into muscle glycogen or fat and most is excreted as CO_2 Pathologically one of the most interesting findings is destruction of the α cells of the pancreas The ackee is probably only one of the factors responsible for this condition

A NEUROPATHIC SYNDROME

Prof E K **Cruickshank** discussed the clinical features of a neuropathic syndrome studied at the University College Hospital The four main features are (*a*) upper motor neurone damage, (*b*) damage to the first sensory neurone, (*c*) retrobulbar neuropathy, and (*d*) eighth nerve deafness The onset is from the second to the sixth decade and may be sudden or gradual The sex incidence is equal Maximum incapacity develops within a few months and the disease thereafter seems to be stationary The diet of the patients varies from good to very poor, but few show overt signs of vitamin deficiency or malnutrition A dietary factor is possibly responsible but there is no definite evidence of this No pathological material has as yet become available for study This, and the related condition of tropical amblyopia described by Dr D W A **Degazon**, are by no means rare in Jamaica, and constitute a public-health problem of some importance On the other hand, demyelinating diseases familiar in Europe, such as disseminated sclerosis, are very uncommon

SOME OTHER PAPERS

In the field of malnutrition, Dr E H **Back** outlined a nutritional survey amongst small farmers in Jamaica, Dr B L R **Symonds** described the clinical syndrome of "sugar baby" in Trinidad, and Dr J **Waterlow** discussed the assessment of protein deficiency in man

Mr R P M **Miles** described the high incidence of rectal stricture in the female in lymphogranuloma venereum, Mr J S R **Golding** gave a survey of bone and joint disease in Jamaica, emphasising sickle-cell disease as a cause of osteomyelitis Dr B B G **Nehaul** of British Guiana, described the clinical manifestations of filariasis, and Dr J A. **Tulloch** discussed certain aspects of diabetes which may be peculiar to the West Indies and outlined the investigations being carried out

FERTILITY AND STERILITY

The Second World Congress on Fertility and Sterility sponsored by the International Fertility Association was held at the Congress Palace of the Mostra d'Oltremare Naples, Italy, from May 18 to 26 It was attended by over 1100 people, representing 68 countries

Implantation of the Ovary into the Uterine Cavity

B S **ten Berge** (Groningen, Netherlands) discussed whether intra-uterine ovarian implantation should be resorted to in cases where both fallopian tubes are absent This procedure has been recommended by several gynæcologists, and pregnancies have occasionally followed, though only in a very small proportion of cases The gynæcologist should not perform this operation unless he is confident that ill effects are unlikely Harmful complications may include postoperative uterine fistula, which may cause leakage of menstrual blood, with formation of adhesions and resulting pain and discomfort A further danger is weakening of the uterine wall with rupture due to stretching during an ensuing pregnancy In 16 patients, in whom this operation was performed subsequent culdoscopic examination proved the absence of adhesions to date none of these patients have become pregnant

Organic Cornual Occlusion of the Tubes

V B **Green-Armytage** (London) said that it is not uncommon in subfertility cases to get a history of abortion before marriage or in the early years of marriage Very often in these cases there is cornual occlusion After excision of the occluded portions, he recommended surgical implantation of the terminal portions of the tubes, with the assistance of solid 'Polythene' rods these may be brought down into the vaginal canal and left there for six weeks

Plastic Operations on the Fallopian Tubes

J P **Greenhill** (Chicago, Ill) reported that, from the literature and personal letters from a large number of gynæcologists interested in plastic operations on the fallopian tubes, he obtained data concerning 2113 such operations There were 405 pregnancies (19%), or 1 pregnancy following every 5 operations There were only 313 living children or 1 living child after every $6\frac{1}{2}$ operations There was 1 ectopic pregnancy after approximately every 6 operations While the results are far better than they were twenty years ago, they are still far short of what they should be to justify indiscriminate plastic tubal operations Furthermore, a high incidence of tubal pregnancies follows these operations

Latent Genital Tuberculosis

I **Halbrecht** (Petah Tiqvah, Israel) investigated 170 cases of tubal occlusion in primary sterility In 68 of these cases, genital tuberculosis was discovered Cultures of menstrual and intermenstrual discharges were employed In 17 out of 27 cases which received combined treatment with streptomycin and *p*-aminosalicylate, there is no evidence of genital tuberculosis four to five years after the treatment

Duration of Function of Corpus Luteum

H H **Knaus** (Vienna) recalled that in 1929 he demonstrated that ovulation takes place on the fifteenth day before the succeeding menstruation, the activity of the corpus luteum normally persisting for fourteen days In cases of sterility, this activity does not last fourteen days, and in consequence, even when the ovum is fertilised, the conditions for proper implantation are not adequate There is no real essential regularity of the length of the menstrual cycle, but there is a real regularity of the activity of the corpus luteum, have a relatively greater effect in depressing blood-cholesterol than in raising B M R Thus, Dr GOOLDEN has shown that a dose of tetrac no greater than is required for the replacement therapy of myxœdema was capable of causing a sizeable drop in the blood-cholesterol of a euthyroid subject Similarly Dr TROTTER has shown that triac was able to lower the blood-cholesterol of 3 euthyroid subjects, without a significant increase in B M R He is hesitant, however, about ascribing these effects to the acetic-acid side-chain, because falls in blood-cholesterol of similar magnitude were produced with triiodothyronine Whatever the significant feature of the molecular structure may be, the fact remains that the new compounds show some promise of being able to lower blood-cholesterol without causing unwanted side-effects If further work confirms these observations, it might be possible to contemplate a large trial designed to test the proposition that lowering the blood-cholesterol will reduce the incidence of coronary-artery disease

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[2] *Ibid* April 14, 1956, p 529

Medicine in the Caribbean

SINCE the recommendations[1] of the Asquith Commission on Higher Education in the Colonies, and of its West Indies committee under Sir JAMES IRVINE, were published in 1945, a University College of the West Indies has been established in Jamaica with faculties of arts, science, and medicine A modern teaching hospital of over 300 beds has been built and staffed from this college, and its clinical instruction was recognised by the University of London as being of sufficiently high standard for the London M B (which was passed by 13 out of the first 15 of the college's students who sat the examination) Moreover, wide research has been put in hand and has already produced notable results, as a recent conference (briefly reported on p 909) reflects But this conference did more than demonstrate these achievements of the University College of the West Indies excellent contributions also came from members of the medical services of the different territories of the British West Indies—contributions which bring credit to the local government medical services and to those who have supported the work from this country and the United States

If the full significance of this medical conference is to be appreciated, it must be viewed against the geographical and social background of the Caribbean Many of us in Britain are apt to forget the enormous sea distances between the countries and islands which make up the British West Indies They form a vast semicircle, which covers over 2000 miles, starting on the central American mainland in British Honduras, and passing through the Cayman Isles, Jamaica, the many Leeward and Windward Isles, Barbados, and Trinidad, to end at British Guiana on the northern coast of South America We forget that the journey from Jamaica to Trinidad is roughly the same distance as that from London to Moscow or Istanbul Yet these scattered lands are closely linked racially, less than 5% of their peoples are of unmixed European descent, and the majority are African Negroes, with a small proportion of East Indians and Chinese They are also linked economically through their agriculture, all of them primarily grow sugar or bananas, with smaller quantities of citrus fruits (Trinidad stands alone in having a rich supply of oil and asphalt) A tropical climate modified by the closeness of the sea is common to them all, and they share too the same historical development It is hardly surprising, therefore, that they have the same medical problems

Anyone from Britain visiting a general hospital in the West Indies would be struck by the amount and variety of the diseases that can be studied there, but nearly always there are the dreadful complications of poverty and malnutrition to modify the clinical picture and hamper treatment Yet, superficially, the similarities to British medicine are perhaps more striking than the differences Typhoid fever, malaria, sickle-cell anæmia, lymphogranuloma venereum, and some specific effects of malnutrition (especially in children) would be the only unfamiliar diseases that the British doctor would commonly see in the general hospital And he would note with interest the extreme scarcity of emphysema, mitral heart-disease, and neurological conditions such as disseminated sclerosis, subacute combined degeneration, and tabes (despite the prevalence of syphilis) On the other hand, acute lobar pneumonia, paraplegia (often due to cervical spondylosis), acute rheumatic fever (in contrast to the rarity of mitral stenosis), hypertension and its complications, and (possibly linked with hypertension) eclampsia are common

The challenge has been ably taken up Malaria has been almost completely eradicated from British Guiana, and at the conference Dr GIGLIOLI described the long work that has led to this great success, to which he has notably contributed Again, the nature of Jamaican "vomiting sickness" has been largely elucidated[2], a new form of liver disease, called venous-occlusive disease, has been described and investigated, research in virus disease in Trinidad and in yaws in Jamaica has been extended, a start has been made at sorting out the neurological syndromes peculiar to the area, and further advances have been made in recognising the all-too-frequent effects of protein malnutrition It seems likely that medical research in the Caribbean may pay big and rapid dividends in the future Apart from the study of specific local diseases, there is a great opportunity for the epidemiological and community-survey approach What precisely is the peculiar distribution of steatorrhœa, and is it related to diet? Is the prevalence of hypertension really as great as it seems? How does the prevalence of hypertension or diabetes compare with racially corresponding groups in Africa? What is the prevalence, class, and locality distribution of the paraplegic syndrome which figures so largely in the neurology of the Caribbean? And there are many other absorbing questions Help in the elucidation of diseases common in Britain may well come from a study of the differences they show in areas like the Caribbean

The rapid fall in death-rate caused by the elimination or reduction of the killing diseases by chemotherapy has increased population pressure in nearly every West Indian island and aggravated the problems of

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[1] Commission on Higher Education in the Colonies H M Stationery Office 1945 See also West Indies Committee of the Commission on Higher Education in the Colonies H M Stationery Office 1944

[2] See *Lancet*, April 14 1956, p 429

In England Now

A Running Commentary by Peripatetic Correspondents

I TURNED thankfully from the chronic depressives, the neurotic necks, the itching unmentionables to the garden—to my potatoes, poking their tardy way up to the spring sunlight, the lettuces in urgent need of watering, the weed-covered borders already herbaceous to the eye of faith But I was followed by the tribe—two small girls and two small boys Eight small feet and eight small hands can undo much in a short time One of my daughters was soon hard at work pulling up lettuces She had been impressed by my transplanting efforts a few days before While I sweated pulling out innumerable weeds among the rows, I cast a friendly eye on my sons digging industriously at the other end of the patch "Let's plant them here," said one What, I wondered, was it going to be this time It soon transpired Triumphantly the seeds flew in all directions, some into the hole they had dug, many more on to the newly weeded potato patch They were dandelions

So Nature redresses the balance impious man presumes to disturb As in the surgery, so in the garden the best motto is "To watch and admire, not harm or destroy" Mrs Brown, late that evening, must have been impressed by the philosophical attitude of the doctor she had called to see her, as usual quite unnecessarily Had she known, the garden soil, still clinging to his shoes, was the clue

* * *

"I'm afraid you have the wrong number," my mother said in the determined voice of the slightly deaf I had telephoned to inquire after her health and was about to convince her of my identity, but she went on almost without pausing for breath

"Isn't it annoying the way they never take the trouble to get the right number for you? I should certainly complain to the operator if I were you My husband—I should say my late husband—always said people simply won't take the trouble these days Those operators on the telephone exchange have nothing to do but sit there and get the right numbers, but they always seem to get them wrong somehow And I expect you're a busy person, aren't you?"

Hurriedly I said, "Yes, I'm the wife of a busy doctor I haven't much time to spare"

My mother was plainly delighted "A doctor!" she exclaimed "Now isn't that strange, one of my daughters is married to a doctor She lives in Hertfordshire you do too! Well the world is a small place I wonder if you know my daughter She's next to the youngest I have five girls I did have three boys but unfortunately I lost them all Have you any children? One girl? My daughter, the one that's married to the doctor has one little girl What a strange coincidence! Actually her little girl is adopted Venetia, that's my daughter you know, lost her own baby boy but her husband thinks the world of this child He simply idolises her but then he would He's a most charming man His name is a household word here where I live You see before he married my daughter he had a practice here in the very road where I live It was the talk of the whole neighbourhood when they were married Actually they eloped Of course it was all very romantic but I can't say I was entirely pleased about it at the time After all, every mother wants to see her daughter married in white, doesn't she?"

I was about to scream into the telephone, 'Mother, how dare you tell all your business to a stranger?' when I realised it was an accusation I couldn't make and anyway I hadn't the chance She went on

'But as I said, he's the most charming man I don't know what I would do without him I certainly wouldn't ever have a night's sleep if it weren't for the tablets he gives me He's what they call Nature's gentleman, you've heard the expression haven't you?"

I mumbled something in a voice as unlike my own as possible and listened, fascinated while she continued

"Two of my other girls are married too But they are as unlike Venetia as it's possible for sisters to be Both very fair and if I may say so, pretty too Venetia isn't She's very dark I suppose she takes after my side of the family I don't mean to say she's ugly, far from it In fact only the oth day I came across a photograph of her when she was a ba lying naked on a rug kicking her chubby legs in the a I must show it to her some time Mothers aren't suppo to have favourites among their children but you can't he it When I had my duodenal ulcer, Venetia was the on one I wanted near me She was the greatest comfort to m And of course good looks aren't everything, are they m dear?"

Very hot, with a rapidly rising blood-pressure, said, 'I'm afraid I must go now" My mother was once concerned

"I'm afraid I've kept you too long I'm so sorry my dea but it's been so nice to have a chat I do hope you get yo number right next time"

I watched the clock and let a quarter of an hour sl by before I telephoned her again This time I left doubt as to my identity My mother said

"My dear, I've been thinking about you A charm girl just got on to me by mistake The operator gave her t wrong number and would you believe it, she's married to doctor and lives in Hertfordshire too I wonder if you kn her"

* * *

Wouldst taste the Elixir of Youth, Dr Faust? Th take a postgraduate course Dig out the old college sc the baggy flannels Lay in a stock of notebooks, gol blocked on the cover with the grand old motto *predicamento tuo non curo, Jack* There stands t geriatrics class of '56, huddled at the end of the wa waiting for the Chief Sister eyes them warily, at t first bar of "Come, boys, let's all be gay, boys!" s will move in among them with her terrible swift swo There's Flashman, stuffing a midday edition and bulldog pipe into the pocket of his tweed jacket, a there's Tom Brown, edging up to that vivacious brunet with the silver threads among the black "Golden da when you're young, golden days!" If Tom were not he he might be advising Mrs Peripatetic "Keep him bed a few days more, Mrs P, and a *very* light die *Cave*, chaps, here's the Chief Done those lines, Flash He never forgets

* * *

In recent *months*, the *attention* of pædiatricians h focused on a mysterious disease, hitherto unknown, t protean manifestations of which have been recognised forming the Davy Crockett syndrome *Pandemic* distribution, equally prevalent in both sexes, and w no respect for site or season, it has become increasin clear that a new clinical entity has appeared While t most florid examples of the condition are to be found childhood, a not uncommon secondary form of t syndrome also occurs in adult life

This fascinating disease may present in all manner guises and almost all the special *departments of a* hospit may meet with one or other of the many clinical variant In skin clinics, the characteristic coronal distribution the lesions extending band-wise to the skin of the cervic and upper *thoracic* spine, should give rise to no difficult Outbreaks of spring catarrh and hay-fever, in the absen of both spring and hay, may perplex ophthalmologists a E N T surgeons, whilst allergists may be misled by extr *ordinary reactions to scratch-testing* with the usu allergens Gastro-intestinal disturbances are not infr quent and a Davy Crockett trichobezoar is a recogni complication Some of the features of the syndrome hav been attributed to an increase in mouse-borne infectio on the grounds that the heavy demand for feline fur h left an insufficient number of cats to keep the *mou* population down to a sanitary level Several pædi tricians have expressed the view that enuresis, co stipation, and acidosis are also part of the syndrome, b the evidence is not convincing However, psychologic disturbances are certainly encountered and usually tak the form of outbursts of aggressive behaviour It h been shown that, in most cases such behaviour is due t the social inferiority consequent upon *not* possessing Davy Crockett hat

* * *

Overheard in Queen Square "You've passed — now you have to take the Harryplattic oath!"

thiopentone level was highest in those babies delivered at the earliest moment after maternal injection of the drug, and the level fell exponentially with an increase in the time before delivery Moreover, the maternal and fœtal serum levels of thiopentone at the time of delivery were approximately equal in every case, whatever the time between injection into the mother and the birth of the child The placenta apparently offers little or no barrier to the passage of thiopentone, and Crawford believes that the length of delivery after the induction of anæsthesia by a single small dose of thiopentone is of no significance

CAUSE OF HYPOGLYCÆMIC SYMPTOMS

Since 1924, when Cannon et al.[1] showed that insulin hypoglycæmia caused a release of adrenaline into the blood of animals, it has been generally accepted that adrenaline is largely responsible for hypoglycæmic symptoms in man The obvious difficulty in accounting for the sweating which is usually a prominent feature of hypoglycæmia, but which does not follow intravenous or intra-arterial injections of adrenaline,[2 3] could be overcome by postulating that adrenaline release was part of a general hyperactivity of the sympathetic nervous system, due to central stimulation by hypoglycæmia Though it is mediated by the sympathetic system, the innervation of sweat glands is cholinergic, and the abolition of sweating by atropine [4] and by hexamethonium [5] is compatible with this hypothesis But other explanations are not ruled out, and observations pointing to another mechanism have been accumulating Recently Weil-Malherbe,[6] using a chemical method of assay, recorded a drop in plasma-adrenaline after insulin His measurements of the normal adrenaline level are at variance with the figures reached by biological assay, and although differences in technique partly reconcile the results of the two methods, the difference of opinion on the effect of hypoglycæmia [7] remains unresolved

von Euler and Luft [8] demonstrated in man that urinary adrenaline excretion is much increased after insulin French and Kilpatrick [4] have confirmed this, and they have recently tried to elucidate the part played by adrenaline in causing the symptoms of hypoglycæmia They found that although sympathectomy prevents adrenaline release, as measured by urinary excretion, it does not significantly alter the hypoglycæmic symptoms It is hard to estimate the significance of their finding that sweating was invariable in their sympathectomised subjects, without knowing more about the methods used to assess it, for, especially as far as sweating is concerned, sympathectomy is seldom complete because there are ganglia in those rami which escape removal [9] Since peripheral nerve block, atropine, and hexamethonium stop hypoglycæmic sweating, it is hard to believe that it is not mediated by the sympathetic nervous system and that failure to abolish it is not due to the incompleteness of the sympathectomy

Chalmers and Keele,[2] having demonstrated that local injections of adrenaline cause sweating, saw no reason to challenge the concept of a solely cholinergic nerve-supply to sweat glands It is of interest that in two clinical conditions in which adrenaline release occurs—hypoglycæmia and phæochromocytoma—sweating is a prominent symptom "Too much significance," Chalmers and Keele remark, "should not be attributed to the failure of intravenous and intra-arterial adrenaline to elicit sweating our experience has been that acetylcholine and mecholyl (methacholine) may also produce little or no sweat response when given systemically The possibility that under certain conditions sweating might be caused by circulating adrenaline has not been excluded "

After the administration of insulin, there is a considerable increase in hand blood-flow in normal persons,[4] and a decrease in those with a sympathectomised upper limb whose vessels, as a result of denervation, are sensitised to adrenaline [10] This suggests that, although adrenaline is released, there are nervous influences which more than counteract its effects in normal persons Evidence for a decrease in the activity of adrenergic nerves has been produced by von Euler and Luft,[8] who found a reduction in the amount of noradrenaline in the urine in hypoglycæmia They say that the chief source of urinary noradrenaline is adrenergic nerve endings There is also the well known vagus mediated increase of gastric secretion in insulin hypoglycæmia to support the conclusion of French and Kilpatrick that "there is much evidence for a general activation of the cholinergic nerves"[4] in this condition But every nerve arising in the central nervous system and ending outside it is cholinergic, whether it passes to the neuromuscular junction, to an autonomic ganglion, or to the suprarenal gland, so this conclusion serves to underline the fact that a great deal still remains to be discovered and that it will probably have to be sought in the central nervous system itself—no easy task What does seem to be clear, however, is that "adrenaline is not the main agent in determining the clinical features of hypoglycæmia in man "

LEUCOTOMY AND THE FAMILY

Frontal leucotomy produces changes in those important but ill defined aspects of behaviour which are termed "personality " The changes may be considerable and are not always desirable [11] They were first clearly demonstrated by workers such as Rylander, who sought their evidence in the home, from friends and relatives Here the effects of leucotomy were found to be greater and more complex than was at first suggested by observation of patients in hospital It follows that the home, to which it may be hoped patients will return, and particularly the personalities of friends and near relatives—above all, wives and children—with whom they will have to live, are of the greatest importance in measuring the success or failure of the operation Nevertheless, this information is often very cursorily gathered A brief and sometimes stereotyped report from a psychiatric social worker, or an interview with the one relative thought to be mainly concerned, may be taken as sufficient, and the complex psychodynamics of the family is neglected When the patient returns home, usually largely relieved of his more prominent symptoms, the effect on the family may sometimes be disastrous

A recent detailed study [12] of 19 women who returned to family life after operation is illuminating The hazards are potentially greatest when the patient is a mother of small children, though the determination to keep a home together may be a stabilising influence Even with single women living with relatives, however, the previous social unit may break down completely Lane's inquiries [12] emphasise the overwhelming importance of the personalities of those who have to live intimately with the patient after operation Detailed information on this score must be regarded as essential before deciding on operation, and more particularly in planning postoperative care The information will also be valuable in determining what kind of preparation to give relatives before they meet the changed personality, and how much and for how long they will need help in dealing with their new situation This is one aspect of social psychiatry pudendal-block anæsthesia In all outlet forceps and most mid cavity, including occipitoposterior positions, in the absence of a contracted pelvis, and in breech deliveries this method can be used, and a high percentage of success can be achieved with but little practice The dangers of inhalation of vomit or regurgitated acid stomach contents are thus entirely avoided

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[1] Cannon W B McIver M A, Bliss S W *Amer J Physiol* 1924 69 46

[2] Chalmers T M Keele C A *J Physiol* 1951 114 510

[3] Barcroft H Swan H J C Sympathetic Control of Human Blood Vessels London, 1953

[4] French, E B Kilpatrick R *J clin Sci* 1955 14 640

[5] Laurence D R Stacey R S *Brit J Pharmacol* 1952 7 255

[6] Weil Malherbe, H *J ment Sci* 1952 48, 565

[7] Holzbauer M Vogt M *Brit J Pharmacol* 1954 9 249

[8] von Euler U S Luft R *Metabolism* 1952 1, 528

[9] Boyd, J D Monro, P A G *Lancet* 1949, ii 892

[10] Freeman N E Smithwick, R H White, J C *Amer J Physiol* 1934 107, 529

[11] See *Lancet* 1954 i 1223

[12] Lane M A *Brit J Psychiat soc Work*, 1956, 3, 18

The best technique for pudendal block has been described by many writers and consists of injecting 10 ml of local anæsthetic around the internal pudendal nerves in the region of the ischial spines It is essential to use a 5 inch, 20 gauge needle and inject at three points, just below the spines, in the nerve canal, and in the greater sciatic notch behind the spines in order to catch all the nerve branches No further injection is required, and the anæsthesia obtained covers a much greater area than the anatomy books would lead one to expect and lasts long enough to repair the perineum after delivery

Spinal needles are too short for this purpose, and their base is not sufficiently strong The needles I use had to be specially made since none was obtainable in London, which would suggest that this technique is not receiving the attention it deserves, and at a recent survey made among candidates at a higher examination I found that less than half had seen a pudendal block and few had performed one

There is, therefore, at present, ample opportunity of using a safe method of anæsthesia I would further suggest that all students should be taught the technique of pudendal block and all candidates for higher obstetric degrees should give evidence of having had practice in the method Experience would be obtained by using pudendal block for normal deliveries, and where the use of forceps is anticipated this will allow early application Excellent muscle relaxation is also obtained by this means, but the patient usually has to be told to push in the absence of local sensation

A qualified anæsthetist should, if possible, give the remaining anæsthetics This is particularly essential where some abnormality is present, such as prolonged labour, for cæsarean sections, or in patients who are fat and thick-set or nervous All hospitals should be able to arrange for this

Many modern methods, especially when newly introduced, as you state, can be dangerous, except in the hands of the anæsthetic specialist, and the house surgeon or anæsthetic registrar should not employ them in obstetrics For instance, thiopentone in small doses can cause laryngeal spasm and fœtal death from anoxia, and maternal death with an average dose in the presence of anæmia, a closed circuit with certain anæsthetics, and lack of facilities for lung inflation with relaxant drugs, have been seen to result in maternal and fœtal death

If the domiciliary patient cannot receive a pudendal block, or be brought into hospital, then the help of a qualified anæsthetist should be available and paid for by a domiciliary visit

These suggestions attempt to answer the questions in your annotation and will go a long way towards lessening the growing dangers of anæsthesia in hospital and domiciliary obstetrics

London W 1

D J MacRae

SIR,—The technique outlined by Dr Coleman and Dr Day is a bold attempt to solve an outstanding problem While I agree with the general principle of employing a cuffed endotracheal tube, I should like to endorse the comments in your annotation—namely, that a quicker induction is probably obtainable with 50% cyclopropane and oxygen, and that intubation should only be performed in the head up position advocated by Morton and Wylie[1] I have now seen three cases of massive regurgitation when succinylcholine was administered in the horizontal and head down positions, but no trouble has so far resulted from the head up position

A series of cases such as that described serves only as a pointer to future lines of investigation The next step is to obtain a properly controlled series of cases comparing the new technique with that of, say, nitrou oxide/oxygen/ether It could then be determined whether in fact the technique of Coleman and Day had any advantages over the older method, when both techniques were utilised by experienced anæsthetists It would become apparent whether the success of the new method was due solely to the technical facility of its originators

I further suggest that the studies should be extended to include the fœtus By a method of assessment such as that of Apgar,[2] the effects of anæsthesia on the fœtu can be compared Only in this way is it possible to obtain a thorough appreciation of such a new technique

University College Hospital,
London, W C 1

L Kaufman

SIR,—Your annotation ends with the question "Wh are students to be taught about obstetric anæsthes and how are they to be equipped to deal with a emergency in domiciliary practice?" May I diffidently suggest that the answer to this is that they should be taught to give anæsthetics? The revival of this useful but now virtually discarded branch of teaching might even result in the young doctor being able to cope with the baffling problem of providing a few minutes' anæsthesia for a healthy young mother while the forceps are put on

Windsor

Douglas Belfrage

FATS AND DISEASE

SIR,—Permit me to refer to Dr Sinclair's fascinating letter of April 7 and the article by Dr Bronte Stewart and his colleagues (April 28), both emphasising the importance of adequate content of essential fatty acid (E F A) in our diet They involve important conclusions, especially the one expressed by you in your leading article (April 28) "If these results are substantiated coronary-artery disease becomes in part a preventable disorder—but at a cost of a complete revolution in our present-day dietary habits The hydrogenation plant of our modern food industry may turn out to have contributed to the causation of a major disease" It can be concluded also that it is wrong to advertise margarine containing hardened fats as properly vitaminised

Bronte Stewart et al 's figures indicate that in a high fat diet the E F A content of fats should be above 5% if an increase in serum cholesterol is to be avoided, 15% being adequate or possibly more than adequate In the diets used, this is equal to above 6 g and below 19 g E F A per 2500 calories With eggs, however, the result is quite different, although they contain much E F A That eggs contain cholesterol may be the explanation

Shapiro and Freedman[3] showed that the hypercholesteræmic response to cholesterol feeding in rats on a sulphur-deficient protein diet was largely prevented by the use of dietary fat containing E F A A calculation based on their figures shows 16 5 g E F A per 2500 calories to be adequate

As to the "etcetera" of Dr Sinclair's letter, he refers to my letter on hardened fats and lung cancer[4] I should like to refer also to the further three letters[5] in which I tried to show that the food consumed domestically in the U K had a decreasing content of E F A If the diets included in my calculations were representative the average consumption of linoleic acid fell between 1939 and 1952 from about 5 to 3 g per head per day, and of

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[1] Morton H J V Wylie W D *Anæsthesia* 1951 6 190

[2] Apgar V *Curr Res Anesth* 1953 32 260

[3] Shapiro S L Freedman L *Amer J Physiol* 1955, 181 441

[4] Nyrop J E *Lancet* 1954 ii 1288

[5] Nyrop J E *Ibid* 1955, i 253 872 1178

Special Articles

FLOUR

MEMORANDUM OF A CONFERENCE * APPOINTED BY THE MEDICAL RESEARCH COUNCIL TO PREPARE EVIDENCE FOR SUBMISSION TO THE GOVERNMENT PANEL ON COMPOSITION AND NUTRITIVE VALUE OF FLOUR

Nutritional Requirements

The most recent authoritative assessment of nutritional requirements in this country is contained in the report of the Committee on Nutrition of the British Medical Association published in 1950[1]. The nutritional levels recommended in the report were formulated not only on the results of research but also on the general basis that a high standard of health had been maintained on the diet prevailing in Great Britain during the war and that the nutrient content provided by that diet might reasonably be accepted as a satisfactory standard for the population as a whole. The B.M.A. recommendations take account within broad limits, of differences of age, sex and physical activity, and allow a margin for individual variation. With the reservation that the number of people in the community whose requirements may be significantly different is unknown, the council's conference are agreed that the B.M.A. recommendations are a fair assessment of average requirements with a reasonable, and not excessive, margin of safety; that in the absence of other evidence they represent a level to which it is reasonable to expect the diets of all to attain; and that they should be used as the standard in considering the effects of any changes in the national diet.

Food Consumption in Relation to Nutritional Requirements

The National Food Survey Committee of the Ministry of Agriculture, Fisheries and Food conducts an annual survey of the domestic food consumption and expenditure (allowance being made for meals eaten outside the home) of a randomly selected sample of households (over 11,000 in 1954) in some sixty parliamentary constituencies throughout Great Britain. In addition to the figures for 1952 which have been published,[2] those for 1953[3] and 1954 have been made available by the Ministry to the council's conference. Table I is taken from the findings of the survey and shows for certain selected nutrients the extent to which the B.M.A. requirements were met in these years. During this period average expenditure on food was rising, and, with the gradual end of rationing, a wider variety of foods was becoming available; while even after the decontrol of flour in August 1953 the bread consumed continued to be made almost entirely from National flour which was required under the Flour Order 1953 to be of 80% extraction or its equivalent. Table I shows that the B.M.A. standards were in general being met, but the figures also suggest that, on the average, large families, and particularly those with adolescents as well as children, were in some respects barely meeting them, although they were not falling short to any substantial degree. The classification of households given in table I does not, however, distinguish between different income groups and may therefore to some extent obscure conditions in the families in the lowest income group. Reliable information on these, the least favoured families cannot be obtained from the survey because the sample is too small, but the Ministry has been asked to prepare figures for food consumption in families with four or more children in the two lowest income groups, which taken together represent about 30% of the total number of such households and will provide a sample large enough to give valid results. The analysis when completed will be considered by the conference and forwarded to the Panel.†

Contribution of Bread and Flour to Nutritional Requirements

In this country bread is the largest and most important single item of the diet, providing between one fifth and one-third of the calories and protein and a high proportion of other essential nutrients (table II). It can therefore be expected that a reduction in the extraction-rate of flour will affect the intake of nutrients, and particularly so in the largest families which are most dependent on bread. Table III shows the concentrations at different extraction rates of some of the nutrients present in flour, and it will be seen that there are some significant differences between 80% and 70% extraction flours. From the figures in table I it is evident that a change in extraction-rate from 80% to 70% would entail a less favourable nutritional standard, particularly for the most vulnerable groups.

Nutrient Content of Flour and Fortification

A reduction in the extraction-rate of flour affects the levels not only of vitamin B_1, riboflavine, nicotinic acid,

TABLE I*—THE EXTENT TO WHICH CERTAIN NUTRITIONAL REQUIREMENTS WERE MET IN HOUSEHOLDS IN 1952, 1953 AND 1954, EXPRESSED AS A PERCENTAGE OF THE B.M.A. RECOMMENDATIONS

Element	Year	Extraction rate of flour (%)	Households with 1 male and 1 female and					
			Children only				Adolescents only	Children and adolescents
			1	2	3	4 or more		
Calories	1952	80	105	101	99	101	96	93
	1953	80	107	102	99	100	99	95
	†1954	80	109	105	100	99	102	97
Total protein	1952	80	112	102	96	95	100	90
	1953	80	112	102	95	93	101	89
	†1954	80	112	102	95	90	100	89
Iron	1952	80	115	106	102	101	108	99
		70	107	100	95	94	92	92
	1953	80	116	108	103	100	110	100
		70	110	101	96	94	104	95
	†1954	80	118	111	103	100	112	102
		70	112	105	97	93	105	96
Vitamin B_1	1952	80	140	130	129	131	127	121
		70	110	102	100	103	97	90
	1953	80	139	131	127	128	130	121
		70	111	106	100	99	102	96
	†1954	80	139	131	126	124	128	120
		70	113	113	100	98	102	91
Riboflavine	1952	80	121	113	109	104	104	96
	1953	80	120	113	107	101	104	95
	†1954	80	120	114	108	101	105	95
Nicotinic acid	1952	80	139	129	123	121	131	119
		70	115	107	104	101	111	99
	1953	80	142	130	124	122	134	121
		70	127	116	108	106	118	105
	†1954	80	140	130	121	116	136	119
		70	124	116	106	100	119	105

* The figures in this table are derived from the findings of the National Food Survey. The contribution of bread and flour to the diets in these households is calculated on the basis of the mean figures for the composition of flour at different extraction-rates which were obtained from the Ministry of Agriculture, Fisheries and Food and which are given in table III. The flour normally used during these years was National flour which was required under the Flour Order 1953 to be of 80% extraction or its equivalent. The figures for 70% extraction have been included for comparison.

† Provisional figures only.

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* The members of the conference were: Sir ALAN DRURY, F.R.C.P., F.R.S. (chairman), Prof. S. J. COWELL, F.R.C.P., Dr D. P. CUTHBERTSON, Prof. R. A. MCCANCE, F.R.C.P., F.R.S., Sir RUDOLPH PETERS, F.R.C.P., F.R.S., Prof. B. S. PLATT, M.B., Dr W. P. H. SHELDON, Dr H. M. SINCLAIR, Prof. A. W. WOODRUFF, F.R.C.P., Prof. F. G. YOUNG, D.SC., F.R.S., and Dr R. H. L. COHEN (secretary).

† These figures were subsequently considered by the conference and were found to accord with the conclusions in this paragraph.

1. British Medical Association. Report of Committee on Nutrition 1950.
2. Domestic Food Consumption and Expenditure, 1952. Annual Report of the National Food Survey Committee. H.M. Stationery Office, 1954.
3. Domestic Food Consumption and Expenditure, 1953. Annual Report of the National Food Survey Committee. H.M. Stationery Office, 1955.

anæsthetics Whilst I myself am convinced of the greater safety of the extradural nerve block, I fully realise that sometimes a spinal may be either the only possible method or the method of choice In such a case, where the anæsthetist believes that the possible complications of the method are outweighed by the probable ill effects of not using it, he should have the backing of his colleagues

London S W 15 G C STEEL

MEDICINES FOR HOSPITAL OUTPATIENTS

SIR,—Dr Tuckman's letter (May 26) calls attention to an aspect of the health service which has rightly received much publicity in recent months—namely, extravagance in prescribing There are, however, one or two points with which I cannot agree

The normal procedure in hospitals is to supply medicines on a time basis—usually a sufficient quantity to last the patient until the next visit to the outpatient department, though in the case of a patient returning for treatment to his general practitioner it is usual to supply medicine for one week only Generally speaking, the issue of antibiotics to outpatients is very carefully controlled, and I doubt very much whether a similar control can be said to exist with regard to prescriptions issued by general practitioners

St Peter s Hospital
Chertsey Surrey

A E GRIMSHAW
Chief pharmacist

ORAL STREPTOMYCIN IN BACILLARY DYSENTERY

SIR,—I was interested to read Dr Sangster's article (May 19), showing that oral streptomycin is an effective treatment for sonne dysentery

During the last three months of 1955 there was an epidemic of Sonne dysentery in this village, in which fifteen families were involved, with 43 individuals with positive stools

Of these 43, (*a*) 11 were cases of diarrhœa seen by me in an attack, (*b*) 12 gave a history of previous mild diarrhœa to the school medical officer investigating the epidemic, and (c) 20 were symptomless carriers, detected when the families of (*a*) and (*b*) had their stools examined 38 of the 43 with positive stools were school children or children under school age

Early in the epidemic an organism isolated from one of the cases was reported as having the following sensitivity reactions in vitro sensitive to streptomycin, chloramphenicol, oxytetracycline, sulphadimidine, phthalylsulphathiazole, partially sensitive to sulphanilamide and sulphaguanidine, resistant to penicillin, aureomycin, erythromycin, succinyl sulphathiazole

It therefore seemed reasonable to give every case a five day course of phthalylsulphathiazole, of which stocks were held in the dispensary, in the first instance And it was decided, after consultation with the M O H of the rural district, to give patients whose fæces remained positive after this treatment a course of oral streptomycin In the event plain oral streptomycin was not obtainable locally, and Guanimycin' (Allen & Hanburys) was used This preparation contains streptomycin 0 25 g and sulphaguanidine 2 g per fluid ounce The doses given were as follows

Adults —Phthalylsulphathiazole 0 75 g q i d , guanimycin 1 ounce four hourly to a total of 8 ounces

Children over 3 —Phthalylsulphathiazole 0 5 g q i d , guanimycin ½ ounce four-hourly to a total of 4 ounces

Children under 3 —Phthalylsulphathiazole 0 25 g q i d guanimycin 2 drachms four hourly to a total of 2 ounces

Of the 42 patients with positive stools who were given phthalylsulphathiazole 32 remained positive after the course —a failure rate of just over 75% These 32 were then given a course of guanimycin with the following results

Time (weeks) to become negative *

Under 1	*1–2*	*2–3*	*3–4*	*4–5*	*5–6*	*6–7*	*7–8*	*8–9*
20	2	0	1	1	2	3	2	1

* Until the first of three consecutive negative stools

Of the 32 cases, 20 became negative in less than one week and a further 2 during the second week, representing a failure rate of a little over 30% Of the 10 cases remaining positive after this treatment 7 came from two families who had had clinical dysentery of moderate severity, and the impression was that reinfection was occurring after clearance (The effect of a repeat course of guanimycin given simultaneously to all the household was not tried)

The question remains, of course, as to which of the two constituents of guanimycin was responsible for the improved result It seems reasonable to suppose that it was the streptomycin, because (1) the organism was reported as being sensitive to streptomycin in vitro, but only partially sensitive to sulphaguanidine, (2) the cases had not cleared after phthalylsulphathiazole, which is said to be more effective than sulphaguanidine in this disease, and which was given for a longer period

Benington Boston Lincs J S RIVER

Parliament

Medical Problems on the Roads

ON the report stage of the Road Traffic Bill in the House of Commons on May 31, Mr GODFREY NICHOLSON moved a new clause to give the Minister power to prescribe definite specifications for crash-helmets and to make their use compulsory for people riding or being carried on motor-cycles Mr HAROLD WATKINSON, Minister of Transport, said that he could not accept a mandatory clause imposing on him the duty of making the failure to wear crash-helmets illegal The police advised him that it would not be possible to enforce this Casualties involving motor-cyclists were 22% higher in 1955 than in 1954 He was impressed with the need to do something about these severe casualties, and if the clause were withdrawn he promised to consider whether a clause could be introduced when the Bill reached the House of Lords to give the Minister permissive powers enabling him, if the voluntary use of crash-helmets did not improve at a satisfactory rate, to make regulations so that the wearing of crash-helmets became obligatory Any clause which the Government introduced would cover both wearing and standards Mr Nicholson withdrew the new clause

Mr RONALD BELL moved a new clause providing that diesel vehicles should not be used on any public road in the Metropolitan police district He was sure that fumes from traffic played a large part in causing respiratory diseases among people in London The number of non smokers who died of cancer of the lung was nearly ten times as high in the cities as it was in the country There could be little doubt that in one way or another that was due to atmospheric pollution The council of the British Medical Association had called the Minister of Transport's attention to the possible dangers of diesel fumes and had stated that they viewed with alarm the proposal to replace electric trolley buses by diesel engined buses The Minister had replied that he could not hold up the normal commercial development of road vehicles without more definite information as to its effect on public health than was at present available Mr Bell suggested that it was for London Transport and the Minister to show that this change would not be harmful to the health of Londoners Mr MOLSON, parliamentary secretary to the Ministry, said a revolutionary clause such as that proposed by Mr Bell could be accepted by the Government only if a case for it were fully made out The effect of diesel fumes was being investigated by the Fuel Research Station and the Medical Research Council So far there was no evidence that exhaust fumes from diesel-driven vehicles had any measurable effect on the health of those who breathed them Unless and until research was able to establish the need for something like this clause the Government could not accept the proposal The clause was by leave withdrawn

Safety, Health, and Welfare in Agriculture

On the motion for the third reading in the House of Commons on May 29 of the Agriculture (Safety, Health and Welfare Provisions) Bill, Mr HEATHCOAT AMORY the Minister in charge of the measure, said that the alterations made in the Bill during the discussions had protein, that these undernourished children should have shown a greatly increased growth-rate that was not dependent on the rate of extraction of the flour. It is also to be noted (see table III) that the 70% extraction flour used in the feeding trial in Germany was rich in some nutrients and indeed, on the analyses available, in some respects more nearly resembled the 80% than the 70% flour used for breadmaking in this country.

These considerations are of importance in assessing the relevance of the results of the trial to conditions likely to obtain in this country. The conference agree with the first conclusion drawn by Dr Widdowson and Professor McCance on p. 68 of their report, which emphasises that caution should be exercised in generalising from results obtained in one experimental setting.

The Effects on Health

The conference do not suggest that a reduction of the extraction rate of flour from 80% to 70% would in itself be likely to give rise to widespread illness in the present favourable circumstances in this country. If, however, for any reason the population had to rely on bread for a greater proportion of their nutritional requirements than they do today, the different nutrient content of breads made from flours of different extraction rates might become important, particularly in the more vulnerable groups. Moreover, the absence of recognisable illness in an individual is not a sufficient criterion that his diet is nutritionally sound. An iron deficiency, for example, invariably affects efficiency; yet the resulting anæmias may vary in intensity from those detectable only by laboratory tests to others which are completely incapacitating. Again, a person may live for long periods on a diet supplying marginal amounts of vitamin B_1 without suffering from beriberi, and then under some additional stress collapse with fulminating beriberi. Great caution is therefore needed before making changes which may lower the nutritional value of a nation's staple food.

Conclusions

The conference therefore conclude that in the light of present scientific and medical evidence:

1. Flour of 80% extraction is a more complete source of nutrients than unfortified or partially fortified flours of lower extraction rates.
2. On the evidence available at present, there are families which, with bread made from unfortified 70% extraction flour, would not be obtaining all their nutritional requirements in full, as recommended by the British Medical Association Committee on Nutrition in 1950.
3. The consumption of a 70% extraction flour, even if this is partially fortified, would lead to a reduced intake of some nutrients. Although such a reduction would not necessarily lead to an increase in recognisable illness, it would, in the present state of knowledge, constitute a risk which can be avoided.

INVALID HOISTS AND SIMILAR NURSING AIDS

H. R. Rishworth

C.B.E., V.D., F.R.C.S., D.P.H.

Increasing attention is being paid to mechanical aids to lighten the labour of nursing helpless patients. The present shortage of nurses may be a cause but there are other factors at work.

The tendency to manipulate the body as a whole and in one unit in spinal conditions and in affections of the major joints, demands an increase in the effort necessary on the part not only of the nurse but also the patient.

Injuries of the spine now receive care to an extent which nurses probably did not experience before the world wars.

Patients with severe paralytic poliomyelitis who in past years might not have survived, can today, after careful nursing and attention to the respiration and skin, attain in the course of a year or two a considerable measure of happiness and comfort if regularly assisted each day from bed to chair, commode, or bath and back to bed—a manœuvre which has aptly been described as "bridging the gap" (Vinden and Bayne 1955).

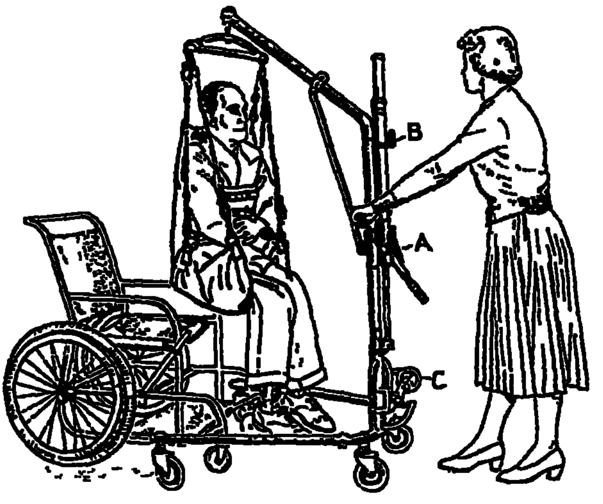

Fig. 1—'Easicarri' hydraulic hoist: A, hydraulic lift handle; B, hydraulic release valve; C, wheel for opening and closing base.

Aged patients receive more scrupulous and exacting attention; indeed longer survival into increasing helplessness of many old people is certainly a factor in directing attention to mechanical devices. In many cases, especially in patients above normal weight, efficient movement and turning are almost impossible without some mechanical aid or a great deal of labour on the part of several assistants.

Some Apparatus in Use

Russell and Schuster (1956) describe several devices developed by them and in use at Headington Hill Hall Rehabilitation Centre, Oxford: one is a modification of the mobile 'Sherpa' industrial truck; two others are types of crane fixed either to the wall or to the head of the bed. Two of the three are operated hydraulically and the third by a counterpoise arrangement of weights.

The Huddleston hoist (*Nursing Mirror* 1954), manufactured by John Bell & Croyden, 50, Wigmore Street, London, W.1, is of duralumin and makes it possible for a nurse to deal single-handed with a bedridden patient. The whole apparatus can be transported and assembled at the bedside without special tools.

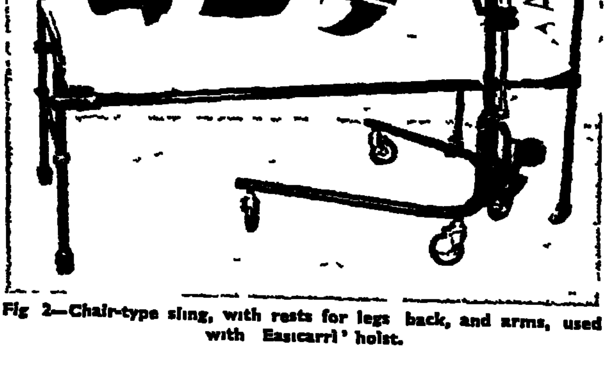

Fig. 2—Chair-type sling, with rests for legs, back, and arms, used with 'Easicarri' hoist.

feature, have had a remarkably fertilising effect on many aspects of health work in European countries The withdrawal of the Eastern European countries from W H O was a matter of deep regret to Begg He knew from his own earlier work in Poland how much both W H O and the countries which withdrew had to gain by continued participation He was always confident that in time the 'inactive members" would return, and he did everything he could to prevent anything being said or done on either side which would make that impossible It is tragic that he should have died when negotiations are taking place which make likely the early return of the Eastern European countries to active work with W H O

A D writes "Norman Begg was one of several Aberdonians who were prominent in the L C C fever service One of them, Andrew Topping, who always had the highest regard for Begg's ability, urged me to second Begg for work in Poland I recall that when an extension of his secondment was under consideration Dr Martha Eliot of the Children's Bureau, Washington, who had just returned from a visit to Poland, told me that Begg had more influence in Warsaw than any other person from the Western countries His work for UNRRA and W H O brought him into contact with a host of people of many nationalities He was genial, friendly, and highly esteemed by all with whom he had official relationship, including his own office staff, who were devoted to him"

"Bright blue eyes and a dark complexion," writes an ex-colleague, "gave Norman Begg a striking and handsome appearance As he listened in silent scrutiny one s lucid exposition began to seem—what it so often was—mere incoherent and irrelevant babbling Many of his colleagues found this daunting, but all recognised the value of his work and his ability as an epidemiologist and medical administrator In the treacherous cross-currents of post-war Warsaw, Begg s obvious competence, impartiality, reticence, and persistence earned the respect of all the warring interests Later, as the first director of W H O's European regional office, he began a long struggle to remove the office from Geneva, where—in his view—it was too much overshadowed by headquarters, and to give it a physically independent existence The decision last year to move it to Copenhagen was in part a tribute to his success as its director and must have given him great satisfaction"

G R H writes "Norman Begg had a combination of qualities which is unusual, especially in a physician He was an excellent administrator and at the same time a man keenly interested in scientific developments relevant to medicine As an administrator he was completely free from the faults of the bureaucrat, and his wide interest in scientific developments always carried with it the practical question 'What may the development of this knowledge one day make possible for public health practice?' When he was appointed to his important international post he was young and comparatively unknown in public-health circles in his own country Many doubts were expressed when he was chosen, but not by those who knew him He filled it with great distinction He had an extraordinary combination of far-seeing vision, quiet unruffled administrative efficiency, and deep modesty He had no idea what a remarkable man he was and that he was making a greater contribution to European unity than any politician His early death is a serious setback for international health work in Europe It is a personal loss to those who knew him and worked with him"

ELEANOR JOYCE PARTRIDGE

F R C S

Dr Joyce Partridge, who died on May 11 in Switzerland, was born in Devon in 1893 and was educated at Bedford High School She studied medicine at the Royal Free Hospital, qualifying in 1917 After holding posts at the Royal Free Hospital and the Elizabeth Garrett Anderson Hospital she took the F R C S in 1921 Later she went into general practice, and her growing realisation that many of her patients needed more than medicine and surgery to get them well led her to study psychology and especially the methods of C G Jung She joined the staff of the Tavistock Clinic, and became a member the Society of Analytical Psychology Shortly before late war she moved to Devon and began to practise psychiatrist in Exeter Later she combined her con sultant practice with the medical directorship of stone Grange Nursing-home and the appointment visiting psychiatrist to Withymead Centre at

E A N writes "Joyce Partridge was a very person first and a psychiatrist second I had known as a friend and colleague for close on eleven years, and during that time I had come to see something of wisdom and calmness which she brought to her work She was never hurried and she gave of her best to patients striving at all times to make them feel that were worthwhile people Perhaps one of the things remember best about her was her insistence on rhythm of life She felt strongly that in this world rush there must be real times of relaxation to balance the periods of stress and work The problem of death was problem to her When the apple was ripe it fell Those of us who knew her and mourn her loss know that would have felt that there was a rightness about death, and in her own words, 'It was just part of God pattern'"

She is survived by her husband, Mr Edward Wenham whom she married in 1931, and by one daughter

JOHN CHRISTOPHER EYRE PESHALL

M A Camb, M R C S

Dr Peshall, who died on May 30, at the age of was the only son of the Rev C J E Peshall, D S O a former archdeacon of the Fleet He was educated at Stowe, Trinity College, Cambridge, and St Thomas's Hospital After qualifying in 1944 he went as medical office on an expedition to Antarctica, and on his return was for a time one of the resident medical officers at the General Lying-in Hospital, York Road, London He was also a surgeon lieut-commander in the R N V R In 1952 he joined a general practice in Bermondsey and recently he had taken over the editorship of the gazette of the South London faculty of the College of General Practitioners

W B M, one of his partners, writes "Chris Peshall entered into the busy round of medical work with boundless zest and energy He was particularly interested in geriatrics and took endless trouble in helping many elderly folk, often taking them out in his car while on his rounds The secret of his happy life was a simple faith in God which reflected itself in all his doings"

Dr Peshall leaves a widow and two young sons

Appointments

BARR MARGARET N MB BSc Ldin, F F A R C S D OBST research asst in anæsthetics, Queen s College, Dundee

BERNSTEIN CYRIL M R C S medical registrar Bath group of hospitals

CANTRELL, G L M B Manc D O consultant ophthalmic surgeon Exeter clinical area

ROBERTS MAIDEN A W, M B Dubl F R C S I M O (surgical specialist), Sarawak

Manchester Regional Hospital Board

BOUND, J P M D Lond M R C P D C H consultant pædiatrician, Blackpool and Fylde group of hospitals

FORRESTER R M M B Camb M R C P D C H consultant pædiatrician Wigan and Leigh Hospitals

KIRWAN ROSALIE M M B N U I, D P M asst psychiatrist S H M O Lancaster Moor Hospital

ROBINSON W A M M B Lpool D P M consultant psychiatrist and medical superintendent Whittingham Hospital and Blackpool and Fylde Hospital Centre

WRIGHT, J K M B Manc F R C S consultant orthopædic and traumatic surgeon Blackpool and Fylde group of hospitals

Births, Marriages, and Deaths

BIRTHS

LICHTER—On March 8 in Johannesburg to Heather (née Lloyd) and Ivan Lichter—a son Barry Michael

STOWERS—On May 28 at Maryfield Hospital Dundee to Mary (formerly Alabaster) M B wife of John Stowers M D M R C P —a son patient, and readjusting the pillows Transport to the bath is effected with a special canvas sling (fig 6), and continuous support in a semi-reclining position can also be arranged with a suitable harness This is in some cases more satisfactory than the usual back-rest with its tendency to allow the patient to slip down the bed

The geared block (fig 3) incorporates a clutch which provides for instant release for winding up without any danger of slipping and is light, elegant in appearance, and easily cleaned

The traverse beam can be attached to the ceiling without much difficulty by a competent builder The apparatus is made by the Invalid Equipment Company, 22, Ashley Park Road, Walton-on-Thames, Surrey, founded by the patient in spite of his physical handicap

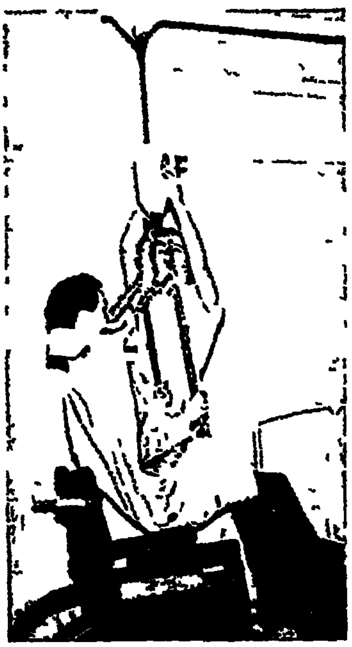

Fig 6—Canvas sling for transferring patient to bath

I am indebted to the *Nursing Mirror* for permission to use drawings (figs 2 and 3) based on photographs taken by the staff of that journal

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USE OF HOSPITAL RECORDS IN RESEARCH

At a meeting of the medical section of the Royal Statistical Society in London on May 29 the use of routine hospital records in research was discussed

Dr A C **Dornhorst** dealt with the nature of clinical records The history was neither a statement of fact nor a record of what the patient said It was rather an aide memoire, a personal document to remind the writer of an interview at which the patient's statements were largely determined by the nature of the questions asked and the manner of their asking It was the record of a conspiracy between the patient and the doctor and was subject not only to errors of memory and reporting but also to the moods and current ideas of the reporter The observer error in recording physical signs and radiographic appearances, and the experimental error of laboratory estimations, were becoming increasingly well known It was an interesting paradox that, despite all these difficulties and inconsistencies, there was in general little difference in the conclusions reached from them The physician did not, in fact, arrive at his diagnosis by logical inference from what he recorded Clinical records tended to become shorter as the writer grew older, and with increasing experience fewer words were required to remind him of his attitude of mind at the time the record was made Research from routine records might be worth while, but it would be interesting to inquire further into what such records really were

Dr J R **Bignall** said that routine hospital records could give valid answers only if they were asked the right questions Every question must be put in such a form that it was nowhere assumed that what was recorded in the notes was true Each part of the question should then be examined to estimate the probability that the recorded statement was a statement of fact Only by having an intimate knowledge of the special subject of the study was it possible to estimate these degrees of reliability and hence to make valid inferences Much research from hospital records used comparisons, and in these the effect of inaccurate reports might be cautiously neglected, if it could be reasonably assumed that the reliability of particular statements in the questions asked was not influenced by the nature of the characteristics being compared Much research from routine records was undoubtedly a waste of time But properly conducted it could be as logically correct and as useful as research in the laboratory

Mr M P **Curwen** said that research included not only the answering of precisely formulated questions but also the observation and reflection that necessarily preceded the making of such questions It was for this purpose that routine hospital records were most useful The precise question might be answerable only by planned prospective surveys, but retrospective study of hospital records, however inaccurate, usually determined what questions were to be asked There were some statistical difficulties associated with such studies For instance, in general there was no justification for using tests of significance with the type of material obtained from routine hospital records This was especially so where arbitrary classifications of symptoms, signs, and pathological reports were being used, for slight changes in the arbitrary groupings might radically affect the interpretation of such tests The tests were useful as rough guides to the investigator in judging whether the inferences he was drawing were reasonable, but they should not be relied on too much, nor should they usually be published in the final report

GENERAL MEDICAL COUNCIL

SESSION MAY 29–JUNE 1

There were a number of new faces at the General Medical Council on May 29, for elections and changes in Crown and university appointments have brought about an extensive alteration of composition The meeting was the last to be attended by dentists representing the Dental Board, which, as Sir **David Campbell**, the council's president, said in his address (reported last week), is to be replaced by the General Dental Council in July

The President, in bidding farewell to the dental members, said that they had been colleagues in one of the most difficult tasks which the council had had to perform, for in considering dental disciplinary cases the council was not in a position to hear the evidence but could accept the recommendation of the Dental Board or send the case back

Sir **Wilfrid Fish** replied that they had always realised the enormous value they had received from the council, he was sure that this had not been appreciated by the public as much as it should have been The dental profession, he remarked, must have gone through the whole gamut of emotions during the eighty-eight years it had been associated with the General Medical Council Sir Wilfrid declared that one of the greatest sources of pride to the dental profession was that its tradition was based on that of medicine Then, as time went on, they had had another emotion—that of frustration—to a certain extent Now independence rid them of the feeling of inferiority which was inevitable when under the tutelage of some other body

THE CAMBRIDGE LONG VACATION

In his report on the Cambridge medical school for 1954–55, Sir Lionel Whitby, the regius professor of physic, mentions that the facilities offered to medical undergraduates during the long vacation now cover not only the preclinical and transitional periods of study "but also provide unique opportunities for continuing a general education in the arts" The faculty of modern languages gives elementary courses of 24 lectures in German, Russian, French, and Italian, designed to give science and medical students a working knowledge of the language, and also more advanced courses Similarly, the faculty of English arranges for students in scientific faculties a special series of lectures in English literature and poetry In both faculties the courses are open without fee to all medical students in residence

A NEW INDIAN HOSPITAL JOURNAL

The second issue of the *Journal of the J J Group of Hospitals and Grant Medical College* appeared in April It is to be published quarterly and papers should be submitted to the hon secretary of the journal, J J Hospital, Byculla, Bombay, 8 The editor is Dr J G Parekh

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University of Cambridge

On May 26 the degree of M B was conferred on D J Blomley and (by proxy) on R B Bennet

University of London

Dr W S Peart, senior lecturer at St Mary's Hospital Medical School, has been appointed to the university chair of medicine at the school

Dr Peart graduated M B with honours from St Mary's in 1945 and took the M R C P the following year With a Medical Research Council studentship he was attached to the department of physical chemistry at St Mary's Later he was appointed junior lecturer in the medical unit there and last year he became senior lecturer He has published papers on splenic sympathin, phæochromocytoma, and hypertensin

University of Liverpool

Mr I W MacPhee has been appointed to a senior lectureship in the department of surgery

Queen's University, Belfast

Sir Frank Montgomery, F F R, has been appointed pro chancellor of the university Dr K W Newell has been appointed lecturer in preventive medicine and Dr W H T Shepherd part time lecturer in radiology

University of Western Australia

The following appointments to chairs in the newly established medical school of this university are announced

Dr D C Sinclair university demonstrator in human anatomy in the University of Oxford, to the chair of anatomy Dr E G Saint director of the clinical research unit in the Royal Perth Hospital, Western Australia, formerly of the staff of the department of industrial health King's College, Newcastle upon Tyne (medicine), Mr N F Stanley, D SC director of the institute of epidemiology and preventive medicine and director of microbiology, Prince Henry Hospital Adelaide (microbiology) Mr Gordon King F R C S F R C O G at present professor of obstetrics and gynæcology in the University of Hong Kong (obstetrics and gynæcology) - Mr C W D Lewis F R C S senior assistant and senior lecturer in the surgical unit Welsh National School of Medicine (surgery)

Royal College of Surgeons of England

A limited number of tickets (£2 10s) for the Buckston Browne dinner on July 11 will be available to fellows and members Applications should be sent immediately to Mr W F Davis, deputy secretary of the college, Lincoln's Inn Fields, London, W C 2

Ryle Memorial Prize

The Medical Association for the Prevention of War is offering a prize (£75) for an essay from a doctor or medical student on a World Approach to Human Survival and Health Further particulars were given in Dr Glaister's letter in our columns (*Lancet*, April 21, 1956, p 509)

United Kingdom Committee for Poliomyelitis

At a meeting held at the Royal College of Physicians of London, representatives of medical and lay organisations agreed to found this committee with the object of ' contributing to the study of all the problems arising from poliomyelitis and especially those relating to its prevention and treatment ' Sir Russell Brain P R C P was elected chairman of the committee and Dr W Ritchie Russell, hon secretary

Research into Ageing

The Ciba Foundation is offering five awards (£300 each) for papers on research " relevant to basic problems of ageing" Entries should reach Dr G E W Wolstenholme, 41, Portland Place, London, W 1, not later than Jan 31, 1957

International Congress of Internal Medicine

This year the International Society of Internal Medicine will hold their congress at Madrid from Sept 19 to 23, under the presidency of Prof C Jiménez Diaz The programme includes discussions on the present situation of internal medicine, the rôle of the adrenals in the pathogenesis and evolution of internal diseases, and bronchial asthma and emphysema The address of the secretariat is Hortaleza Madrid

Medical Golfing Society

At the summer meeting of this society, held at Swinley Forest, the *Lancet* cup (scratch medal) was won by Mr R H Maudsley (6) with a score of 74

CORRIGENDUM *Aldosterone*—The initials of Dr Ivor H Mills were given incorrectly in the letter by Dr Garrod and his colleagues last week

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Diary of the Week

JUNE 10 TO 16

Monday, 11th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, *Ducane Road* W 12
4 P M Dr A F Foster Carter Broncho pulmonary Anatomy
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY, Queen Charlotte's Hospital, Goldhawk Road, W 6
4 30 P M Mr H MacLennon Contracted *Pelvis and Disproportion*

Tuesday, 12th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street W 1
8 P M *Psychiatry* Dr W Mayer Gross, Dr D M Leiberman Dr M Shepherd Pharmacological Approach in Psychiatry
WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, St *Mary's Hospital* Medical School, W 2
5 P M Prof Ronald Hare Transmission of Infections of the Respiratory Tract (Almroth Wright lecture)
INSTITUTE OF DERMATOLOGY *Lisle Street W C 2*
5 30 P M Dr G C Wells Drug Eruptions

Wednesday, 13th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Dr Derrick Rowley One Aspect of Natural Immunity
INSTITUTE OF CARDIOLOGY
5 P M (1 Wimpole Street, W 1) Dr Wallace Brigden Rare Forms of Myocardial Disease (St Cyres lecture)
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P M (Hammersmith Hospital W 12) Prof W C W Nixon The Maternal Services in the Future
INSTITUTE OF DISEASES OF THE CHEST
5 P M Dr C M Fletcher Coalminers Pneumoconiosis
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Mycotic Disease

Thursday, 14th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn Field W C 2
5 P M Dr C Marks Surgical Sequelæ of Bilharzial Disease (Hunterian lecture)
ROYAL SOCIETY OF MEDICINE
5 P M *Ophthalmology* Mr D P Greaves Dr *J Gloster* Some Ocular Effects of Diencephalic Stimulation in Experimental Animals
UNIVERSITY COLLEGE Gower Street W C 1
5 15 P M Dr Roy P Forster (Dartmouth College New Hampshire) Active Transport in Cells of Mammalian Renal Tubules Studied in Vitro
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P M (Hammersmith Hospital W 12) *Prof C G Lennon* Cæsarean Section
INSTITUTE OF DERMATOLOGY
5 30 P M Dr H Haber Cytodiagnosis in Dermatology
NUFFIELD ORTHOPÆDIC CENTRE *Oxford*
8 30 P M Mr J H S Scott The Fractured Scaphoid
HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place Edinburgh) Prof G L Montgomery Morbid Anatomy of Coronary artery Disease

Friday, 15th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A M Prof J C Goligher Carcinoma of the Rectum
4 P M Prof C N H Long (Yale University) Experimental Obesity

Saturday, 16th

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY Chelsea Hospital for Women S W 3
11 15 A M Prof Ian Donald Infertility

postponed in respect of convictions in 1953 and 1954 under the Dangerous Drugs Regulations, 1937, and the Dangerous Drugs Act, 1951

In view of the satisfactory information concerning the doctor's conduct the committee did not direct the Registrar to erase his name from the Register

BREACH OF THE PEACE

Robert Lindsay, registered as of 8, St Ninian Drive, Inverness, M B Glasg (1945), appeared for postponed judgment following convictions for a breach of the peace in 1951, 1952, and 1955, and one of being found drunk in 1954 Judgment was postponed for a further year

OFFENCES ASSOCIATED WITH ALCOHOL

Last May the committee was not satisfied that the evidence concerning the habits and conduct of *Patrick Joseph Conlin*, registered as c/o Barclays Bank Ltd, Dudley, Worc, M B N U I (1920), were such as to justify them discharging the case at that time He had been convicted in 1950 of being under the influence of drink so as to be incapable of having proper control of a motor vehicle The Registrar was now not directed to erase Dr Conlin's name

Joseph John McMenemy, registered as of Burnside, Bargeddie, Glasgow, L A H Dubl (1947), was found to have been convicted at the Sheriff Court at Airdrie in 1954 of being in charge of a motor vehicle when under the influence of drink, when he was fined £15 and disqualified for twelve months, and at York City Magistrates' Courts in November, 1955, of driving a motor car when under the influence of drink, when he was sentenced to three months' imprisonment, ordered to pay £3 3*s* doctor's fees and £5 3*s* 11*d* witnesses' fees, and disqualified for three years The committee postponed judgment for a year

Andrew Francis Amerherst Gallen, registered as of 20, Orchard Drive, Giffnock, M B Glasg (1932), had been convicted at the Glasgow Sheriff Court in 1954 and 1956 of driving a motor vehicle when under the influence of drink or drugs On the first occasion he was fined £15 with an alternative of sixty days' imprisonment, and was disqualified for a year On the second the fine was £30 with three months' imprisonment as the alternative, and the disqualification was for two years Judgment was postponed for a year

BIRTHDAY HONOURS

The list of honours published on May 31 contains the names of the following members of the medical profession

Baron

Sir Henry Cohen, M D Lpool, F R C P, J P
Professor of medicine in the University of Liverpool, for services to medicine

Knights Bachelor

Samuel Phillips Bedson, M D Durh, F R C.P, F.R S
Professor emeritus of bacteriology in the University of London

Joseph Welsh Park Harkness, C M G, O B E, M B Glasg
Medical adviser to the Comptroller for Development and Welfare in the West Indies

Arthur Massey, C B E, M D Leeds
Chief medical officer, Ministry of Pensions and National Insurance

James William Tudor Thomas, M D Wales, F.R C S
Ophthalmic surgeon, United Cardiff Hospitals

C B (Military)

Air Vice Marshal Reginald Horace Stanbridge, O B E, M.R C S, R A F retd

C M G

Theodore Farnworth Anderson, O B E, M D Camb
Director of medical services, Kenya

Edward George Sayers, M B N Z, F R C P
Senior visiting physician, Auckland Hospital, for public services

Kenneth William Starr, O B E, E D, M S Melb, F.R C S
Councillor of the Royal Australasian College of Surgeons, for services to the medical profession

C V O

Francis Galloway Leslie, B A Camb, M R C S
Physician in ordinary to H R H the Princess Royal

C B E (Civil)

William Donald Wykeham Brooks, D M Oxfd, F.R C P
Consulting physician to the Royal Navy, physician to St Mary's Hospital, London

Patrick Wimberley Dill Russell, M R C S
Director of medical services, Cyprus

George Matthew Fyfe, M B Aberd, F.R C P E
Medical officer of health for Fife

Philip D'Arcy Hart, M D Camb, F R C P
Director, tuberculosis research unit, Medical Research Council

James Peter Speid Jamieson, M D Edin, F R A C S
Formerly medical superintendent, General Hospital, Nelson, New Zealand

Hallam Grey Massiah, M D
For public services in Barbados

Graeme Mitchell Mill Menzies, M B Aberd
Deputy chief medical adviser, federal government, Federation of Nigeria

Leonard James Ternouth Pellew, M B Adelaide, F R C S, F R A C S
For services to the Fire Brigade and other services in the State of South Australia

Hugh Stannus Stannus, M D Lond, F.R C P
Medical officer, Board of Inland Revenue

Frank Edward Tylecote, M D Manc, F R C P
Chairman, public health committee, Association of Municipal Corporations, professor emeritus of medicine, University of Manchester

Robert Bruce Wallace, D S O, M C, M B Glasg
For medical services in Kedah, Federation of Malaya

Frank Clare Wilkinson, M D Lpool, F D S R C S
Director of Eastman Dental Hospital and dean of Institute of Dental Surgery, University of London

O B E (Military)

Wing Commander John Nigel Carlyle Cooke, M D Lond, R A F

Colonel John Matthew Dwyer, E D, M B Adelaide, R A A M C

Major Maurice Francis Ronayne, M B E, M B N U I, R A M C, T A

Lieut Colonel Ernest Albert Smyth, M B Dubl, M CH ORTH Lpool, F R C S, R A M C

Lieut Colonel John Joseph Sullivan, M B, R A M C

O B E (Civil)

Edward Armstrong, M D Belf
Senior medical officer, ministry of health and local government, Northern Ireland

Thillaiampalm Balasingham, L.M S
Senior lecturer in pathology, University of Malaya

Enid Constance Evans, M R C S
Senior medical officer, H M Treasury

Horace Primrose Smith Gillette, M B Edin
Superintendent medical officer (specialist) malariologist, Trinidad

James Kellock Hunter, M B Glasg
Deputy director of medical services, Uganda

William Charles Donald Lovett, M D Lond
Senior medical officer, Somaliland

Cyril John Aloysius O'Kelly, F R C S I
Lately surgeon at the Royal Hospital, Basra

Albert John Orchard, M B Edin
Medical practitioner in Christchurch N Z for over 50 years

Cyril Seymour Coode Prance, M B Lond, J P
Commissioner, St John Ambulance Brigade for Plymouth, South West Devon, and East Cornwall

Alexander Noble Roxburgh, M B Edin, F R C S E
Consultant surgeon, Scottish Northern Regional Hospital Board

Anthony Andrew Russo, L R C P I
For medical and public services in Gibraltar

Charles Ernest Salt, M B Birm, J P
For public services in Denbighshire

Hope Trant, M B E, M D Dubl
Medical research officer, East African Medical Survey and Research Institute

Vera Cecil Veitch, M B Edin
Deputy principal school medical officer, Stoke on Trent

Though not definable in precise terms, scientific value can as a rule be reliably assessed Its appraisal is required and depended upon every day in the process of advancing and disseminating science Referees consulted by journals have to judge whether the scientific interest of a contribution would justify the expense of its publication Others have to decide whether the award of a research grant is worth while Scientists must be able to recognise what is manifestly trivial, just as what is manifestly false When the distinguished German physicist Friedrich Kohlrausch (1840-1910) declared, in a discussion about the aims of natural science, that he would be pleased to determine accurately the speed of water running through the gutter, he was talking utter nonsense He made no false statement of fact, but he completely misjudged the *nature of scientific value*, *for the accuracy of an* observation does not in itself make it valuable to science

The foolish promise made by Kohlrausch was of course not his true intention He was merely expounding a false theory of science more consistently than is usual relying on it, no doubt, that the errors of philosophy are only ridiculous and its extravagances do not influence our lives[2] But in doing so he demonstrated involuntarily that such absurd conclusions can be avoided—without inconsistency—only by abandoning altogether the ideal of a strictly objective science

To this revision of our scientific ideal we may find a clue in Kepler's title *Harmonices of the World* It suggests that we should acknowledge our capacity for recognising scientific value by our sense of harmony—by our emotional response to the intellectual beauty of science And since no part of science can be said to be beautiful unless it is also believed to be true, we must claim for this emotional response also that it makes contact with reality A discovery is beautiful if it reveals a new vision of reality This is the news to which the scientist's heart goes out this the object of his scientific passion

Discovery reveals new knowledge, but the new vision which accompanies it is not knowledge It is *less* than knowledge, for it is a guess , but it is *more* than knowledge, for it is a foreknowledge of things yet unknown and at present perhaps even inconceivable Our vision of the general nature of things is our guide for the interpretation of all future experience

Such guidance is indispensable Theories of the scientific method which try to explain the establishment of scientific truth by any purely objective procedure are doomed to failure Any process of inquiry unguided by intellectual passions would inevitably spread out into a desert of trivialities Our vision of reality, to which our sense of scientific beauty responds, must suggest to us the kind of questions that it should be reasonable and interesting to explore It should recommend the kind of conceptions and empirical relations that are intrinsically plausible and which should therefore be upheld, even when some evidence seems to contradict them , and tell us also, on the other hand, what empirical connections to reject as specious, even though there is evidence for them and we may as yet be unable to account for this evidence on any other assumptions

In fact, without a scale of interest and plausibility based on a vision of reality nothing can be discovered that is of value to science , and only our sense of scientific beauty, responding to *the* evidence *of our senses*, can evoke this vision Such is the *selective* function of scientific passion

This function is continuous with another, coming out clearly in the part of Kepler's text which precedes the words I quoted before He writes there

> "What I prophesied two and twenty years ago, as soon as I discovered the five solids among the heavenly orbits—what I firmly believed long before I had seen Ptolemy's Harmonics—what I had promised my friends in the title of this fifth book, which I named before I was sure of my discovery—what sixteen years ago I urged to be sought—*that for which I have* devoted the best part of my life to astronomical contemplations, for which I joined Tycho Brahe at last I have brought it to light, and recognised its truth beyond all my hopes So now since eighteen months ago the dawn, three months ago the proper light of day, and *indeed a very few days ago the* pure Sun itself of the most marvellous contemplation has shone forth—nothing holds me , I will indulge my sacred fury "

It is clear from this that intellectual passions not merely affirm the existence of harmonies which foreshadow an indeterminate range of future discoveries, but that they can also evoke intimations of specific discoveries and sustain their persistent pursuit through years of labour The appreciation of scientific value merges here into the capacity for discovering it , even as the artist's sensibility merges into his creative powers Such is the *heuristic* function of scientific passion

But the words of Kepler show us also that this truth bearing passion is far from infallible Kepler rejoiced in his discovery of the five solids among the heavenly orbits , he thought that the solar distances of the six planets known to him corresponded to the sizes of the successive Platonic bodies, as measured by the radii of inscribed and circumscribed spheres This is nonsense, and we would regard it as nonsense today, however accurately it corresponded to the facts merely and simply because we do not believe any longer that the fundamental harmonies of the universe are disclosed in numbers and geometrical figures But though this view of reality led Kepler astray in this case, it was close *enough to the truth to guide him aright to the* discovery of his three laws of planetary motion Therefore Kepler remains a great scientist to us, in spite of his erroneous reference to the Platonic bodies It is only when he talks of such things as the mind residing in the sun which listens to the planets, and puts down in musical notation the several tunes of the planets, that we no longer regard him as a scientist, but as a mystic We draw here a distinction between two kinds of error—namely, between ***scientific guesses*** which have turned out *to be* ***mistaken,*** and ***unscientific guesses*** which are not only false, but ***incompetent***

* * *

Scientists—*that* is creative scientists—spend their lives in trying to guess right They are sustained and guided therein by their heuristic passion We call their work creative because it changes the world as we see it, by deepening our understanding of it The change is irrevocable A problem that I have once solved can no longer puzzle me , I cannot guess what I already know Having made a discovery, I shall never see the world again as before My eyes have become different , I *have made myself into a person* seeing and thinking differently I have crossed a gap, the heuristic gap which lies between problem and discovery

To the extent to which discovery changes our interpretative framework, it is *logically* impossible to arrive at it by the continued application of our previous interpretative framework In other words, discovery is creative also in the sense that it is not to be achieved by the diligent application of any previously known and specifiable procedure Its *production* requires originality The application of existing rules can produce valuable surveys, but they can as little advance the principles of science as a poem can be written according to rule We have to cross the logical gap between a problem and its solution by relying on the unspecifiable impulse of our heuristic passion, and must undergo as we do so a change of our intellectual personality Like all ventures in which we comprehensively dispose of ourselves, such an intentional *change of our* personality requires a passionate motive to accomplish it Originality must be passionate

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[2] Hume D A Treatise on Human Nature Book I part iv section vii

No register of health visitors is recommended but their qualification should continue to be protected by statutory regulations

Training should be financed from central funds provided mainly by appropriate contributions from local health authorities A uniform scale of training allowances should be payable by training centres to students willing to serve for a specified period in certain conditions

MAN-POWER AND RECRUITMENT

On the standards set by the working party, a target establishment of 11 500 full-time staff—an increase of some 3500 full-time workers—is needed To meet the need within ten years the number of students trained each year would have to rise from about 640 to 1100 The working party realise that the number of suitable trained nurses likely to be available each year is too small to guarantee expansion They therefore recommend concentration on direct entrants and the establishment of adequate integrated courses to attract them

The report advocates a vigorous recruitment policy in which an important place is given to the enhanced status of health visitors, the elimination of inessential work, and better conditions of work and pay

Infectious Diseases in England and Wales

Disease	Week ended May			
	5	12	19	26*
Diphtheria	5	6	6	8
Dysentery	1635	1590	1664	1146
Encephalitis				
Infective	1		5	1
Postinfectious	3	6		3
Food poisoning	234	398	311	269
Measles excluding rubella	2176	3076	3373	3234
Meningococcal infection	28	33	30	32
Ophthalmia neonatorum	38	30	41	25
Paratyphoid fever	11	19	27	9
Pneumonia, primary or influenzal	459	461	364	339
Poliomyelitis				
Paralytic	11	15	15	16
Non paralytic	10	11	12	9
Puerperal pyrexia	245	225	243	170
Scarlet fever	778	737	691	553
Smallpox				
Tuberculosis				
Respiratory	729	705	686	559
Meninges and C N S	14	12	13	13
Other	89	91	81	68
Typhoid fever	4	2	1	
Whooping cough	1844	1750	1563	1351

* Not including late returns

Conferences and Congresses

MEDICAL RESEARCH IN THE CARIBBEAN

THE first scientific meeting to be held under the auspices of the newly formed Advisory Committee for Medical Research in the West Indies met at the University College of the West Indies, Jamaica, on April 8 and 9, under the chairmanship of Sir HAROLD HIMSWORTH The large audience included representatives from seven West Indian territories 32 papers were presented, 3 being read by title Many papers were interim reports on current research The proceedings of the meeting and many of the papers are to be published in the *West Indian Medical Journal*, and there follow summaries of a few of the contributions

MAYARO VIRUS

Dr W G DOWNS, of Trinidad, reported that in 1954 his team at the Regional Virus Research Laboratory had isolated a new virus, later called the Mayaro virus, from the blood of 5 febrile patients They were also able to demonstrate the presence of antibodies to this virus in the blood of a number of Trinidad residents, using an antigen prepared from mouse serum In the same year the virus was isolated in Brazil and Bolivia, and possibly also in Uganda, but this latter virus may be a close relative rather than the Mayaro virus itself Nothing is known as yet of its epidemiology or of its importance as a human disease producing agent, but it is of interest that the virus was not isolated in Trinidad during 1955

CONTROL OF MALARIA

Dr GEORGE GIGLIOLI outlined the investigations which he had undertaken from 1923 onwards into the epidemiology of malaria and blackwater fever in British Guiana He was able to identify *Anopheles darlingi* and to establish that it was the sole malaria carrier of practical importance in British Guiana He studied the breeding, biting, and resting habits of this vector, and he noted that acidity of the water in certain areas prevented breeding But in the cultivated and settled coastal lands of British Guiana (low level, sea defences, immense irrigation canal network, flood fallow, and rice cultivation) control by the methods then available—before the first world war—was impossible

The advent of dicophane (D D T) brought a new significance to these researches, and the results achieved with its use were more complete than might have been hoped for Only occasional cases of malaria are now recorded in British Guiana and these are from the far interior, mainly along the Brazilian border The geological formations inland from the coastal belt, which drain very acid waters, form a barrier to the spread of *A darlingi* This, together with periodic application of dicophane to the houses along the alluvial banks of the rivers and smaller water courses, has eradicated this mosquito from the coastal plains and also prevents re invasion from the forest areas Malaria is thus a thing of the past in the coastal plain of British Guiana

Dr H P S GILLETTE described investigations showing the development of resistance to dicophane by *Aedes Ægypti* Field observations made during the yellow fever campaign of 1954 have been confirmed by detailed laboratory work

YAWS

Dr F J GOODEY, Dr C C GORDON, and Prof K R HILL (University College of the West Indies) indicated some limitations of the modern methods of treatment of yaws in the field, and described this disease as produced experimentally in the hamster Detailed long-term observations made in a small closed country community suggested three main points (1) serological reactions are of little assistance in the control of framboesia in the community, (2) approved medical methods of control are often both impractical and unsuccessful, (3) a large proportion of frambœsial lesions are not recognised as such The experimental work suggested that during a remission there is residual latent infection at the roots of the hair follicles This might explain the exacerbation of the disease at the site of an old scar in human cases Professor Hill and his colleagues also reported work on some immunological aspects of leprosy

VENO OCCLUSIVE DISEASE OF THE LIVER

Dr K L STUART outlined the clinical features of veno-occlusive disease of the liver[1] Infants between 1½ and 3 years of age are primarily affected by the acute disease, but older children and adults do not escape Most affected children are not malnourished In the acute stage, there is a sudden onset of abdominal distension due to a smooth, firm, slightly tender liver enlargement, which is often associated with an acute ascites Many patients recover rapidly, at least clinically, with or without treatment, but there may be (*a*) rapid death due to liver failure, (*b*) persistence of the disease been replaced some 50 years ago by the exact sciences, is now once more dug up by pseudo scientists from the lumber room of human fallacies, and like a trollop, newly attired in elegant dress and make up, is smuggled into respectable company, to which she does not belong "

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[1] See *Lancet* 1955 ii 1284

Now, in a second paper,[7] he gave as a further example of this aberration an account of van t'Hoff's work which he "would have ignored like many other efforts of its kind" but for "the incomprehensible fact" of its warm recommendation by so distinguished a chemist as Wislicenus So Kolbe wrote

> "A certain Dr J H van t'Hoff, employed by the Veterinary Academy at Utrecht, appears to have no taste for exact chemical research He *found it more convenient* to mount Pegasus (borrowed no doubt from the Veterinary Academy) and to proclaim in his *La Chimie dans l'espace* how on his daring flight to the chemical Parnassus the atoms appeared to him disposed in world space "

Kolbe's comment on the introduction given by Wislicenus to van t'Hoff's theory reveals the principles of his criticism in further detail Wislicenus had written of "this real and important step in the advancement of the theory of carbon compounds, a step which was organic and internally necessary " Kolbe asks What is "the theory of carbon compounds? What is meant by saying that 'this step was organic and necessary' "? And he goes on "Wislicenus has here expelled himself from the ranks of exact scientists and has joined instead the nature philosophers of ominous memory who are separated only by a slender 'medium' from the spiritists "

Scientific opinion eventually repudiated Kolbe's attack on van t'Hoff and Wislicenus, but his suspicion of speculative chemistry ("paper chemistry") continued to be shared by most of the leading chemical journals, which refuse up to this day contributions containing no new experimental results In spite of the fact that chemistry is largely based on the speculations by Dalton,[8] Kekule, and van t'Hoff, which were initially unaccompanied by any experimental observations, chemists still remain suspicious of this kind of work Since they do not sufficiently trust themselves to distinguish true theoretical discoveries from empty speculations, they feel compelled to act on a presumption which may one day cause the rejection of a theoretical paper of supreme importance in favour of comparatively trivial experimental studies So difficult is it even for the expert in his own field to distinguish scientific merit from incompetent chatter by applying the criteria of empiricism

Nor does this apply only to purely theoretical discoveries The great controversy on the nature of alcoholic fermentation which, starting in 1839, went on for almost forty years, showed that the verification of an experimental observation may run into precisely the same difficulties From 1835 to 1837 no less than four independent observers (Cagnard de la Tour, Schwann, Kützing, and Turpin) had reported that yeast produced during fermentation was not a chemical precipitate, but consisted of living cellular organisms which multiplied by budding, and they had concluded that fermentation was a living function of yeast cells [9] But this went against the overmastering intellectual passion of contemporary scientists In 1828 Wohler had synthetised urea from inorganic materials and had triumphantly disproved thereby the existence of powers hitherto ascribed exclusively to living beings Liebig had followed suit by laying the foundations of a chemical approach to all living matter, and Berzelius had recognised that platinum could speed up reactions occurring in its presence, in the same way in which fermentation was caused by yeast All three great masters poured scorn on the claims which they regarded as a fantastic resurgence of the kind of "vitalism" they had banned for ever Wohler and Liebig published an elaborate skit making fun of these absurd speculations [10]

In 1857 Pasteur entered the lists on the side of the "vitalists" His investigations on yeast and putrefaction involved him at the same time in another fierce controversy of longer standing—the question of "spontaneous generation" In this, too, he was on the side considered at the time reactionary (and is still so considered in the Soviet Union), which denied that living beings could be produced experimentally from dead matter [11]

The reason why both these controversies dragged on indefinitely is revealed by a remark of Pasteur concerning his own arguments for regarding fermentation as a function of the living cells of yeast "If anyone should say that my conclusions go beyond the established facts [he wrote] I would agree, in the sense that I have taken my stand unreservedly in an order of ideas which strictly speaking, cannot be irrefutably demonstrated "[12] This order of ideas was therefore separated by a logical gap from that entertained by Liebig, Wohler, and many other great men of his time The schism was eventually bridged by a conceptual reform, induced by Buchner's discovery in 1897 of zymase in the liquor squeezed out of yeast cells The agent of fermentation was proved a dead catalyst of the kind imagined by Liebig and Berzelius but it also proved a vital organ of yeast cells, as Pasteur and his precursors since Cagnard de la Tour had affirmed the new conception of intracellular enzymes combined these two aspects [13]

* * *

The great scientific controversies which I have just recalled were conducted in passionate accents, as was inevitable between contestants who shared no common framework within which a more impersonal procedure could be followed Kolbe could not argue against van t'Hoff He quoted with ironical glee van t'Hoff's description of the disposition of atoms in spirals, which to him was sufficient evidence that the new theory was a tissue of fancies From his own point of view he was right in refusing to enter into any detailed argument on these lines, since he denied that one could argue rationally in terms of such wild ideas The ironical travesty by which Wohler and Liebig replied to the papers of Cagnard de la Tour, Schwann, and others, claiming that fermentation is a function of living yeast cells, sprang from the same view that an argument believed to be wholly specious cannot be seriously discussed point by point A Western scientist challenged to answer Lysenko's biological theories would similarly refuse to discuss them on the Marxist-Leninist grounds on which they were put forward, while Lysenko would refuse to consider the statistical evidence

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[7] Kolbe A W H *Ibid* 1877 15 473 The above summary of the first paper is quoted from the second paper

[8] For the case of John Dalton see H E Roscoe and A Harden A New View of the Origin of Dalton's Atomic Theory London 1896 p 50

[9] Dubos R J Louis Pasteur London 1950 pp 120–121

[10] Wohler and Liebig *Ann Pharm* 1839 29, 100

[11] See for example, the violent attacks on Pasteur by Pisarev published in 1865 (Coquart A Dmitri Pisarev Paris 1946 p 336 ff) Experiments acknowledged today in the Soviet Union as proofs of the spontaneous generation of cellular organisms were carried out by Lepeshinskaia (see Th Dobzhansky Proceedings of the Hamburg Congress on Science and Freedom *London, 1955, p 219)*

[12] Dubos, R J Op cit p 128 J B Conant in Pasteur's and *Tyndall's Study of Spontaneous Generation* (Harvard University Press 1953), suggests (p 15) that the most convincing evidence for the impossibility of spontaneous generation is to be found in the whole fabric of the results of the study of *pure* (bacterial) cultures in the last sixty or seventy years The author implies here that all the experiments made to decide this question from the inception of Spalanzani's studies in 1768 up to 1880–90 could be interpreted in terms of either opposing systems of thought

[13] The way an apposite new conception can reconcile two alternative systems of interpretation which hitherto completely excluded each other is illustrated by Braid's conception of 'hypnosis' which acknowledged the reality of the very features of Mesmerism which were hitherto taken to prove its fraudulence while rejecting the evidence for 'animal magnetism' which had been regarded as its claim to scientific solidity but was in fact illusory

Correction of Uterine Retroversion

M. MOORE WHITE (London) said that the correction of uterine retroversion as an aid to fertility has fallen into disrepute, but if performed for certain indications it is worth while. The faulty position of the uterus can hinder access of sperm to the cervix, cause kinking of the tubes at the uterine angles (a condition manifested when carbon dioxide fails to enter the tubes, on insufflation, until the uterus has been elevated), result in œdema both of the uterus and prolapsed ovaries, and be a cause of pelvic pain, backache, and dyspareunia. Operative correction is indicated if manual reposition is unsuccessful, the method varying according to the condition found at operation.

Iatrogenic Sterility

W. T. POMMERENKE (Rochester, N.Y.) reported an analysis of 9200 consecutive operations in the gynæcological service of a general hospital over a seven year period, 1948–54. This showed that 2035 (22.1%) of those operations were of such a nature that infertility would have been an inevitable consequence if the women had been otherwise functionally and anatomically intact. True, a significant number of patients had already been doomed to infertility because of age or pelvic disorder. However, the high incidence of sterilising procedures in young women in whom the desire for child bearing is paramount hardly bespeaks the ultimate in diagnosis or treatment. The rightful place of surgery in gynæcology is admitted, but quite apart from other unpredictable sequelæ, sterility may follow as a result of ill advised or heedlessly radical surgery. The number of absolute indications for sterilising operations is decreasing.

Urinary Hormone Determinations in Chronic Aborters

M. ROLAND and E. VEPROVSKY (New York City) stated that the value of urinary hormone determinations in chronic aborters, particularly of pregnanediol, appears to be limited at present—chiefly because we do not know the exact mechanism of progesterone metabolism. The methods now used account for only 20–30% of the converted progesterone. Even this estimated amount appears to be a "pregnanediol complex" which includes pregnanolone as well as different types of pregnanediol. Our interpretation will remain inaccurate and of limited value until we know more of progesterone metabolism. When a sudden drop in the urinary pregnanediol excretion occurs in chronic aborters, particularly during the first trimester of pregnancy, it is usually too late to attempt any type of therapy. When substitutional therapy has been started at the initiation of pregnancy, studies of the urinary hormone excretion may be of considerable value. In habitual aborters where the endometrial biopsy premenstrually demonstrates poor secretory activity, it is advisable to determine whether this is due to a lack of progesterone or to an endometrium which responds poorly to this hormone. The pregnanediol determination, evaluated together with the endometrial biopsy, may aid in ruling out one of these possibilities. Where a lack of progesterone is evident, replacement therapy might be indicated. High doses of oral progesterone were used as therapy in this series.

Therapeutic Experiments in Female Infertility

A. SHARMAN (Glasgow) stated that until ten years ago he performed tubal insufflations routinely both as a diagnostic and as a therapeutic procedure in all cases of primary sterility at the sterility clinic and in the wards of the Royal Samaritan Hospital for Women, Glasgow. Since then the procedure has been discontinued at the sterility clinic, as a routine measure, so that comparative experiments might be carried out, not only to assess the results of other methods of treatment but also to attempt a critical evaluation of the therapeutic merits of insufflation. A total of 2089 primary sterility patients were followed for twelve months, 893 after insufflation, 253 after the passing of a uterine sound, 286 after bimanual examination, 198 after commencing injections of progesterone combined with œstradiol benzoate, 300 after the oral administration of a mixture of ethisterone and ethinyl œstradiol, and 159 after the oral administration of inert tablets. The pregnancy rates at the end of the year were respectively, 17.4%, 17.8%, 10.8%, 16.6%, 14.3%, and 12.0%. In a series of nontreated and unexamined patients (355), who were merely interrogated and asked to return after their next period, 3 had no period following their visit to the clinic and were subsequently found to be pregnant (0.8%). Of 301 hospital inpatients, who were treated while the above hormone studies were proceeding, 67 (22.3%) became pregnant within twelve months of their stay in hospital.

Functional Aspects of Uterine Irritability and Tubal Occlusion

J. A. STALLWORTHY (Oxford) suggested guides to the clinician responsible for advising on infertility problems. (1) Every case should be investigated in full before advising on any one aspect of it. This demands knowledge of the male factor, ovulation, the uterus and endometrium, and tubal function. Unsuspected lesions, such as tuberculosis, will be discovered in this way. (2) Functional occlusion is more common than organic blockage. (3) Unilateral cornual occlusion in the absence of previous surgical intervention is most likely due to uterine irritability. (4) The radiological picture of bilateral functional cornual occlusion is identical with that of organic blockage following postabortal or puerperal sepsis. (5) Repeated negative tests by both insufflation and salpingography are not conclusive evidence of organic blockage. Reassurance, sedatives, and spasmolytics will reduce but not eliminate, errors. (6) The final diagnosis between functional and organic blockage is made only at operation and even then may be difficult. Retrograde insufflation should precede tubal implantation. The pathological report on tissue excised is the ultimate proof—or reproof!

Bilateral Ovarian Wedge Resection

I. F. STEIN (Chicago, Ill.) followed, for as long as twenty five years patients on whom bilateral ovarian wedge resection was performed for bilateral polycystic ovaries. He is convinced that this operative procedure, performed in carefully selected cases which conform to the definite syndrome restores reproductive function. He stated that in the entire series there has been no recurrence of bilateral polycystic ovaries, nor has there been a single instance of carcinoma of the endometrium. In some instances, as at cæsarean section and at hysterectomy, he has had the opportunity of inspecting the ovaries previously resected, and found them normal in appearance. In a few patients, postoperative fibrous adhesions were observed at laparotomy or by culdoscopy. However, pregnancy occurred despite the ovarian adhesions. He emphasised that the bilateral ovarian wedge resection is the treatment of choice and the beneficial effects are not self limited but last throughout the reproductive life of the woman.

Conception Following Tubal-patency Tests or Endometrial Biopsies

G. I. M. SWYER and H. H. FOURACRE BARNS (London) spoke of the prevalent belief that tubal patency tests have a therapeutic as well as a merely diagnostic value. It is further commonly held, they said, that conception is more likely to follow hysterosalpingography, especially if this be carried out with an oily rather than a non oily medium, than to follow uterotubal insufflation. However, no acceptable evidence in support of these views seems to be available, and they sought to provide this by comparing the incidence of conception in the arbitrarily chosen period of six months following a tubal patency test (in women with no obvious infertility factors, and with apparently fertile husbands) with that in a similar period following the performance of an endometrial biopsy—for which no special therapeutic value has ever been claimed. The differences in these incidences of conception are of doubtful significance and do not provide clear evidence in support of the above mentioned beliefs.

Donor Insemination

P. T. TOPKINS (New York) reported that approximately 80% of regularly menstruating, gynæcologically normal women who undergo donor insemination become pregnant. Conception occurs within six months in almost 90% of successful cases, within three months in almost 75%, and during the first month in about 33% of the cases. If conception does not occur within the first six months it becomes increasingly difficult to attain. The most productive method of determining insemination time is the Ogino Knaus calculation. Of those who conceive, approximately 15% ultimately abort.

Functional Significance of the Cervical Mucus

B. ZONDEK (Israel) gave a short review of the physical and chemical properties of the cervical mucus; the phenomena of arborisation with crystallisation of the dried mucus was discussed in detail.

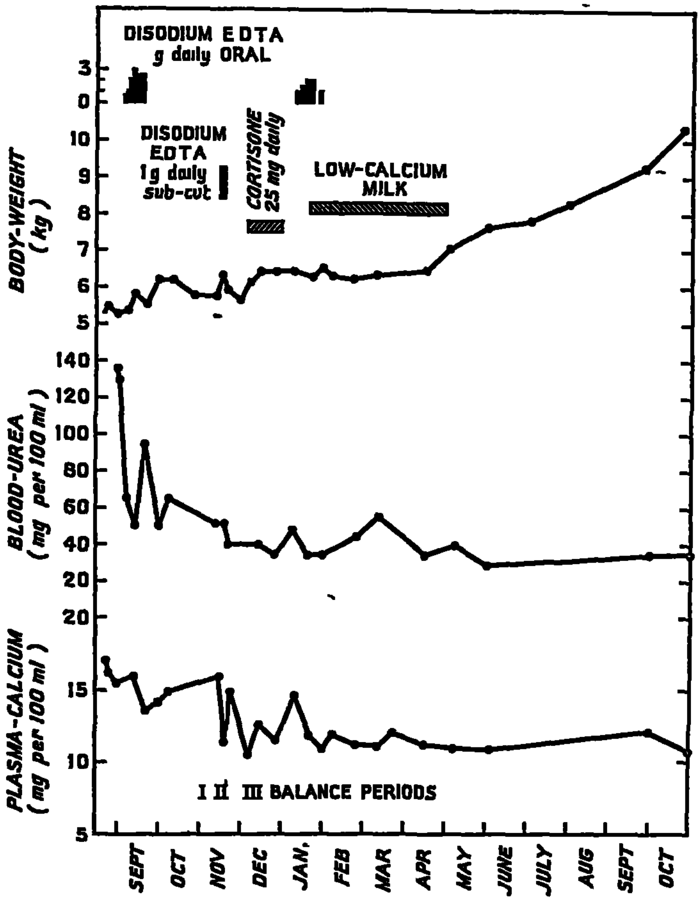

Fig 1—Case 1 variations in plasma calcium and blood urea levels and weight in response to EDTA, cortisone, and low-calcium milk (details in table I)

was started, 2 pints being given daily for ten days The amount of EDTA required to decalcify 2 pints is about 4 g, but we began with 0 5 g and increased this over a week to a daily dose of 3 g After two days at this level several loose stools were passed, and the dose was reduced to 2 5 g daily Soybean milk, still with EDTA 2 5 g daily, was then substituted for the breast milk but was not taken well Vomiting, frequent stools, and dehydration developed during the following week Both EDTA and soy feeds were then stopped The plasma calcium level had fallen to 13 6 mg per 100 ml Fresh cow's milk thickened with corn flour proved the best diet for restoring lost weight and general well being, but the plasma calcium level had risen to 14 8 mg per 100 ml after fourteen days on this diet (Oct 6, 1954)

Balance studies were started on Nov 3, 1954, the details are shown in table II and fig 2 After the control period disodium EDTA 1 g was given subcutaneously once daily for five days until signs of gastro intestinal disturbance developed By the third day of treatment the plasma calcium level had fallen from 15 7 to 11 4 mg per 100 ml, but it rose again to 14 7 mg per 100 ml a day after the EDTA had been discontinued After nine days without treatment a course of oral cortisone 25 mg daily was started on Nov 30, 1954, and this was followed by a gain in weight (balance period III) There was a striking improvement in appetite and general well being, and it became possible to add gravy and potatoes to the diet The plasma calcium level fell to satisfactory levels but rose after the cortisone therapy was stopped on Jan 1, 1955 Breast milk and oral EDTA (up to 2 g daily) were then given until low calcium milk ('Locasol,' Trufood) was obtainable on Jan 21, and thereafter the plasma calcium level remained below 12 mg per 100 ml By Feb 11 the child was feeding well enough to be sent home on locasol and a low calcium mixed diet In May she began taking cow's milk and bread with the standard fortification with calcium In July her Hb had decreased to 6 56 g per 100 ml, and iron was given In September, 1955, at the age of 20 months, she had just begun to walk and to wave her hand The systolic murmur was less intense than formerly, but the ocular pareses were unaltered She was very bright and happy

Case 2—A boy, born on Jan 11, 1954, by forceps delivery because of disproportion, weighed only 5 lb 5 oz although he was said to be overdue He was the first child of healthy young parents, there was no relevant family history He was breast fed for a week and then changed to half cream National dried milk because appendicitis developed in his mother His progress was satisfactory, and at the age of 3 months, when mixed feeding was started, he weighed 12 lb 8 oz About the age of 4 months he began to vomit occasionally after feeds but continued to gain weight Until he was 6 months old he passed one soft stool daily, but thereafter his stools became hard and less frequent At 7 months the vomiting began to increase in frequency and severity, and his family doctor prescribed 'Milk of Magnesia' In spite of this the constipation and vomiting continued, and the boy began to refuse feeds and to lose weight He was therefore admitted to Dundee Royal Infirmary on Sept 2, 1954, at the age of 8 months, under the care of Prof J L Henderson At this time he was on a diet of full cream National dried milk, strained soups sieved vegetables and fruits, and cereal foods He had also had half a teaspoonful of National cod liver oil compound (400 I U of vitamin D) daily since the age of 2 weeks

On admission he was pale and rather irritable and weighed 12 lb 15 oz He had general muscular hypotonia with lax skin but no clinical dehydration His anterior fontanelle admitted a finger tip No murmur or other cardiovascular abnormality was present, and electrocardiography showed no prolongation of the P–R interval There was slight inflammation of the right tympanic membrane

Investigations—The urine contained no protein or sugar and only a few pus cells Its pH was 7 5, and it was sterile on culture Radiography of the heart, lungs, skull, and long bones showed no abnormality The plasma calcium level was 14 8 mg per 100 ml and the blood urea level 50 mg per 100 ml Values for other electrolytes are given in table III

Treatment and progress—During the first six weeks in hospital the infant was given fresh cow's milk with no added vitamin D His general condition improved and vomiting became less frequent, but in spite of this his weight gradually fell and the plasma-calcium level rose to 18 8 mg per 100 ml Further culture of the urine grew *Escherichia coli*, and streptomycin was given for six days

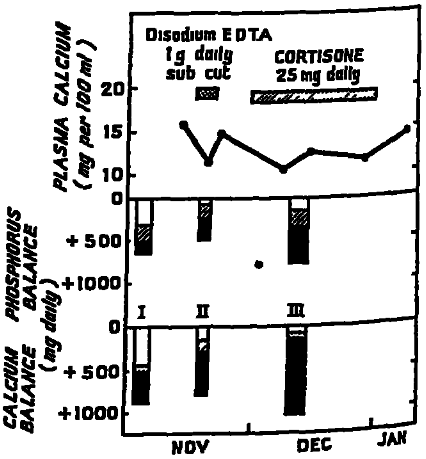

Fig 2—Case 1 balance data for calcium and phosphorus Intake is plotted downwards from baseline faecal output (black) and urinary output (hatched) are then plotted upwards A positive balance (excess of intake over output) is shown by a clear space below the base line (details in table II)

Balance studies were started on Oct 19, 1954, the details are shown in table IV and fig 3 The administration of cortisone from Oct 27, 1954, produced a dramatic improvement in the child's general well being, his weight increased, his appetite improved, and he lost his fretfulness and irritability This improvement coincided with a fall in the plasma calcium level, and on the one occasion during ten weeks on cortisone when the plasma calcium level rose to a high value after the dosage had been reduced, the irritability and anorexia returned, to disappear again as the plasma calcium level fell when the dosage of cortisone 25 mg was resumed

Letters to the Editor

ANÆSTHESIA IN OBSTETRICS

SIR,—I would like to comment on a few of the points raised by Dr Coleman and Dr Day in their interesting article (May 19) and by your annotation in the same issue.

I am not convinced that Coleman and Day have solved, by the method they advocate, the problem which they have posed. The results of their experience with a method involving endotracheal intubation are impressive, but no better than those which should be—and I feel are—obtained by equally competent anæsthetists working with drugs and equipment to which they are accustomed.

Those who claim that vomiting is a perpetual hazard in obstetric cases, however skilfully the anæsthetic be administered, indicate that it is most likely to occur during the induction period—the phrase “stormy induction” occurs with great regularity in the tales of disaster of this class. Yet Coleman and Day make no special provision for this period other than the prophylactic one of having suction apparatus handy. I calculate that, unless the anæsthetist in charge has a medically competent associate working with him in the labour ward or the theatre (a rare event except in teaching units), the time elapsing between application of the anæsthetic mask and inflation of the endotracheal cuff is likely to be more than four minutes. Attempts to hurry induction, or premature attempts to intubate, would merely invite regurgitation or vomiting. You go some way towards making this point in your annotation, but I feel that even so you are too confident about the modification you suggest.

I believe that Coleman and Day introduce an unnecessary hazard into the anæsthetic management of these cases. If the postulate that “the woman in labour presents problems similar to those in cases of intestinal obstruction” is accepted, then naturally the management of each must follow a similar pattern. It is now accepted teaching that a large-bore gastric tube (definitely not a Ryle's tube) should be passed preoperatively on each patient with intestinal obstruction. To comment as do Coleman and Day that the passage of such a tube increases the “fear and distress” of the woman in labour is merely to invite the reply “better that than a disastrous induction.” The observation of Coleman and Day that “commonly the quantity of fluid and debris recovered is small” must mean that if the gastric tube was of wide enough bore, the stomach was virtually empty.

There are, however, two other aspects of this question which I consider to be of very considerable importance. Coleman and Day reiterate the long held contention that during labour the gastric emptying-time is prolonged. I have recently attempted to show,[1] with the help of Dr F. Hutton, radiologist at the Central Middlesex Hospital, for whose cooperation I am grateful, that this is by no means true. We performed barium-meal examinations on twelve women in established labour, and the times of gastric emptying showed the same range of variation as in the normal subject (from 2 hours to over 8 hours in our series). This generalisation we can apply only to patients who are on fluid or semi solid diets of the type which should by now be the rule for all patients in labour.

The conclusion to be drawn from this investigation was that the renowned hazard of obstetric anæsthesia is not due to “the inevitable retention of gastric contents in labour.” I feel that the important factors are the choice of agents used for induction of anæsthesia and the competence with which the anæsthetist is able to use these agents. Most anæsthetists in this country use thiopentone for induction in the majority of their cases. Yet in their obstetric practice they revert to a sequence of inhalation anæsthetics which in the non-sedated patient invites the hazards that may be grouped under the term “stormy induction.” Thiopentone provides a smooth and rapid induction, and, at least in a dose of about 250 mg., exerts no undue depressant effect upon the child regardless of how long the obstetrician takes over the delivery.[2]

The employment of thiopentone is often opposed on the ground that it demands a high standard of professional competency. I feel that no practitioner lacking that degree of competence should be permitted to indulge in obstetric anæsthesia. Although I claim that the method I suggest is the most satisfactory, it would be stupid to deny that any method, willingly undertaken by a competent anæsthetist in a large series of cases, will be associated with a very low disaster-rate.

This of course, as you suggest at the conclusion of your annotation is the real crux of the matter. I read with great interest Professor Russell's article (May 12) and your editorial comment. I feel very strongly that, just as “dabbling in midwifery must be discouraged, in much the same way as dabbling in surgery is discouraged,” so should the employment of an “occasional” anæsthetist be countered as far as possible, and also the application of the “occasional” technique for potentially poor-risk cases (i.e., non-routine inductions for obstetric patients). I have long believed that there should be a general-practitioner anæsthetists' list analogous to the G.P. obstetricians' list. I fail to understand why anæsthetics has been allowed to assume the place it now holds in the curriculum of undergraduates. Students on the general surgical and obstetric “firms” are rarely permitted to do more than assist in the theatre, or to perform a vaginal examination before the obstetrician applies forceps. Yet they are expected to conduct up to twenty major and minor anæsthetic cases (albeit under supervision) and are then encouraged to consider themselves competent to conduct such cases (in hospital or domiciliary practice) as soon as they qualify. Surely it would be enough that undergraduates be given a short course of lectures on anæsthetics and be taught how to maintain the airway of an unconscious patient? This would help to reduce an already overburdened curriculum, and might also possibly enable the senior anæsthetists to supervise more closely the work of their graduate trainees in the labour wards—at least in the daytime. It would also help to discourage general practitioners not on the anæsthetists' list from giving occasional anæsthetics.

To summarise: I suggest that if (*a*) domiciliary anæsthetics (which are mainly for obstetric cases) were given only by doctors who have had postgraduate experience in the specialty, and (*b*) the routine of induction of anæsthesia for obstetric cases in both domiciliary and hospital practice were similar to those used by the individual anæsthetist for the majority of his general surgical cases, we would be much closer to solving this pressing problem than we are likely to get by pursuing some panacea in the form of a fool-proof anæsthetic.

London, W.1. J. SELWYN CRAWFORD

. We refer to Dr Crawford's work on thiopentone levels in an annotation on p. 898.—ED. L.

SIR,—You leave unanswered several important questions in your annotation regarding the future of obstetric anæsthesia.

The problem, as you state, has become increasingly important in the post-war years as one of the major causes of maternal mortality and morbidity in hospital obstetrics. Its dangers can, however, be greatly reduced and strictly circumscribed.

It is possible to conduct the large majority of hospital and almost all domiciliary forceps deliveries under

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[1] Crawford, J. S. *Brit. J. Anæsth.* 1956, 28, 201.

[2] Crawford, J. S. *Ibid*, p. 146.

TABLE III—BIOCHEMICAL DATA AND BODY-WEIGHT IN CASE 2

Date	Wt (kg)	Plasma calcium (mg per 100 ml)	Plasma phosphorus (mg per 100 ml)	Blood urea (mg per 100 ml)	Plasma sodium (m eq per litre)	Plasma potassium (m eq per litre)	Plasma chloride (m eq per litre)	Plasma bicarbonate (m eq per litre)	Plasma cholesterol (mg per 100 ml)	Plasma protein (g per 100 ml)	Plasma albumin (g per 100 ml)	Other
Sept 3 1954	5 9	14 8	3 8	50			97 4	23 3	225	8 0	5 4	
„ 20	5 6	18 8	5 1	55			104	24 2	250	7 5	4 1	
Oct 19 „	5 5	16 6		55					275			
„ 20–24 „		*Period I*										
23	5 5	18 5	4 1									Hb 12 7 g per 100 ml
27 „	5 6	19 0	4 9									
27–31 „		*Period II*										
Nov 2 „	5 9	12 6	3 5	30	139	5 0						
8	6 2	12 4	3 9									Magnesium 3 0 mg per 100 ml
„ 9–13 „		*Period III*										
„ 15	6 4	12 0	3 0	30	150	4 1	100	17 3	160	7 2	4 2	
„ 22 „	6 8	12 5	4 0	30	134					8 1	4 9	
„ 25–29		*Period IV*										
„ 30 „	6 5	17 2	4 1	45	154	5 4		26		8 7	5 1	
Dec 7 „	6 4	11 8	2 7	30	157	3 5		25 3	250	7 4	4 5	
14	6 7	11 0	3 6	25	150	3 4		37	250	6 9	4 1	Ceph flocc neg Thymol turb ' unit
19–23 „		*Period V*										
„ 24	6 7	11 8	2 7	20	139	4 4		26	250	6 7	3 8	
„ 31 „	6 5	10 1	6 4	95				20 6				–

I–III, with added custard in period IV and added apple in period V Samples of the diets for each period were analysed

The bulked stools were strongly acidified with hydrochloric acid before being mixed mechanically Fæcal and dietary samples were ashed in silica crucibles, dissolved in three washings of hot 2*N* hydrochloric acid, and made up to volume

Urine was mixed, strongly acidified, and allowed to stand at least a week (to precipitate uric acid), and the supernatant fluid was sampled (Badenoch and Fourman 1954)

For the calcium determinations McCrudden's method, modified slightly from Hawk et al (1947), was used on the extracts and on the urine, and also, in case 1, on samples of ashed urine For the phosphate determinations the method of Fiske and Subbarow (1925) was used

All the results represent at least two estimations on each of two samples

Balance Studies

The results of balance studies are given in tables II and IV and figs 2 and 3 Certain features are common to both cases In the control periods there was a large absorption of calcium (57 5% and 61%) and of phosphorus (74% and 84%) producing a strongly positive balance despite relatively large outputs in the urine At this time each infant had severe hypercalcæmia and moderate azotæmia, and therefore only one control balance study was made

Oral cortisone 25 mg daily in each case more than doubled the fæcal calcium and phosphorus and diminished the retention of calcium by about 330 mg a day and of phosphorus by about 130 mg a day The urinary calcium increased from 45 to 87 mg a day in case 2 but diminished from 55 to 21 mg a day in case 1, although the latter balance study was not started until the tenth day of treatment with cortisone The amount of urinary phosphorus was not significantly altered The plasma calcium and plasma-phosphorus levels returned rapidly to near normal, and the clinical status improved greatly A week after the start of cortisone therapy the plasma-calcium level had dropped from 19 0 to 12 6 mg per 100 ml in case 2 and from 14 7 to 10 6 mg per 100 ml in case 1

Subsequently in case 1 the cortisone was discontinued after a month, and later the plasma-calcium level rose from 11 5 to 14 5 mg per 100 ml , it fell again while oral EDTA and breast milk, and later locasol (fig 1), were being given

In case 2 clinical improvement on cortisone permitted a much greater intake of milk during period III, and the retention of calcium and phosphorus then exceeded that of the control period, although the proportion of each

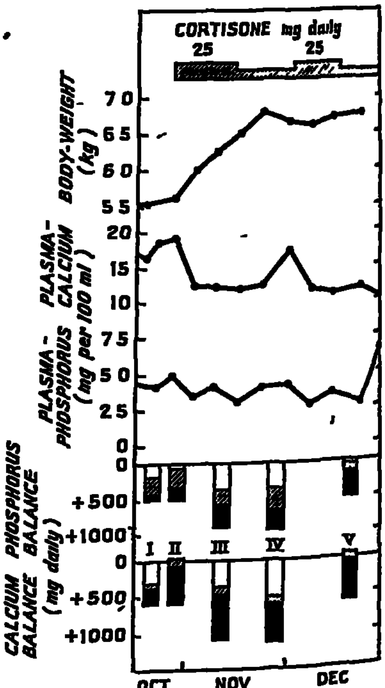

Fig 3—Case 2 balance data (details in table IV)

TABLE IV—BALANCE FINDINGS IN CASE 2

Period	Therapy	Calcium (mg daily)						Phosphorus (mg daily)					
		Excretion			Diet	Balance	Absorption (%)	Excretion			Diet	Balance	Absorption (%)
		Fæces	Urine	Total				Fæces	Urine	Total			
I(Oct 20–24)	Nil	228	45	273	587	+314	61	80	230	310	493	+183	84
II(Oct 27–31)	Cortisone 25 mg daily	510	87	597	587	–10	13	178	261	439	493	+54	64
III(Nov 9–13)		664	80	744	1104	+360	40	342	212	554	894	+340	62
IV(Nov 25–29)	Cortisone 12 5 mg daily	574	80	654	1171	+517	51	280	327	607	948	+341	70
V(Dec 19–23)		625	41	666	630	–36	1	380	106	486	510	+24	25

arachidonic from 0 8 to 0 3 g In 1952 the E F A content was about 3 2 g per 2500 calories An idea of the human requirements of E F A was indicated by mentioning the 13 3 g E F A per 2500 calories of human milk This figure is strikingly close to the figures mentioned above

Copenhagen　JOHAN E NYROP

LYMPHATIC DRAINAGE OF THE BREAST

SIR,—The pathways of lymphatic drainage of the breast have been studied by intravital methods Solutions containing iron and patent blue, and in some cases a radioactive tracer, have been injected into the tissues of the breast A proportion of this is taken up by the lymphatics thus demonstrating the lymphatics during operation and in cleared surgical and post-mortem specimens[1]

In addition to the commonly described axillary and internal mammary pathways, lymphatic vessels can be seen to accompany the lateral perforating branches of the intercostal blood vessels that supply the breast, these drain into the posterior intercostal lymph nodes lying between the necks of the ribs in close relation to the vertebræ

Post-mortem examination of the posterior intercostal nodes has shown that they may be invaded by carcinoma of the breast, and there is also evidence that this pathway may be involved fairly early in the spread of the tumour in some cases If routine postoperative radiotherapy is employed in the treatment of this disease, it would seem rational to include these nodes in the treated area

Middlesex Hospital
London W 1　R T TURNER-WARWICK

DIABETES AND PARITY

SIR,—The data which Dr Pyke has reported in his article of June 2 are of great interest, and his interpretation of them—that the chance of a woman developing diabetes after the age of 45 increases with the number of children she has had—is probably correct The alternative explanation—that women who are genetically predisposed to diabetes are more fertile than normal women —must be carefully considered, however, and perhaps Dr Pyke could report further details of his patients which might help to answer the problem

Diabetes mellitus has such a high frequency in the population that recurrent mutation alone cannot account for its gene frequency having reached the estimated 15% It is likely therefore that the diabetic genes confer some biological advantage to counter their loss from the population due to young diabetics failing to reproduce in the generations before insulin therapy was introduced The disease is usually inherited as a recessive character, and the simplest mechanism by which the polymorphism could be maintained in the population would be by individuals heterozygous for a diabetic gene being generally more fertile than individuals without the gene, data published previously suggest that this may indeed be so, as the parents of diabetics have in several series been found to have more children than do the general population If the heterozygotes are more fertile than normal people, it would be reasonable to expect diabetics also to be more fertile than normal before they develop the disease, and it would be of great interest to know if Dr Pyke's data support this expectation or not

One would expect to find a higher percentage of diabetic women in the higher parity groups, and a lower percentage in the lower parity groups, than is found with normal women Dr Pyke's tables II and IV show that this is what he finds His percentage of nulliparæ (19 6%) is so very much lower than the normal (32 6%) that it would be of interest to know what proportion of them remained unmarried up to the menopause, compared with the proportion found in the nulliparæ of the general population If the proportions in the two groups are similar it could be regarded as evidence in favour of the explanation of the data being that parity increases the chances of developing diabetes, but if the proportion of unmarried is higher in the diabetic nulliparæ it would favour the hypothesis that the diabetic genes increase fertility

Heredity Clinic
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SIR,—Is the apparent "effect of parity" on women due to parity as such, or to the "stress" involved in bringing up more children under present conditions? Is there, I wonder, any difference in the incidence of diabetes in mothers with and without domestic help?

Sanderstead Surrey　EVE STRATON

HOME CONFINEMENTS

SIR,—The four London regional obstetric committees have been concerned for a long time that practitioners who are admitted to the list of general-practitioner obstetricians should have had adequate experience Since 1948 they have admitted to the list practitioners who have been responsible for 30 confinements within a period of three years or who have held a resident obstetric post

They have now decided that, save in exceptional circumstances, practitioners who have qualified since Jan 1, 1951, and who wish to be included in the London list of general-practitioner obstetricians must, as from May 1, 1957, have held a resident house job in obstetrics for a period of six months

Any applications received before May 1, 1957, will be considered in the light of the standards mentioned in the second sentence of this letter

J A SCOTT
Public Health Department　Chairman London
County Hall London S E 1　Local Obstetric Committee

PARAPLEGIA FOLLOWING SPINAL ANÆSTHESIA

SIR,—Sir Francis Walshe's usual, delightful, pellucid English for once leads him into obscurity Paragraphs 8 and 9 of his letter (June 2) detract from what is otherwise a logical theoretical argument which arrives at an incontrovertible conclusion "There is some special risk in spinal anæsthesia"

Had the corpus of anæsthetists been present, as I was, at a symposium in Bangalore in 1946 on Complications of Spinal Anæsthesia, and seen the wardful of paraplegia and spinal osteomyelitis there assembled, they would have arrived at the same conclusion as Sir Francis on the evidence before their eyes

They would have resolved, as I did, never to introduce foreign bodies into the theca again

Anæsthetists Sir Robert Macintosh amongst them, need not ' substitute their naïve optimism for knowledge " No further research is needed Abandon spinal anæsthesia

London S W 3　L H LERMAN

SIR,—This subject is, as the correspondence shows, one fraught with difficulties Without wishing to add to these, I would like to mention that I have injected into a patient with inoperable carcinoma the phenol glycerin mixture of Maher[1] into the theca below L5, without any neurological changes whatsoever ensuing A week later the injection was repeated, this time using phenol-glycerin-water Whilst the perineal pain for which it had been given was slightly improved, no other neurological changes immediate or remote were demonstrable

In addition, I feel that we must go in for some hard thinking regarding the justification of the use of spinal stated that addition of the vitamin to the milk mixture in manufacture may be uneven (Spur 1953), hence there may be an unknown difference between the estimated and the actual dosage. The inaccuracy of the methods of assaying vitamin D and the need to ensure a product of at least the required potency are likely to lead to excessive supplementation with the vitamin. The importance of the relative potency of the different forms of vitamin D cannot at present be assessed (Bicknell and Prescott 1953).

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[1] Turner Warwick R T *Lancet* 1955 ii 1371

[1] *Lancet* 1955 i 118

The apparent absence of idiopathic hypercalcæmia in the United States (H. E. Harrison, personal communication) and Canada (D. A. McGreal, personal communication) and its rarity in Sweden (Mellander 1955) may be related to the smaller intake of vitamin D in milk in these countries. The contrast is striking, for in the United States fortified whole milk and reconstituted evaporated milk contain about 400 I.U. per U.S. quart (946 ml.) (American Medical Association 1955), whereas in the United Kingdom reconstituted National dried milk has contained at least 1400 I.U. per quart (1152 ml.) for the past ten years. In Finland, where milk is not fortified, hypercalcæmia has been reported in 59 cases of interstitial plasma cell pneumonia (Hallman 1955), but 58 of these infants had had previous massive dosage of vitamin D (500,000–3,000,000 I.U.) as a prophylaxis against rickets.

If hypervitaminosis D, due either to overdosage or to increased sensitivity, is the main cause of hypercalcæmia, other signs of overaction of the vitamin might well be found. The nephrocalcinosis and renal insufficiency in case 2 and in other fatal cases might be explained by vitamin-D overactivity. Renal disease can increase the toxicity of vitamin D in rats (Opper 1941) and man (Anning et al. 1948, Chaplin et al. 1951), and this interrelationship may lead to a vicious circle when hypercalcæmia has begun to impair renal function, as it always does eventually. The recurring urinary infections in idiopathic hypercalcæmia also presumably increase the susceptibility to the vitamin's action.

Neither of our patients showed the lines of abnormally dense bone near the epiphyses of the long bones as described in hypervitaminosis D by Ross and Williams (1939). Possibly, however, the osteosclerosis in some severe cases of chronic hypercalcæmia (Schlesinger et al. 1956) may partly be due to this vitamin. Low plasma alkaline phosphatase levels, hypercholesterolæmia, and hyperglobulinæmia have been recorded in some cases of this syndrome, and also in hypervitaminosis D (Ross and Williams 1939, Anning et al. 1948, Powell et al. 1948, Payne 1952, Bonham Carter et al. 1955).

Action of Cortisone

Under the influence of cortisone the plasma calcium levels of our patients rapidly fell to normal or near normal values. Cortisone could achieve this result by increasing the urinary excretion of calcium, increasing the secretion of calcium into the gut, decreasing the absorption of calcium from the gut, or redistributing calcium within the body.

Increased elimination of calcium in the urine could have played no significant rôle in our patients, because in case 2 the increase was only about 40 mg. a day, whereas in case 1 there was a decrease of more than 30 mg. a day in spite of a larger intake.

On the other hand, the effect of cortisone in increasing the fæcal calcium was in each case large, indeed so large that this change alone could account quantitatively for the rapid fall in the plasma calcium level.

We could not, however, determine whether increased secretion or decreased absorption of calcium was mainly responsible for the increased fæcal calcium. If cortisone acts as a direct antagonist to vitamin D, as suggested by Anderson et al. (1954) in reference to hypercalcæmic sarcoidosis, it must do so by decreasing the absorption of calcium. Nevertheless cortisone may also increase the secretion of calcium into the gut. Thus a patient with Cushing's syndrome, receiving corticotrophin 50 mg. a day, excreted in the fæces an amount of calcium which exceeded the dietary intake (773 mg.) by 1400 mg. a day (Soffer et al. 1950). We have obtained a similar result in a four-day balance study of a man with asthma receiving 200 mg. cortisone daily. The fæcal calcium (554 mg. a day) exceeded the dietary calcium (291 mg. a day) by 263 mg. a day (unpublished work).

The results of our balance studies do not require us to invoke any other mechanism for the decrease in the plasma calcium level by cortisone than the action of increasing the fæcal calcium, but there may well have been some redistribution of calcium within the body. This is suggested by the relatively low plasma calcium levels in case 2 during period III, when there was a large retention of calcium.

Treatment

The clinical improvement in our patients accompanied pari passu the fall in the plasma calcium level whether this was due to cortisone, E.D.T.A., or simply a small intake of calcium. The first essential in treatment is therefore the reduction of the hypercalcæmia. This is effected by a diet without added vitamin D and containing as little calcium as possible, certainly not more than 300 mg. a day (cow's milk contains about 1400 mg. of calcium per quart). The basis of such a diet may be a low calcium milk powder (e.g., locasol) or cow's milk treated with a cation exchange resin which substitutes sodium, potassium, and magnesium for calcium, supplemented when possible in either case by a cereal containing little calcium—e.g., 'Farola' and 'Glaxo Low Calcium Cereal Food' (available at present only through hospitals). The cation exchange process is complicated and time consuming and is becoming less necessary with the increasing availability of commercial low calcium milk powders. Using such diets Ferguson and McGowan (1954) found that the serum calcium level became normal in two to six weeks. Supplementary iron should be given with these modified milks.

During the initial phase of treatment no vitamin D supplements should be given. After normal blood calcium levels have been attained, the intake of calcium can be gradually increased, preferably as fresh cow's milk, and later a small amount of vitamin D should be added to prevent rickets. Alkalis should be avoided because they are likely to favour the deposition of calcium in the kidneys, and a generous intake of fluid will minimise the possibility of metastatic calcification in the renal tract.

Cortisone should be used whenever it is desirable to achieve a more rapid return of the plasma calcium level to normal, but it is unnecessary to use it in the more common mild cases. The balance data in case 2 show that cortisone was effective in reversing the positive calcium balance only when the dietary calcium was restricted to about 600 mg. a day. Cortisone 25 mg. daily for an infant aged up to 1 year produces a satisfactory clinical and biochemical response. Whenever cortisone is given for more than a few days, it is wise to supplement the diet with potassium chloride, unless the child has significant uræmia.

We do not recommend treatment with E.D.T.A., although we found it effective in reducing hypercalcæmia, because of the gastro-intestinal irritation. Moreover a tendency to hæmorrhages and renal tubular damage may follow the intravenous administration of large doses of E.D.T.A. (Wishinsky et al. 1953, Dudley et al. 1955).

The absorption of calcium might be effectively decreased by giving oral sodium phytate. This has been

been sound rather than spectacular The safety regulations under Clause 1 and any orders extending the scope of the Bill under Clause 17 would be subject to an affirmative-resolution procedure, as also any orders made under the new clause for preventing overlapping with the Factories Acts He had no illusion that by passing the Bill Parliament would automatically achieve its objectives Everything would depend upon the regulations This task would be undertaken in earnest and every effort would be made to ensure that the regulations should be effective and sensible

QUESTION TIME

Registration of Medical Auxiliaries

In answer to a question Miss PATRICIA HORNSBY SMITH, parliamentary secretary to the Ministry of Health, said that the Minister did not propose to publish the report of the working party set up to inquire into the possibilities of State registration of medical auxiliaries, since it was prepared for confidential circulation only He was considering the views of all the bodies concerned and hoped to make a further statement soon

Obituary

WILFRID PATON PHILIP

M C , M B Aberd , Hon M A Camb , D M R E , D P H

FOR 36 years, until his retirement last year, Dr Paton Philip had been responsible for the tuberculosis services of the county, city, and university of Cambridge He will be especially remembered as a pioneer in the use of X rays, for he was one of the first to appreciate the value of the proper screening of patients

He was born at Stonehaven and he studied medicine at the University of Aberdeen After graduating M B in 1912 his first posts were in Merseyside where he served as house officer in the Stanley Road Hospital, Liverpool, and later as assistant tuberculosis officer and bacteriologist at Bootle During the 1914–18 war he served with the R A M C and won the Military Cross Soon after demobilisation he went to Cambridge, at first as assistant medical officer at Papworth Village Settlement In 1919 he succeeded Sir Pendrill Varrier-Jones as tuberculosis officer to the county A few years later he began to use X rays for diagnosis, and G L C recalls how "in those difficult days of administrative control by small and poor local government authorities, Philip's first apparatus in the then tuberculosis dispensary was bought out of his own pocket—and he was an Aberdonian" In 1929 he took the D M R E and in 1931 the D P H

He renewed his early association with Papworth when he became physician to the settlement, and his special interest in preventive medicine and in diagnosis was of great value to the Cambridge University Health Service With the establishment of the National Health Service he became consultant in chest medicine to the East Anglian Regional Hospital Board and he was also consultant chest physician to the United Cambridge Hospitals In recognition of his work the university in 1950 conferred on him the honorary degree of M A , and in the same year he was elected a fellow of the American College of Chest Physicians Two months ago, soon after his retirement, his colleagues and associates in teaching gave him a presentation 'in token of their gratitude and affection"

A L B writes "Philip was by nature an artist, with all the advantages and some of the disadvantages of the artistic temperament There can be few physicians in the long history of medicine who were so well beloved as he was by his patients and his fellows He had, like all great clinicians, that sixth sense which led him to the true heart of a difficult case The mere words 'P P does not think so' were enough to dispose of alternative diagnoses He was a big man physically, of striking appearance, and always well dressed His emotions were easily aroused, and it could be an embarrassment to walk down King's Parade with him while he discussed, with a wealth of gesture, some rare case His temperament was such that he found official rules and regulations particularly irksome, and the unfortunate officials whose duty it was to administer them sometimes felt the weight of his anger His oratory on such occasions was impressive For a long time I represented 'the Ministry' in his mind and so I, perhaps better than most men, can pay tribute to his selflessness In all the years I knew him he never sought anything for himself, other than recognition of the importance of the work on which he was engaged and proper provision for this It was fortunate that in the latter years of his life, when his clinical skill and wisdom were at their peak, he was given membership of the University, consultant status in the National Health Service, and an in-patient unit of his own I think that he would have agreed that the last ten years were the happiest of his professional life Now it has ended, and we in Cambridge mourn the loss of a man who did so much to maintain the reputation of medicine and the standing of the physician"

Dr Philip leaves a widow two sons, and a daughter

NORMAN DARROCH BEGG

M D Aberd , D P H

Dr Norman Begg, director of the European region of the World Health Organisation, died in London on May 23, after a short illness, at the age of 49 At the closing meeting of the World Health Assembly in Geneva a tribute was paid to his work

He was born of Scottish parentage at Kuling, China, and educated in Aberdeen, where he graduated M B in the University in 1929 He took the D P H in 1932 and joined the fever-hospital service of the London County Council in 1934 at the North-Eastern Fever Hospital A year later he went to Southend-on-Sea as medical superintendent of their fever hospital where he also acted as epidemiologist on the staff of the medical officer of health and was much in demand for domiciliary consultation In 1937 he returned to the L C C service as medical superintendent of the Eastern Fever Hospital at Homerton As with other London fever hospitals, a section was set aside for air-raid casualties The district was heavily bombed on many occasions and Begg faced courageously and with conspicuous success the many demands on his administrative and clinical skill

From the early days of the war he had applied repeatedly to be allowed to join the medical services of the Armed Forces, but he was required to continue his civilian work In 1945, however, when the air-raids on London ceased he was permitted to accept an invitation from the United Nations Relief and Rehabilitation Administration to work in Poland His secondment was in the first place for one year, but it was extended year by year until 1948 when the fever hospitals were transferred to the regional hospital boards Shortly before this Begg had been appointed medical superintendent of the North-Eastern Fever Hospital, but he never took up the post, and in 1948 he resigned from the hospital service to accept an appointment with W H O which had just been established He remained in Poland for some time and was later appointed chief of W H O 's special office in Europe, with responsibility for the reconstruction of the health and hospital services in the war-devastated countries of Europe After the decentralisation of the work of W H O into regions in 1951 he was appointed director of the regional office for Europe, which included several countries in North Africa and the Near East His post was one of the most difficult in public-health administration Most countries in the region are not like those in other parts of the world, preoccupied with the need to obtain outside assistance in developing health services from an existing rudimentary level Each has already reached a high level of development in health work, their future advance cannot be based merely on the lessons of experience elsewhere It was the recognition of this that led him to plan a European programme which differed sharply from the activities in other regions It was characterised by cooperative activities from which the health workers of many countries benefited, rather than assistance which benefited only a particular country It concentrated especially on the interchange and spreading of knowledge and practice within Europe, and the international seminars, which were a prominent

MANAGEMENT OF "IDIOPATHIC" HYPERCALCÆMIA IN INFANCY

THOMAS STAPLETON
D M Oxfd, M R C P
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W B MACDONALD
M D Melb, M R A C P
LECTURER IN PÆDIATRICS

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M D Lond, F R C P
DIRECTOR, PÆDIATRIC UNIT

ST MARY'S HOSPITAL MEDICAL SCHOOL, LONDON

THE purpose of this paper is to record the management of an infant with "idiopathic" hypercalcæmia by means of a diet which was almost free of calcium The results of this trial not only confirm that such treatment may restore the raised serum calcium to a normal level (Creery and Neill 1954, Ferguson and McGowan 1954, Russell et al 1954, Stapleton and Evans 1955, Bonham Carter et al 1955, Macdonald and Stapleton 1955), but also demonstrate the possibility of reversing certain of the cardiovascular and renal changes in the severe grades of the disorder

Case-report

A male infant was born three weeks after the expected date, weighing 5 lb 10 oz Labour was induced, but was uncomplicated His mother had had no added vitamins during her pregnancy There was one sibling, a healthy girl aged 3 years

The infant was breast fed for six weeks From the age of 18 days he received a complement of 1 fluid ounce of reconstituted half cream National dried milk (containing not less than 280 I U vitamin D per dried ounce) to each feed At the age of 6 weeks breast feeding was discontinued and he was fed on half cream National dried milk He progressed well, physically and mentally, until the age of 8 weeks when he weighed 9 lb From this time he failed to thrive, and at the age of 10 weeks he began to vomit His feeding was changed to full cream National dried milk (containing not less than 280 I U vitamin D per dried ounce), then successively to 'Ostermilk' no 2 (containing not less than 320 I U vitamin D per dried ounce), Nestle's Sweetened Condensed Milk (containing no added vitamin D), full cream dairy milk, and half cream National dried milk He received 1 teaspoonful of orange juice per day from the age of 3 months, and for four days only he was given 2 drops of 'Radiostoleum' per day He received no other vitamin supplement Despite these changes in diet, vomiting persisted, and his weight remained about 9 lb He was constipated from the age of 3 months He took water eagerly without vomiting At the age of 3 months he was attempting to raise his head, and was grasping at objects, but from this age he became hypotonic and h neuromuscular development did not progress He wa contented baby in spite of his failure to thrive

On admission to Southend General Hospital, at the age of months, his weight was 8 lb 15 oz "Idiopathic" hyp calcæmia was diagnosed (serum calcium 14 0 mg per 100 ml On Sept 10, 1955, aged 5 months he was transferred to S Mary's Hospital for special study He was alert and co tented, but weighed only 9 lb 1 oz His muscle tone w poor, but the deep reflexes were active His appetite w poor and he was constipated His skeletal measurements a skull circumference were normal (see table) and the anter fontanelle was patent A moderately loud systolic bru which had not been recorded previously, was found T heart was not enlarged His systolic blood pressure when was quiet was 170–185 mm Hg (flush method) Radiologic examination showed no abnormality in the long bones, b in the astragalus and os calcis on each side there were peripher zones of greater density surrounding relatively transluce central cores No centres of ossification were seen in t carpal bones

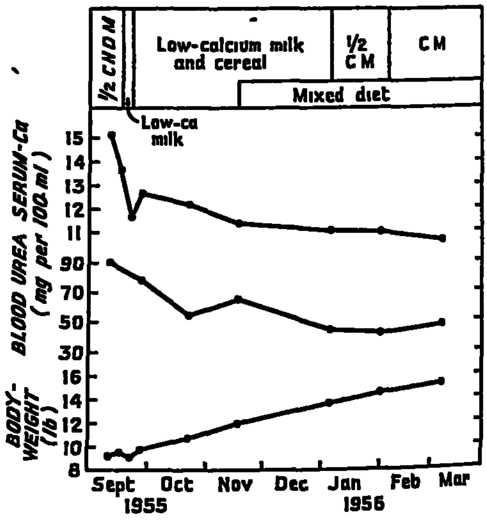

Fig 1—Treatment related to serum-calcium and blood urea levels a body weight Symbols as in table

Serum biochemistry confirmed the diagnosis of hyp calcæmia There was azotæmia and the serum alkalin phosphatase level was low (see table) There was no glyc suria, albuminuria, or amino aciduria Microscopy of t urine showed an occasional pus cell, a slight growth protous was believed to be a contaminant An electr cardiogram was normal

The sudden onset of the illness at an early age the failu to gain weight, hypertension and systolic murmur an azotæmia indicated a moderately severe grade of the disea

CLINICAL AND BIOCHEMICAL PROGRESS WITH CHANGES IN DIET, FROM TIME OF ADMISSION TO ST MARY'S HOSPIT

Date	Age (mos)	Diet	Weight (lb oz)	Length (in)	Skull circ (in)	Cardiac murmur	Systolic blood pressure (mm Hg)	Serum calcium (mg per 100 ml)	Serum phosphorus (mg per 100 ml)	Blood urea (mg per 100 ml)	Serum cholesterol (mg per 100 ml)	Serum alkaline phosphatase (K A units)
Sept 10 1955	5	½ C N D M	9 1	23	15¹/₈	Loud systolic	170 185	15 1	4 8	90	139	4
Sept 16	5	Low calcium milk commenced	9 3			Loud systolic		13 7	4 8			
Sept 21	5¹/₄	Low calcium milk + cereal	8 14			Loud systolic		11 8	3 5			12
Sept 27	5¹/₂	Low calcium milk + cereal	9 8			Loud systolic	120	12 7	2 9	80	213	16
Oct 22	6¹/₄	Low calcium milk + cereal	10 9	23³/₈	15³/₄	Nil	108	12 2	3 3	55	148	11
Nov 16	7	Low calcium milk + cereal + mixed diet	11 13	23³/₄	16¹/₈	Nil	112	11 5	4 4	66	139	20
Jan 4 1956	8¹/₂	½ C M low-calcium cereal + mixed diet	13 10	25³/₈	16³/₈	Nil	120	11 2	4 6	46		20
Jan 31	9¹/₄	½ C M low calcium cereal + mixed diet	14 10	26¹/₈	16⁵/₈	Nil	110	11 2	4 2	44		1
March 7	11	Full mixed diet C M	15 4	26³/₄	16³/₄	Nil		10 0	5 5	49	120	

½ C N D M = half cream National dried milk Low-calcium milk = locasol (Trufood) prepared in distilled water Low calcium mil and cereal = locasol and low calcium cereal (Glaxo) Mixed diet = vegetables eggs broth &c ½ C M = milk consisting of equal part reconstituted locasol and whole cow's milk with no added vitamin D C M = whole cow's milk with no added vitamin D

Notes and News

CHANGES IN SOCIAL RESPONSIBILITY

In a Cantor lecture to the Royal Society of Arts on May 29 Dr Roger Tredgold pointed out that some people who speak of the decline in social responsibility do so with 'righteous indignation'—a mixture of anger and self-complacency not uncommon in our society—while others are indulging in the tendency to praise the past at the expense of the present. Criticisms of this kind give pleasure to the speaker, and flatter his pride by the implication of his own admirable social responsibility, but their effects on the listener are not pleasant at all: they are accepted very seldom and acted on less.

Admittedly there are no direct statistics and no yardstick, so no final diagnosis of the situation is possible. But, in their patients' interests, doctors are often obliged to recommend some treatment before their diagnosis is final. One may indulge, therefore, in a little speculation.

Social irresponsibility, Dr Tredgold felt, occurs in two forms: (1) in people whose early upbringing is so deficient in affection that adequate social relationships cannot be formed (the antisocial psychopaths—known variously to other authorities) and (2) in those who can respond to environmental influences and in particular to the expectation in the family, at school, and in the various media of communication. The late war, for instance, showed that a changed expectation can awaken and satisfy social responsibility. The individual "has felt loyal, and been heroic." Unfortunately this expectation is now less: we have lost sight of individual responsibilities in our proper desire for individual rights. "'No rights without responsibilities' would be a better slogan than many which have won an election."

On the whole, therefore, Dr Tredgold was compelled to conclude that in this country "the responsibility of each of us for the welfare of each other citizen" is getting less. Among the reasons for this he put "the break-up of many families, the lessened skill and security of both parents and teachers, the lessened influence of the citizen who is responsible on him who is not, and conversely the greater influence of irresponsible and self-centring propaganda by press, wireless, and other means, and so the lack of expectation of responsibility in the community", and finally the misuse of leisure. These conditions, he thought, are increasing in their scope and power, and will do so faster as social irresponsibility increases. There is then a vicious spiral.

Are we, he asked, aware of this? "The majority are unaware and complacent, a minority has some vague sense of it, and is anxious and ill at ease. But this anxiety, tragically, leads to no appropriate action; indeed it does the reverse, for it may well lead, as we have seen, to criticism, anger, and superiority. And this is unlikely to cause anything but stubborn ill will, and a hardening into self-interest, self-righteousness, and perhaps a narrow loyalty to a small group." In international relations the same lack of responsibility towards other people is reflected: national interests are consistently put first, just as within nations the interests of small groups are preferred to the nation's. The truth that "charity begins at home" is often used to mean "charity stops at home."

Among the remedies he proposed Dr Tredgold put first the improvement of the quality of parenthood. "We must try to inculcate the idea that we are no more born good parents than we are born good children. We must recognise that it is a skill and not just 'mother love'; factors which influence development are there to be studied, and a skill is there to improve with practice." Secondly teachers must be selected and trained to be more secure than now, and more skilled: "can anyone feel that the average teacher's value to society is in any way reflected in his or her possible earnings?" Thirdly, the State should not financially penalise parents who want to send their children to public schools where social responsibility is taught. And fourthly, as individuals and as members of professions each must do what he can to influence public opinion, and those who mould it, so as to increase a sense of responsibility where possible—an up-hill task. "We must try to get recognised those trends which decrease responsibility in childhood, adolescence, military service, work, and leisure. But we must also ensure that this recognition does not lead to pontifical criticism." As a final slogan the lecturer suggested "No criticism without construction."

THE RIGHT SORT OF APPEAL

Mental hospitals all over the country are short of nurses, and everywhere efforts are being made to attract suitable men and women to this worth-while profession. The booklet which has lately been issued by a Birmingham hospital management committee is an example of stimulating recruiting technique. *The Story of Mental Nursing and of Rubery Hill and Hollymoor Hospitals* shows the variety of work in a mental hospital today. As the well-chosen illustrations make clear, the hospital itself is a complex organisation run by a mixed team including doctors, nurses, tradesmen, typists, and therapists. It is also backed by the mental health services of the city of Birmingham which offer aftercare to the patient who has returned to his home. The booklet thus shows a community doing its best to deal with a community's problem: it is a persuasive appeal to others to share this responsibility.

FAMILY PLANNING ASSOCIATION

At the annual general meeting of this association on June 2 Sir Russell Brain, P.R.C.P., was elected president in succession to the late Lord Horder. Addressing delegates from more than 200 branches Sir Russell said: "It seems to me that there can be few Associations in existence which have such opportunities of contributing to human happiness as this, and I mean that in two senses, the happiness of the individual in contributing to the security of happy married life, and in the broader sense of human welfare. I believe that we are faced at present, with a crisis in the evolution of the human race, and unless we can solve the population problem the consequences will be really disastrous." Mrs Pandit, the High Commissioner for India, who also spoke, said that in India the problem was not one of propaganda but of machinery and of the need for a simpler contraceptive. Each State now had a long-term programme; though population must go on increasing before this could have any effect, at least a start had been made.

HOME FOR HANDICAPPED WOMEN

The Oxfordshire branch of the British Red Cross Society has opened a home for physically handicapped women, aged 16–40, at Andrew Duncan House, Shiplake, near Henley-on-Thames. Admission is on medical recommendation, but mental defectives or those with fits or incontinence are not accepted. The cost is 5 guineas a week. Full information can be obtained from the County Civilian Welfare Officer, British Red Cross Society, 101, Banbury Road, Oxford.

APPROVED NAMES FOR DRUGS

The British Pharmacopœia Commission has issued the following supplementary list of approved names:

Approved name	*Other names*
Chlorotrianisene	Tri-(p-methoxyphenyl)-chloroethylene Tri-p-anisylchloroethylene TACE
Edetic Acid	Ethylenediamine tetra-acetic acid
*Levorphanol	(−)-3-Hydroxy-N-methylmorphinan Levorphan Dromoran is the tartrate
Mephentermine	N, α, α-Trimethyl-β-phenylethylamine Mephine
Meprobamate	2-Methyl-2-propyl-1,3-propanediol dicarbamate Equanil, Miltown
Mercaptopurine	6-Mercaptopurine Puri-nethol
Methyprylone	3,3-Diethyl-5-methylpiperidine-2,4-dione Noludar
Nitrofurantoin	1-(5-Nitro-2-furfurylideneamino)hydantoin Furadantin
Nystatin	An antibiotic produced by *Streptomyces noursei* Mycostatin
Phensuximide	N-Methyl-α-phenylsuccinimide Milontin
Pyridostigmine	3-Dimethylcarbamoyloxy-1-methylpyridinium Mestinon is the bromide
Sodium Calciumedetate	Calcium chelate of the disodium salt of ethylenediamine tetra-acetic acid

* Replaces levorphan as the approved name.

AMENDMENTS

The approved name methœstrol is withdrawn and the entry under promethœstrol amended as follows:

Promethœstrol	3,4-Di-(4-hydroxy-3-methylphenyl)-hexane Methœstrol

atrioventricular valves (Hjelt et al 1956), it certainly may occur in the absence of hypertension The fall in the blood-pressure in the present case and the disappearance of the murmur in this and in one other of our cases emphasise the value of early treatment Possibly other features of the severe cases are reversible, as well as preventable, by prompt and early treatment

Summary

A case of "idiopathic" hypercalcæmia of infancy was treated with a low-calcium diet

The blood-pressure, which had been raised, reverted to normal and a cardiac murmur disappeared

The advantages of treatment with a low-calcium diet, including a low-calcium cereal, are discussed

Criteria for deciding when to allow the infant to return to a normal diet are suggested

We wish to thank Dr R H Dobbs and his colleagues at Southend General Hospital for allowing us to investigate and treat this case, and Mr I W J Evans who carried out many of the analyses and prepared the charts The blood-urea, serum cholesterol, and alkaline phosphatase estimations were made in the department of chemical pathology, St Mary's Hospital We are grateful to Dr W F J Cuthbertson (Glaxo Laboratories) for especially preparing the low calcium cereal The balance studies would not have been possible without the enthusiastic help of Sister M S Anderson and her staff

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TREATMENT OF AMŒBIASIS WITH RESOTREN

L Pfannemueller

M D

SPECIALIST IN INTERNAL AND TROPICAL DISEASES, GERMAN RED CROSS HOSPITAL, PUSAN, KOREA

CLINICAL studies on 'Resotren'* by Halawani et al (1951), Mohr (1953), Chaudhuri et al (1954), Knorr (1954), Sarsam (1954, 1955), and Scheel (1955) cover more than 300 cases The various reports agree that resotren is effective in both intestinal and extra intestinal amœbiasis

Resotren is a chemical combination of chloroquine and iodohydroxyquinoline and, taken by mouth, is poorly absorbed and reaches the lower bowel in considerable concentration Fuhrmann and Koenig (1953), who studied its pharmacology, report that about half of it is gradually broken down in the small intestine, releasing chloroquine and iodohydroxyquinoline, which are then absorbed The remainder passes into the large intestine, where some is also split up, and thus both chloroquine and iodohydroxyquinoline are brought to the site of infection, where they never are present in such amounts when given separately by mouth

I review here 42 cases seen while I was physician to the Mosul and Hillah hospitals in Iraq These cases are summarised as follows

Type	*No of cases*	*Results**	*Remarks*
Uncomplicated amœbic dysentery	5	Clinical cure and negative stools within 8 days in all patients	No relapses, 3 cases previously treated with aureomycin without permanent success
Amœbic hepatitis complicating amœbic dysentery	31	Clinical cure in 30 (1 did not complete course) negative stools in 29	Rapid disappearance of hepatomegaly in [illegible] cases regression of symptoms and liver enlargement within two days 14 in which amœbic hepatitis had developed after treatment elsewhere with aureomycin rapidly responded to resotren
Liver abscess complicating amœbic dysentery	6	Clinical cure and negative stools in all	Acute severe cases all rapidly responded to resotren without surgery 1 case was 'needled' [illegible] 150 ml of chocolate coloured pus In the first two or three days chloroquine was given additionally

* Search for *Entamœba histolytica* in the stools during six months after treatment gave negative results

Clinical Studies

Uncomplicated Amœbic Dysentery

The first 3 cases included in the table were of typical acute uncomplicated amœbic dysentery with bloody diarrhœa and positive stools The first 2 had been treated with aureomycin elsewhere and relapsed, the 2nd patient had a black hairy tongue due to the antibiotic All 3 patients were rapidly cured with resotren, the clinical symptoms disappearing by the third day Neither trophozoites nor cysts could be found in the stools at the end of the course or during the follow up

Cases 4 and 5 were of chronic uncomplicated amœbic dysentery with only cysts in the stool Both patients were cured of their clinical symptoms by the end of the course, cysts were no longer present in the stool, and the stools were negative during the six-month follow up

Amœbic Hepatitis Complicating Amœbic Dysentery

31 cases of amœbic hepatitis were treated with resotren In all the cases amœbæ or cysts were found in the stools, but, in view of the positive clinical signs present in each case, their absence would not have altered our diagnosis The liver was palpable and generally enlarged to three finger-breadths below the costal margin, and pain on pressure was a constant finding

Treatment with resotren produced striking improvement in all the cases, the liver returned to its normal size and the symptoms disappeared, in some cases within four days of the start of treatment In 2 cases cysts were still present in the stools at the end of treatment, 2 other patients were not examined at the end of the course owing to factors outside our control The remaining 27 had negative stools after treatment, 14 of them had previously been treated elsewhere with the broad spectrum antibiotics, aureomycin or oxytetracycline, before they came to this hospital

Liver Abscess Complicating Amœbic Dysentery

6 cases of acute amœbic liver abscess were treated with resotren Results were excellent, the clinical symptoms rapidly disappeared, and the stools became negative both for trophozoites and cysts by the end of the course The temperature returned to normal, usually by the third day of treatment, and radiography before and after treatment confirmed the impressive clinical effect of resotren

DOSAGE

Usually a course of resotren consisted of 40 tablets given as follows

1st day	3 × 2 tablets	= 6
2nd–5th day	4 × 1 tablet	= 16
6th–10th day	3 × 1 tablet	= 15
11th–12th day	3 × 0 5 tablet	= 3
12 days		40

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* Resotren is a product of Farbenfabriken Bayer A -G, Leverkusen, Germany

PASSION AND CONTROVERSY IN SCIENCE *

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M D Budapest D Sc Princeton D Sc Leeds F R S
PROFESSOR OF SOCIAL STUDIES IN THE UNIVERSITY OF MANCHESTER

My title may sound shocking for the first thing you know about science is that it is dispassionate Science is said to describe *facts* which are there whether you like them or not facts derived from the experience of *things* that can be seen and touched Scientific knowledge is therefore regarded as matter-of-fact, impersonal objective in sharp contrast to our moral convictions, religious beliefs, and other persuasions that are charged with emotion

The father of empiricism, John Locke, has said that whatever is not capable of demonstration by experience 'is not unless it be self evident capable to produce knowledge how well grounded and great soever the assurance of faith may be wherewith it is received , but faith it is still and not knowledge , persuasion and not certainty '[1] How then can passion ever participate in producing knowledge ? How can it indeed do aught but adulterate objective demonstration by an admixture of unwarranted persuasion ?

Yet there is on record the overwhelming elation felt by scientists at the moment of discovery, elation of a kind which only a scientist can feel and science alone can evoke in him Kepler testified to it in his *Harmonices Mundi*, published in 1619, in which he announced the discovery of his Third Law,' connecting planetary periods and distances He writes

> nothing holds me I will indulge my sacred fury , I will taunt mankind with the candid confession that I have stolen the golden vases of the Egyptians in order to build of them a tabernacle to my God far indeed from the bounds of Egypt If you forgive me I shall rejoice , if you are angry, I shall bear it the die is cast the book is written whether to be read now or by posterity I care not it may wait a hundred years for its reader if God himself has waited six thousand years for a man to contemplate His work '

We have the image of Archimedes jumping out of his bath to rush through the streets of Syracuse shouting Eureka ! And we have it on record how Louis Pasteur rushed out likewise from his laboratory when he first separated lævo and dextro rotatory tartrates and fervently embraced the laboratory assistant in the corridor

The outbreak of such emotions in the course of discovery is well known but they are not thought to affect the outcome of discovery Science is regarded as objectively established in spite of its passionate origins But in my title I mentioned passions *in* science and I do actually want to show that scientific passions are no mere psychological by-play, but have a logical function which contributes an indispensable element to science They respond to an essential quality in a scientific statement and may accordingly be said to be right or wrong depending on whether we acknowledge or deny the presence of that quality in it

What is this quality ? Passions charge objects with emotions making them repulsive or attractive , positive passions affirm that something is precious The excitement of the scientist making a discovery is an *intellectual* passion, telling that something is *intellectually* precious and, more particularly, that it is *precious to science* And this affirmation forms part of science The words of Kepler which I quoted were not a statement of fact but neither were they merely a report of Kepler's personal feelings They asserted as a valid affirmation of science something else than a fact namely, the scientific interest of certain facts the facts just discovered by Kepler. They affirmed indeed that these facts are of immense scientific interest and will be so regarded so long as knowledge lasts Nor was Kepler deceived in this majestic sentiment The passing centuries have paid their cumulative tribute to his vision, and so I believe, will the centuries yet to come

The function which I attribute here to scientific passion is that of distinguishing between demonstrable facts which are of scientific interest, and those which are not And hence also of serving as a guide in the assessment of what is of higher and what of lesser interest what is great in science and what relatively slight I want to show that this appreciation depends ultimately on a sense of intellectual beauty , that it is an emotional response which can never be dispassionately defined, any more than we can dispassionately define the beauty of a work of art or the excellence of a noble action

It is true that the scientific value of an observation usually increases with its generality But unique facts may also possess profound scientific significance Take Tycho Brahe's discovery of a nova a new fixed star in 1572 or the synthesis of urea by Wohler in 1828 The great scientific value of these discoveries lay in the fact that they fundamentally changed our conception about the nature of things The birth of Tycho's new star proved that the empyrean was subject to change Its occurrence invaded the last area of the universe still reserved to the rule of divine principles and annexed it to the realm of accident and necessity a fit subject of empirical science By this discovery Tycho anticipated Newton's demonstration that the same laws governed the stars in their courses and the swing of a clock's pendulum Similarly, Wohler by his synthesis of urea broke through the barrier between the inanimate and the living He proved that no 'life-force" was required for the production of organic matter, and thus opened the path to biochemistry

Discoveries like those of Tycho or Wohler are valued for the breadth of their implications even though they establish no new general laws They offer something more vague and also more profound namely, a truer understanding of a large domain of experience. Generality is indeed but an aspect of profundity in science and profundity itself as we shall see but an expression of the feeling that we are making a new more intimate contact with reality

* * *

The following case of scientific glory blighted by the later progress of science will illustrate this point In 1914 T W Richards, then professor of chemistry in Harvard, was awarded the Nobel prize for his determination of some atomic weights with an accuracy far surpassing that which had been achieved before His results have never been contested But in 1932 Frederick Soddy could write of this type of measurement that it appears now of as little interest and significance as the determination of the average weight of a collection of bottles some of them full and some of them more or less empty For it had been realised that the value of atomic weights resulted from the accidental proportion in which the constituent isotopes happen to be present in the element as found in Nature A magnitude that had seemed to characterise a deep seated feature of the universe had turned out to have no such bearing Though factually correct it had proved deceptive because—contrary to expectation—it did not correspond to anything substantial in Nature When the exact atomic weight of an element had ceased to be of interest to science, what had seemed important had turned out to be trivial

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* A university lecture delivered to the Manchester Medical Society on Jan 31 1956

[1] Locke J Third Letter on Toleration

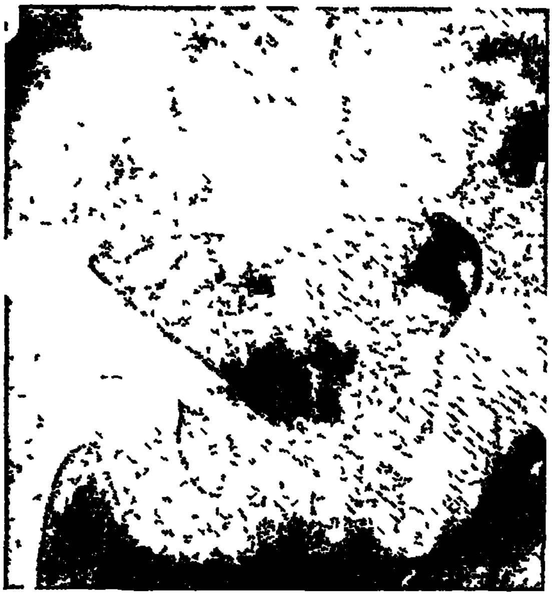

Fig 1—Pelvis (Oct 14, 1954) showing fractures of all pubic rami with gross deformity

Her sternal marrow was normoblastic, with no evidence of carcinoma, myeloma, or leukæmia Her blood contained protein 6 4 g per 100 ml (A G ratio 1 8 1), sodium 320 mg per 100 ml, potassium 15 mg per 100 ml, chloride 610 mg per 100 ml, CO_2 combining power 55 vol %, urea 30 mg per 100 ml, calcium 10 1 mg per 100 ml (average of 8 readings), phosphorus 2 7 mg per 100 ml (average of 8 readings), alkaline phosphatase 28 units, serum bilirubin 0 4 mg per 100 ml, thymol turbidity 2, gold sol test negative, glucose (fasting) 120 mg per 100 ml, and amylase 100 Somogyi units

Glucose tolerance test—The blood sugar level was 90 mg per 100 ml fasting, and at 30 minute intervals after 50 g of glucose 210, 150, 90, and 60 mg per 100 ml, her urine after 30 and 60 minutes contained a trace of sugar, but later specimens contained none

Urine—No albumin, Bence Jones proteoses, red cells, pus cells, or organisms, only occasional traces of sugar, 17 ketosteroids 6 7 mg in 24 hours (average of 3 readings), calcium (on ordinary ward diet) 69 mg in 24 hours (average of 4 readings), and phosphorus 460 mg in 24 hours (average of 4 readings)

Fæcal fat (estimated over a 3 day period after 6 days on a fixed daily intake of 30 g of fat)—Average daily fæcal

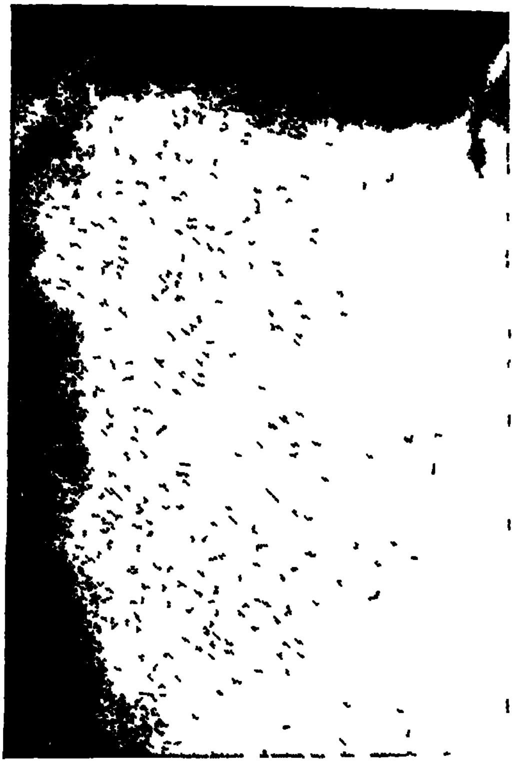

Fig 2—Right 10th, 11th, and 12th ribs (Oct 14, 1954) showing unheal fractures with excessive callus

fat was 18 4 g (only 63% absorption of fat) Of fæcal f 66% was split and 34% unsplit

Test meal—Complete achlorhydria Jejunal secretio contained trypsin and lipase

Radiography of skeleton (figs 1–5)—The pelvis showed striking "squash in" deformity with widely distributed an ill defined patches of decalcification All *four* pubic ra showed unhealed fractures Fifteen ribs were fractured in the lower ribs these fractures were more prominen unhealed, and surrounded by excessive callus Symmetrica false fractures were seen in the lateral borders of both scapul and the lower ends of both fibulæ The long bones showe generalised and somewhat patchy decalcification The vaul of the skull also showed patchy ill defined areas decalcification

Intravenous pyelography showed no renal abnormality

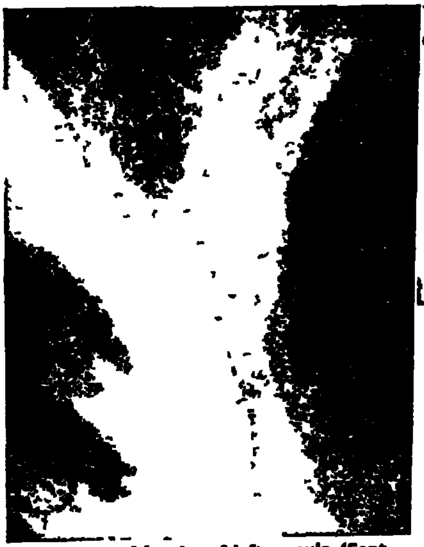

Fig 3—Lateral border of left scapula (Sept 6, 1951) showing Looser s zone

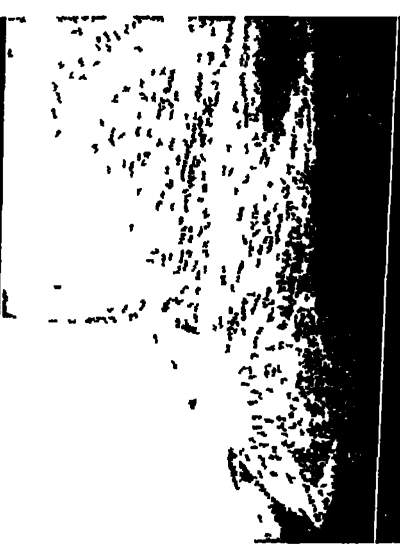

Fig 4—Lower end of left fibula (Oct 14 1954) showing Looser s zone and fracture

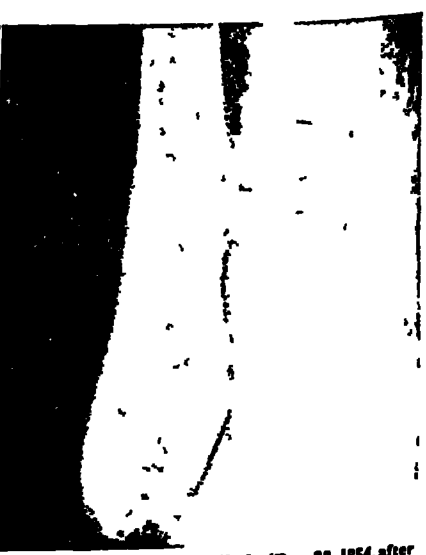

Fig 5—Lower end of right fibula (Dec 29 1954, after six weeks' treatment) showing healing of old Looser's zone and fracture

But this passionate quest seeks no personal possession Intellectual passions are not like appetites, they do not reach out to grab, but set out to enrich the world Yet such a move is also an attack It raises a claim and makes a tremendous demand on other men, for it asks that its gift—its gift to humanity—be accepted by all In order to be satisfied, our intellectual passions must find response This universal intent creates a tension We suffer when a vision of reality to which we have committed ourselves is contemptuously ignored by others For a general unbelief threatens to evoke a similar response in us which would imperil our own convictions Our vision must conquer or die

Like the heuristic passion from which it flows, the *persuasive passion* too finds itself facing a logical gap To the extent to which a discoverer has committed himself to a new vision of reality, he has separated himself from others who still think on the old lines His persuasive passion spurs him now to cross this gap by converting everybody to his way of seeing things, even as his heuristic passion had spurred him to cross the heuristic gap which separated him from discovery

We can now see the great difficulty that may arise in the attempt to persuade others to accept a new idea in science To the extent to which it represents a new way of reasoning, we cannot convince others of it by formal argument, for so long as we argue within their framework we can never induce them to abandon it Demonstration must be supplemented therefore by forms of persuasion which can induce a *conversion* The refusal to enter on the opponent's way of arguing must be justified by making it appear altogether unreasonable

Such comprehensive rejection cannot fail to discredit the opponent He will be made to appear as thoroughly deluded, which in the heat of the battle will easily come to imply that he was a fool, a crank, or a fraud And once we are out to establish such charges we shall readily go on to expose our opponent as a metaphysician, a Jesuit, a Jew, or a Bolshevik, as the case may be, or—speaking from the other side of the Iron Curtain—as an "objectivist," an "idealist," and a "cosmopolitan" In a clash of intellectual passions each side must inevitably attack the opponent's person

* * *

I shall recall here three controversies to illustrate this They occurred in the 19th century and their outcome has had an effective part in developing our present sense of scientific value

The first of these conflicts, though brief, was momentous The quixotic attack of the young Hegel on the empirical method of science and his swift defeat at the hands of the scientists was one of the great formative experiences of modern science In the year 1800 a band of six German astronomers, led by Bode, set out to search for a new planet to fill a gap between Mars and Jupiter in the numerical series of planetary distances discovered by Titius, and known as Bode's law The series is obtained by writing down the number 4, followed by the series $3 + 4, 2\ 3 + 4, 2^2\ 3 + 4, 2^3\ 3 + 4$ &c This gives for the first eight places 4, 7, 10, 16, 28, 52, 100, 196, which can be shown to correspond pretty well to the relative distances of the six planets known in 1800, provided you leave out the fifth number Setting the distance of the Earth arbitrarily at 10 you have the table

Bode's law

	Predicted	*Observed*		*Predicted*	*Observed*
Mercury	4	4	?	28	?
Venus	7	7	Jupiter	52	52
Earth	(10)	(10)	Saturn	100	95
Mars	16	15	Uranus	196	192

The young Hegel poured scorn on an inquiry following up a regularity of numbers which, being meaningless, could only be accidental On the grounds that Nature, shaped by immanent reason, must be governed by a rational sequence of numbers, he postulated that the relative spacing of the planets must conform to the Pythagorean series 1, 2, 3, 4 (2^2), 9(3^2), 8(2^3), 27(3^3)—in which, however, he substituted 16 for 8 This would limit the number of planets to 7, and allow a large gap between the 4th and 5th planets, i e Mars and Jupiter The quest for an eighth planet to fill this gap was therefore nonsensical[3]

However, on Jan 1, 1801, Bode's party of astronomers discovered the small planet Ceres in the region in question Since then over 500 small planets have been found in that neighbourhood,[4] and it may be that these are fragments of a full sized planet that took this place before

Hegel was discomfited and the astronomers triumphed uproariously This was all to the good, for it confirmed a juster sense of scientific value But we should realise that it had little else to support it Whether Bode's law has any rational foundation or has been fulfilled so far by mere coincidence (as Hegel had thought) is still open to question today opinions have changed on the subject repeatedly during the past fifteen years[5] So Hegel may have been right in rejecting the astronomers' grounds for their search for a new planet

Yet I agree that the astronomers were right and Hegel was wrong Why so? Because the astronomers' guess lay within a conceivably scientific system and so it was a kind of guess to which astronomers as scientists are entitled It was a *competent* guess, and—if Bode's law has any truth in it—even a true guess, while Hegel's inference was altogether unscientific, *incompetent* Fortunately Hegel guessed wrong and the astronomers, though their guess was perhaps unjustified, did hit the mark But even if Hegel's guess had proved right and the astronomers' wrong, we would still reject Hegel's vision of reality and cleave to that of the astronomers

In any case, the revulsion of scientists against *Naturphilosophie* was violent and lasting By the middle of the century empiricism ruled unchallenged But unfortunately the empirical method of inquiry—with its associated conceptions of scientific value and of the nature of reality—is far from unambiguous, and consequently conflicting interpretations of it had ever again to fight each other from either side of a logical gap

In his doctoral thesis, presented in 1875 to the university of Utrecht, J H van t'Hoff had put forward the theory that compounds containing an asymmetric carbon atom are optically active In 1877 there appeared a German translation of this work with a commendatory introduction by Wislicenus, a distinguished German chemist and an authority on optical activity This publication evoked a furious attack from Kolbe, another leading German chemist, who had recently published an article called Signs of the Times,[6] in which he castigated the decline of rigorous scientific training among German chemists, a decline which, he said, had led to a renewed sprouting of

"the weeds of a seemingly learned and brilliant but actually trivial and empty Philosophy of Nature, which, after having

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[3] Hegel Dissertatio philosophica de Orbitis Planetarum (1801) Werke Berlin 1834, vol 16, p 28
In his lectures on the Philosophy of Nature Hegel admitted the presence of Ceres and other asteroids in this gap He still referred to the numbers of the Timaeus but he now declared that the law of the planetary distances was still unknown and that one day the scientists would have to turn to the philosophers to find it Bertrand Beaumont in discussing Hegel's position (*Mind* 1954 63, 246) suggests that the Platonic series could be extended beyond the original seven, but in terms of Greek mathematics this is impossible

[4] Turner H H Astronomical Discovery London 1904, p 23

[5] An attempt to interpret Bode's law rationally by deriving it from a theory of the planetary system was made by C F von Weizsäcker in 1943 (*Z Astrophys* 1944 22 319) But from a later paper it appears that the problem is still in flux (see C F von Weizsäcker, Festschrift der Akademie der Wissenschaften in Göttingen, 1951, p 120)

[6] Kolbe, A W H *J prakt Chem* 1877, 14 268

Case-report

A 21 year old woman, mother of two children aged 21 months and 11 months, was admitted unconscious from another hospital on July 22, 1955 The patient's husband had left her in apparently normal condition at 6 P M the previous day When he returned at 9 P M he found her lying unconscious face down on the floor, a douche can containing a soapy solution and a syringe beside her There was no unequivocal evidence that she had actually used these Before the patient was admitted to hospital at 11 15 P M the same night she vomited several times

On admission the patient was unconscious, with eyes deviated to the left and pupils reacting briskly to light The upper limbs were hypertonic and held in flexion, the lower limbs were flaccid with absent tendon reflexes and extensor plantar responses She was about five months pregnant There was a slightly bloodstained discharge from the vagina, the external os of the uterus was closed Urine obtained by catheter contained a trace of albumin The stomach was washed out, nothing abnormal was found in its contents The next day the temperature had risen to 101 8°F, large doses of penicillin were administered During the day she remained unconscious and exhibited twitchings of the left upper limb Intracerebral hæmorrhage or air embolism following a mechanical attempt to produce abortion was suspected, and the patient was transferred to the Department of Surgical Neurology, Royal Infirmary, Edinburgh

On examination twenty-four hours after she had been found unconscious, the woman was still unconscious but moaned and became restless in response to painful stimuli Only the upper half of the body took part in the restlessness, and such response was elicited only by painful stimuli to the face, upper limbs, and trunk, there was no response to pinching or deep pin pricks applied to the lower limbs There was irregular twitching of both upper limbs, which were intensely hypertonic and were held adducted at the shoulder and flexed at the elbow, while there was obviously flaccid paralysis of the lower limbs with extensor plantar responses and retention of urine There were no signs of meningeal irritation Pupillary reactions were normal, the eyeballs were not deviated, and the eyegrounds were normal Lumbar puncture yielded clear cerebrospinal fluid containing 6 cells per c mm and 260 mg of protein per 100 ml, the colloidal gold curve was normal and the Wassermann reaction negative, the fluid mechanics were normal The cervix uteri now admitted three fingers and products of gestation could be palpated

Course —During the subsequent night the patient had a complete spontaneous abortion and the temperature returned to normal Twelve hours after admission re examination showed a sensory level for painful stimuli on the right side at T2, and on the left side at T4 There was no change in the level of consciousness, irregular twitching in the upper limbs continued, and other findings were unchanged Ascending neuronitis of the Landry type due to apiol poisoning with toxic coma and convulsions, was tentatively diagnosed Efforts to find any published suggestions as to the treatment of this condition were unsuccessful, so symptomatic treatment was applied Breathing remained satisfactory and nursing in the respirator appeared unnecessary

Sixty hours after admission the sensory level had risen to T1 bilaterally Twitching was now observed also in the face, otherwise the neurological condition was unchanged Urinary excretion remained satisfactory, and subsequent specimens of urine contained no albumin Absorption of the tube feeds was normal The patient died eighty four hours after she had been found, without regaining consciousness

After her death, the patient's husband admitted that he had seen "black pills, like 'Beecham's pills'" in the vomited matter A neighbour had cleaned the floor after the patient's removal to hospital, and no pills or container were found in the house

Pathological Findings

Post mortem examination showed no external injuries No abnormality of the *cardiovascular system* was seen on naked eye examination, and in particular there was no evidence of air embolism Microscopically there were several minute foci of myocardial necrosis with early polymorph infiltration The *lungs* were congested with early bronchopneumonic consolidation The *gastro intestinal tract* was healthy The *liver* appeared normal on external examination histologically there was minimal focal necrosis of liver cells The *spleen and pancreas* were normal The *kidneys* were completely normal both on naked eye and on microscopic examination The uterus showed evidence of recent, complete abortion There was no evidence of artificial stripping of the membranes or of other trauma to the uterus, vagina, or external genitalia

The *brain* showed slight generalised swelling with compression of both lateral and third ventricles, but no other gross abnormality The meninges, superficial cortical vessels and arteries forming the circle of Willis were healthy Histologically focal necrotic lesions were scattered throughout the brain In these damaged zones there was necrosis of nerve cells and to a lesser extent of neuroglia There was pallor of staining and vacuolation of ground substance with patches of early polymorph cell infiltration and proliferation of microglia with, in some instances, foam cell production In lesions in white matter the axons were swollen These foci of early necrosis affected grey matter more than white matter and cortex rather than subcortical grey matter They did not appear to follow any special anatomical distribution, nor were they necessarily related to blood vessels, though a causal relationship to small arterioles and capillaries could not be entirely excluded since in some instances there was quite distinct endothelial swelling and hyperplasia The leptomeninges overlying damaged areas of cortex showed scanty infiltration with foam cells and mononuclear cells Apart from the vascular changes already described the blood vessels were normal

In the *spinal cord* the 6th, 7th, and 8th cervical and the 1st thoracic segments were swollen, and during removal of the cord the partly liquefied 7th cervical segment disintegrated so that no material from this segment was available for histological examination Sections from the remaining cervical and from dorsal and lumbar segments of the cord showed foci of necrosis in the anterior grey horns identical with the lesions in the brain No abnormality of white matter, meninges, or blood-vessels was seen

Peripheral nerves —Numerous sections were examined from the ulnar, popliteal, and femoral nerves on each side, but despite staining by various methods, no evidence of peripheral neuritis was found

Biochemical analysis of liver and kidney and of bladder and bowel contents yielded no confirmation of the presence of apiol or an adulterant thereof

The lesions in the central nervous system, liver, and myocardium were either toxic or ischæmic and were not characteristic of any infective condition

Discussion

In this case it was evident that the nervous system was diffusely affected, coma and convulsions pointed to widespread cerebral damage The rising sensory level pointed to damage of the spinal cord, peripheral nerve lesions were also suspected, but their presence was not confirmed by post mortem examination Poisoning with triorthocresyl phosphate from taking an overdose of impure apiol was thought to be the cause of the neurological syndrome It was subsequently established that apiol had been supplied to the deceased woman, but the date of supply and amount of apiol could not be ascertained

One of us had seen similar cases on the Continent where the condition had occurred among pregnant women, intent on abortion, who had taken large doses of apiol preparations or so called "female pills" Most of the patients referred to in Continental reports developed weakness and tingling in the periphery of the lower limbs followed by similar symptoms in the upper limbs Some patients developed the syndrome of ascending myelitis or Landry's paralysis The symptoms began usually one to three weeks after the apiol preparation had been taken, irrespective of whether abortion had occurred

Extensive chemical investigations and subsequent animal experiments (ter Braak and Carillo 1932) proved that apiol itself was not responsible for the neurological illness Like other volatile oils, apiol—if taken in excessive doses—produces severe gastro intestinal irritation for Mendelism on the grounds that "in science there is no place for chance".[14]

There are serious questions still open today concerning the nature of things—at least, I believe them to be open, though the great majority of scientists are, as usual, convinced that the view which they hold is right and they meet any challenge to it with scorn. A notorious example is extrasensory perception. The evidence for it is ignored today by scientists in the hope that it will one day find some trivial explanation. In this they may be right; but I respect those too who think they may be wrong. And no profitable discussion is possible between the two.

Another example. Neurologists today accept almost without exception the assumption that all conscious mental processes can be interpreted as epiphenomena of a chain of material events in the nervous system. Some writers, like Prof K W Kapp, have tried to show that this is logically untenable, and I myself believe he is right. But to my knowledge only one neurologist—namely, Prof J C Eccles—has gone so far as to amend the neurological model of the brain by introducing an influence by which the will intervenes to determine the choice between possible alternative decisions.[15] This suggestion is scornfully ignored by all other neurologists, and indeed it is difficult to argue profitably about it from their point of view.

A similar schism is present today between the ruling school of genetics, which explains evolution as a result of a haphazard sequence of mutations, and writers such as Graham Cannon in England, Dalcq in Belgium, and Vandel and others in France, who consider this explanation inadequate and support the assumption of a harmonious adaptive power controlling the most important innovations in the origin of phyla.

* * *

Some people may listen to these illustrations with impatience for they believe that science provides a procedure for deciding any such issues by systematic and dispassionate empirical investigations. However, if that were clearly the case, there would be no reason to be angry with me. My argument would have no persuasive force, and could be ignored without anger.

At any rate, let me make quite clear what I have urged here. I have said that intellectual passions have an affirmative content; they affirm the scientific value of certain facts, as against any lack of such interest in others. This *selective* function—in the absence of which science could not be defined at all—is closely linked to another function of the same passions in which their cognitive content is supplemented by a conative component. This is their *heuristic* function. The heuristic impulse links our appreciation of scientific value to a vision of reality, which serves as a guide to inquiry. Heuristic passion is also the mainspring of originality—the force which impels us to abandon an accepted framework of interpretation and commit ourselves, by the crossing of a logical gap, to the use of a new framework.

Finally, heuristic passion will often turn (and have to turn) into *persuasive* passion, the mainspring of all fundamental controversy. I am not advocating the outbreak of such passions. I do not like to see a scientist trying to bring an opponent into intellectual contempt, and to silence him in order to gain attention for himself; but I acknowledge that such means of controversy may be tragically inevitable.

I certainly affirm that passion, and controversy moved by passion, must continue in science. And I would add to this my belief that, if this amendment to our conception of science be accepted, it would have to be followed by others which would lead to a fairly comprehensive revision of our philosophy of science.

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[14] *Pravda* Aug 10 1948 Quoted by Sidney Hook in Marx and the Marxists New York 1955 p 235

[15] Eccles J C The Neurophysiological Basis of Mind Oxford 1953 p 271

METABOLIC STUDIES ON TWO INFANTS WITH IDIOPATHIC HYPERCALCÆMIA

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WE report here the results of metabolic balance studies on 2 infants with idiopathic hypercalcæmia and the effects of treatment with cortisone. One of these infants was also treated with disodium ethylenediamine-tetracetic acid (E D T A) during the metabolic studies.

Cortisone and corticotrophin have been shown to increase fæcal calcium and to lower a raised serum-calcium level in Cushing's syndrome (Soffer et al 1950), rheumatoid arthritis (Kinsell et al 1950, Moehlig and Steinbach 1954) and sarcoidosis (Shulman et al 1952, Dent et al 1953, Henneman et al 1954). The efficacy of cortisone in lowering the serum calcium level and relieving the symptoms of 4 infants with idiopathic hypercalcæmia has now been reported (Creery and Neill 1954a, Macdonald and Stapleton 1955). This action of cortisone is as little understood as the pathogenesis of idiopathic hypercalcæmia, and the present studies were an attempt to investigate both problems.

Case-reports

Case 1.—A girl, born on Dec 25, 1953 at full term after a normal delivery, weighed 6 lb. Both parents were aged 26 and healthy. The mother had been well during pregnancy and had taken the usual supplements of vitamins. The baby was breast fed till the age of 9 weeks, when the supply failed and she was put on dried milk ('Lactogen,' Nestle). At the age of 6½ months her diet was changed to 2 pints of full cream National dried milk daily. Mixed feeding was started when she was 5 months old. She had been having up to half a teaspoonful of National cod liver oil compound daily (400 I U of vitamin D) between the ages of 1 and 6 months. At the age of 8 months she was admitted to Dundee Royal Infirmary on Aug 23, 1954, under the care of one of us (J T) because for six weeks she had not been taking her feeds well. She had vomited occasionally and three weeks before admission she had vomited all feeds for a week. Scanty stools were passed twice daily.

On admission she weighed 11 lb 5 oz but appeared well nourished. She was small, bright and interested, and slept well. She had prominent epicanthic folds and paresis of both external recti muscles. A systolic murmur of moderate intensity took the place of the first sound all over the precordium; it was maximal at the pulmonary area and was transmitted to the left axilla. No thrill was felt. The blood-pressure at a single reading was 174/110 mm Hg. The history of bottle feeding, loss of appetite, vomiting, and constipation, and the cardiac murmur suggested idiopathic hypercalcæmia.

Investigations.—Electrocardiography showed no prolongation of the P–R interval. The urine was usually acid and contained no protein or sugar and only a few pus cells. Mantoux tests to 1/100 were negative, and radiography of the whole skeleton, heart, and lungs, and iodised oil given by mouth showed no abnormality. Radiographically there was no calcification in the kidneys. The plasma calcium level was 16.8 mg per 100 ml and the blood urea level 135 mg per 100 ml. Other biochemical findings are shown in table I and fig 1.

Treatment and progress.—Two weeks after admission a low calcium diet of breast-milk treated with disodium E D T A

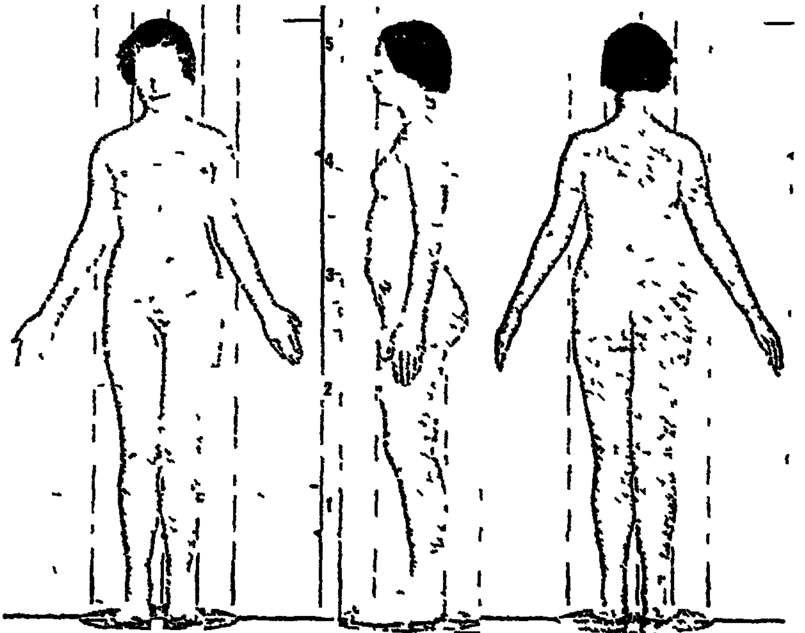

Fig 2—The patient three years after irradiation of her pelvis

Radiotherapy—Three days later the child was transferred to St Bartholomew's Hospital, under the care of Mr I G Williams, and a course of X ray therapy was given to her pelvis A total depth dose of 2150r was given in thirty days by anterior and posterior fields (fig 1) measuring 14 × 12 cm, at 250 kV peak, 60 cm focus skin distance, half value layer 1 75 mm Cu During the course she had an attack of left sided abdominal pain with some muscle guarding This subsided after three days without intervention Her hæmoglobin decreased from 72 to 58% by the end of the treatment, but her white cell count always remained over 5000 per c mm At the end of the treatment the tumour could not be felt per rectum The girl was returned to the Hospital for Sick Children, where her anæmia was corrected by blood transfusion

At a second laparotomy (Mr D I Williams) on Oct 3, 1952, the right ovary, on release from its protective sheath looked healthy and was returned to the pelvis The left ovary, with its sheath, had escaped from the suture to the abdominal wall and had ulcerated into the wall of the pelvic colon, causing a pericolic abscess and fistula The abscess was drained and, to rest the damaged gut while the fistula healed, a transverse colostomy was done This was closed by Mr Twistington Higgins on Nov 26, 1952, when an examination of the child's pelvis revealed no tumour in the sacrococcygeal region

Histology—Dr Martin Bodian reported that the tumour was a neuroblastoma showing very little evidence of differentiation

Follow up—It is now three years since the tumour was treated The patient is 11 years old, weighs 8 st, and is 5 ft 2 in tall She is in good health, her bowel and bladder functions are normal, and there is no clinical evidence of any tumour in the pelvis Her physical development is proceeding naturally (fig 2) She began to menstruate in November, 1954 when she was 10½ years old and now has a regular cycle of twenty eight days

Discussion

Three years after treatment for a pelvic neuroblastoma, with no sign of recurrence of the tumour, the prognosis for life is likely to be good

It remains to be seen what damage has been done by the treatment, in particular damage to the ovaries by the irradiation Since the menarche cannot be established without a functioning ovary, one at least of our patient's ovaries must be virtually intact

The doses of X rays received by the two ovaries differed As can be seen from fig 1, only one ovary was within the beam of the X rays The dose received within a lead sheath of similar dimensions to those used was recently measured, and from these measurements it has been calculated that the left ovary received about 170r during the treatment and the right ovary about 50r

It is known that temporary sterility can be achieved in the adult by 170r in a single dose, and that ovulation ceases after 290r (single dose) The dose received by our patient's left ovary would probably correspond to less than 70r given at one time, and is therefore below the threshold for damage to ovarian function

How much harm has been done to her fertility and what genetic damage has been caused, it is impossible to say at present, but some mutations are almost certain

Summary

A heavy dose of X rays to a malignant tumour was prevented from having a lethal effect on a child's ovaries by fixing lead sheaths round them and by removing the ovaries from the direct beam of X rays

The lead was removed after the course of irradiation, and three years later there was evidence of ovarian function

We are indebted to Mr Twistington Higgins and Mr I G Williams for permission to publish, Dr W M Levitt and Mr D I Williams for help in the management of the patient, Dr Martin Bodian for the histology report, Mr G S Innes for measuring the dose of X rays received, and Mr T C Crichton for constructing the original shells

EUNUCHOIDISM

RESPONSE TO VERY LATE TREATMENT WITH TESTOSTERONE

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A BUSINESS man, aged 40, first seen in late 1951, complained of extreme depression, shyness and feeling of inferiority, lack of energy, muscular weakness, lack of interest in life, and absence of all secondary sexual characteristics

He was the youngest of a family of 5 his brother and 3 sisters were all normal and were all married, with children His childhood was normal, with no serious illnesses His left testis had always been present in his scrotum, but his right testis was undescended, and puberty had never occurred He had never had any trace of secondary sexual characteristics, any facial hair, or any evidence of sexual activity

At the age of 20 he had a discharge from his umbilicus, and a patent urachus was diagnosed and removed

At the age of 25 he had consulted an endocrinologist who diagnosed 'Pituitary dyscrasia with cryptorchidism' and treated it at first with '*orchitic substance*" and later with injections of chorionic gonadotrophin ('Antuitrin S') The injections apparently produced effects growth of pubic hair, penile erection for the first time in his life (without discharge) improvement in his facial skin, and increase in the size of his right testis, which could be manipulated into the scrotum temporarily He continued with the injections for twelve months without further effects No secondary sexual characteristics developed, and he became disheartened discontinued treatment, and regressed to his previous condition He was morose, shy, lonely, had no ambition, had very severe feelings of inferiority, and could not mix with other people He also had periodic attacks of extreme depression lasting several days in which he lost all interest in life He had no sexual feelings, was afraid of women, and had no intention of marrying

On examination he was very obese (weight 13 st, height 67 inches) with striking feminine distribution of fat about his lower abdomen, thighs, hips, and breasts (extreme gynæco

TABLE I—BIOCHEMICAL DATA AND BODY-WEIGHT IN CASE 1

Date	Wt (kg)	Plasma-calcium (mg per 100 ml)	Plasma-phosphorus (mg per 100 ml)	Blood urea (mg per 100 ml)	Plasma sodium (m eq per litre)	Plasma potassium (m eq per litre)	Plasma chloride (m eq per litre)	Plasma bicarbonate (m eq per litre)	Plasma-cholesterol (mg per 100 ml)	Plasma protein (g per 100 ml)	Plasma albumin (g per 100 ml)	Others
Aug 23 1954	5·4	16·8										
26 ,,	5·5	16·1			149	4·7	110	30	300	8·9	4·53	Mg 3·4 mg per 100 ml α globulin 1·05 g per 100 ml β globulin 2·0 g per 100 ml γ-globulin 1·33 g per 100 ml
,, 31 ,,	5·4	15·2	5·6	135								P clearance 1·3 ml a minute Urea clearance 2·25 ml a minute
Sept 1 ,,	5·4			130								Hb 12·5 g per 100 ml
,, 7	5·5			65								B P 175/110 mm. Hg
,, 13 ,,	5·8	15·8		50								
22 ,,	5·6	13·6		95								
29	6·2	14		50								Hb 11·4 g per 100 ml.
Oct. 6	6·2	14·8		65								
,, 27	5·8											
Nov 3–6		*Balance period I*										
,, 15 ,,	5·8	15·7		50								Alkaline phosphatase 8 K.-A units Hb 11·2 g per 100 ml
,, 17–19		*Balance period II*										
19 ,,	6·3	11·4		50								
,, 22	5·9	14·7		40					200			
,, 30 ,,	5·7											
Dec 7 ,,	6·2	10·6			148	6·0						
9–13 ,,		*Balance period III*										
,, 14	6·5	12·6		40	129	5·1						
28	6·5	11·5	4·4	35	143	6·1						
Jan. 10 1955	6·5	14·5		48	137	4·6						Hb 11·36 g per 100 ml
25	6·4	11·8	4·7	35								
Feb 1	6·6	10·9		35								
,, 8	6·4	11·7										Alkaline phosphatase 22 K.-A units
25	6·3	11·2	4·6	45								
March 11 ,,	6·4	11·2	5·2	55								Hb 10·56 g per 100 ml
25 ,,		12										
April 15 ,,	6·55	11·2	5·3	35								Hb 9·44 g per 100 ml
May 6 ,,	7·2	10·9	5·5	40								
June 3	7·8	10·9	6·2	30								Hb 8·64 g per 100 ml.
July 6 ,,	8·1											Hb 6·56 g per 100 ml
Aug 5 ,,	8·65											
Sept. 30 ,,	9·5	12·0	5·7	35								Hb 13·6 g per 100 ml
Oct 28	9·5	10·6	5·5	35						9·0	4·9	Alkaline phosphatase 14 K.-A. units

Further course.—On Dec 10, 1954, the urine, which had never been quite free from pus cells, contained much pus, and two specimens grew proteus, a further course of streptomycin was given, and the pyuria disappeared On Dec 29, 1954, diarrhœa developed and the boy rapidly became dehydrated. His urine again contained pus and proteus sensitive to streptomycin. Three specimens of stool were free from pathogens The plasma-calcium level was 10·1 mg per 100 ml, but the blood-urea level had risen to 95 mg per 100 ml and the plasma-phosphorus level to 6·4 mg per 100 ml Intravenous fluid and electrolytes followed by a transfusion of 150 ml of blood produced rapid recovery, and by Jan 3, 1955 he was beginning to sit up again and to take solid food, although he was still a little subdued. During the night he became extremely ill and died suddenly and unexpectedly on Jan 4 at the age of 1 year

Necropsy (Dr K. Rhaney) revealed gross foci of calcification in the outer part of the renal medulla, with virtually none in the cortex or in the distal pyramids Large thrombi, possibly of embolic origin, were present in many of the pulmonary arteries within the lungs, these thrombi showed different stages of organisation, and the oldest had clearly been present for a week or more There were no pulmonary infarcts Further lesions revealed by histological examination, were acute bronchiolitis, early bronchopneumonia, and mild enteritis There was no other metastatic calcification The immediate cause of death appeared to be the acute bronchopneumonia in the presence of severe pulmonary arterial occlusion The importance of the primary disease could not be assessed in relation to the other causes of death. Full details of the necropsy will be reported elsewhere (Rhaney and Mitchell 1956)

Methods

A metabolic bed was used during the balance studies Fæces dropped directly into waxed cardboard containers Urine was collected through a plastic appliance (designed by Mr D Munro, L D S, of Dundee Dental Hospital) in the case of the female infant and through Paul's tubing strapped to the penis in the case of the male infant

Significant vomiting took place only once during the balance studies (period IV, case 2), and the estimated loss was subtracted from that day's intake

The diet in case 1 consisted of fresh cow's milk thickened with corn-flour (because of its small content of calcium), and in case 2 of fresh cow's milk in periods

TABLE II—BALANCE FINDINGS IN CASE 1

Period	Therapy	Calcium (mg daily)						Phosphorus (mg daily)					
		Excretion			Diet	Balance	Absorption (%)	Excretion			Diet	Balance	Absorption (%)
		Fæces	Urine	Total				Fæces	Urine	Total			
I (Nov 3–6)	Nil	382	55*	437	899	+462	57·5	168	181	349	648	−299	74
II (Nov 17–19)	Disodium E.D.T.A. 1 g daily	340	106*	446	617	−171	45·0	193	205	398	468	−70	59
III (Dec 9–13)	Cortisone 25 mg daily	899	21	910	1040	−130	14·5	446	177	623	798	+176	44

* Excluding loss of not more than 5% of total urine volume

absorbed was 20% less The urinary output of calcium remained large Despite this greater retention of calcium the plasma calcium level remained just over 12 mg per 100 ml For eleven days before and during period IV the dosage of cortisone was halved to 12 5 mg daily, even more calcium was retained, and the plasma calcium level rose to 17 2 mg per 100 ml After a return to the original dosage of cortisone the level again fell Further clinical improvement allowed the introduction of a more mixed diet containing less calcium, and in period V calcium and phosphorus were both in balance under treatment with only 12 5 mg of cortisone daily In comparison with the control period when the calcium and phosphorus intakes were similar, this strikingly different result was clearly due to the increased fæcal output of calcium and phosphorus

The urinary output of calcium remained large throughout periods II–IV despite varying plasma calcium levels but decreased in period V, possibly owing to the virtual lack of absorption of calcium The amount of urinary phosphorus also decreased considerably in period V, again possibly owing to the large amount of fæcal phosphorus

Oral disodium EDTA in case 1 seemed to lower plasma-calcium levels a little on both occasions when it was tried The object was to produce a low calcium diet very simply by adding EDTA powder to milk, because this substance chelates calcium into a soluble, non-ionised, and therefore biologically inactive, compound which is virtually unabsorbed from the gut (Foreman and Trujillo 1954) However, EDTA binds only a tenth of its weight of calcium, and 10 g would have been necessary to produce a calcium free diet on cow's milk, although only about 4 g on breast milk Unfortunately, loose stools developed as a toxic effect whenever the daily intake exceeded 2 g Disodium EDTA was also given subcutaneously (over period II) to combine with the calcium in the body-fluids and thus to reduce the toxic plasma calcium level, since 95% of intravenous calcium EDTA has been shown to be excreted in the urine in twenty four hours (Foreman and Trujillo 1954) The daily dose was 1 g in 100–200 ml of N/5 saline solution, given over four hours The object was to assess its efficacy in treating acute hypercalcæmic episodes No local ill effects appeared The plasma-calcium level fell to normal but rose again the day after the administration was stopped The urinary excretion increased considerably, but not quite to the extent expected from the dosage

Discussion

Incidence

During the two years ending Oct 1, 1955, 15 children with hypercalcæmia were treated in the pædiatric units of Dundee hospitals This condition accounted for 4 6% of all medical admissions of children aged 6–12 months, and ranked fourth in frequency after respiratory infections, feeding difficulties, and otitis media This number represents the approximate incidence of diagnosed cases in a population of 450,000 Idiopathic hypercalcæmia is also a significant cause of death, 4 of these infants died

Ætiology

Theories of causation have to explain not only the hypercalcæmia, with its consequent anorexia and vomiting, but also the spontaneous improvement shown by most of these infants An explanation should be provided too for the apparent increase in incidence in the United Kingdom in the past few years

The ætiological rôle of alkaline medication was suggested by Creery (1953), who noted the clinical resemblance to the "milk and alkali" syndrome of adults (Burnett et al 1949), because a large proportion of the diets of these infants consisted of cow's milk Creery and Neill (1954a), however, conceded that a history of taking alkalis in the form of either magnesium hydroxide or alkaline carminatives was not obtainable in all cases We also have seen hypercalcæmic infants who have not been given any alkali Alkalis cannot therefore be more than a contributory factor

The significance of a large intake of calcium is much more definite, in all the published cases the infants have had either fresh or reconstituted cow's milk They have thus had to contend with intakes of calcium and phosphorus about five times as great as would have been obtained from the same volume of human milk However it is of particular interest that one of our other hypercalcæmic patients was still being breast-fed when the diagnosis was made at the age of 8 months, and only a small amount of cow's milk had been given in milk puddings and with other cereal foods This infant had never been given dried milk but had had one teaspoonful of National cod-liver oil compound (vitamin D 800 I U) daily from the age of $4^{1}/_{2}$ months Cow's milk therefore appears to be a factor in the causation of the syndrome but other factors must exist because idiopathic hypercalcæmia develops in only a very small minority of the many infants who receive a similar intake of cow's milk and alkalis

Hyperparathyroidism, due to parathyroid hyperplasia rather than tumour, was one of several possibilities considered by McCance three years ago (McCance 1954) but is an unlikely explanation in view of the normal plasma-phosphorus level in the absence of severe uræmia, and the tendency to a low plasma-alkaline phosphatase level In addition, the plasma calcium level does not fall after cortisone in hyperparathyroidism (Dent 1956) whereas a striking fall occurred in our cases

Perhaps the most remarkable finding in our own and in previously published studies of the calcium balance of such infants (Creery and Neill 1954a, McCance 1954, Bonham Carter et al 1955) is the high proportion of the dietary calcium that is absorbed—about 60% in some instances This immediately suggests overaction of vitamin D as the probable cause, since this vitamin has the distinctive property of increasing the absorption of calcium from the gut The healthy infant fed on cow's milk without added vitamin D absorbs up to 35% of the calcium ingested (Telfer 1922), if vitamin D is added the absorption of calcium may reach 50% of the intake (Stearns 1931) but is usually less (Jeans et al 1936, Holmes 1945)

Some form of vitamin D has been used as a supplement to the diet in all the cases of idiopathic hypercalcæmia of infants that we have seen, yet in some cases the dosage does not appear to have been excessive Accurate assessment of intake of vitamin D is difficult because so many of the proprietary foods contain it, but, if dried milk fortified with vitamin D, cereals fortified with vitamin D, and the National cod-liver oil compound supplied free are all given to an infant aged 5 months, the total daily intake of vitamin D may easily exceed 2000 I U Such amounts may well be toxic (Jeans and Stearns 1938, Berry et al 1955), and the 2 infants reported here received amounts of vitamin D which were at or near these levels Other infants, however, have developed hypercalcæmia while receiving much less vitamin D, therefore, if vitamin D was the cause of the hypercalcæmia, these babies must have been unduly sensitive to its action (Lowe et al 1954)

The medium in which vitamin D is given may affect the strength of its action, Lewis (1935) reported that calciferol given in milk was several times more potent than when given in corn oil Thus the fortification of milk with vitamin D may be a method of intensifying the vitamin's action (Supplee et al 1936) It has also been

TABLE V—REPRESENTATIVE SOURCES OF VITAMIN D IN THE DIETS OF INFANTS

Food	*Vitamin D content* (I U)
Human milk	5 to 115 per quart
Fresh cow s milk	3 to 50 per quart
Evaporated milk (' Carnation ')	500 per reconstituted quart
* National dried milk	" Not less than ' 1400 per reconstituted quart
* ' Lactogen ' (Nestlé)	1500 per reconstituted quart
* ' Ostermilk (Glaxo)	1600 , ,
* Cow and Gate milk	1600 , , ,
Scott s Midlothian Oat Flour ' (M O F)	600 per oz dry weight
Robinson s Patent Groats '	800 , ,
Farex ' (Glaxo)	1000 , , ,
National cod liver oil compound	Not less than ' 700–800 per teaspoonful
Haliverol ' (Parke Davis & Co)	6000 per gramme

* The vitamin D content of dried milks may in fact be considerably higher than is stated on the label because it is incumbent on the manufacturer to produce a product of not less than the stated level and he has to allow for possible losses in processing or during the period between production and retail sale

done successfully in sarcoidosis with hypercalcæmia (Henneman and Carroll 1955) but we cannot yet confirm its efficacy in idiopathic hypercalcæmia

Prevention

The evidence cited leads us to believe that vitamin D is the most significant factor in the development of hypercalcæmia It is therefore pertinent to consider what amount of vitamin D should be recommended for infants It was conventional pædiatric practice for many years to recommend the addition of 400 I U per day to prevent deficiency, but the official recommendation in the United Kingdom has been 700 I U per day (as fortified cod-liver oil) since 1943, when the British Pædiatric Association advised an increase to ensure an ample margin of safety In the literature there is no general agreement Jeans (1950), Harrison (1954), and others (American Medical Association 1955) agree that 300–400 I U per day is enough to prevent rickets and to allow optimal growth In Sweden 1500 I U daily has been officially recommended (Mellander 1955), and yet 1800 I U daily has been recorded as causing delayed growth (Jeans and Stearns 1938) In the United Kingdom the vitamin-D intake of many infants may be even larger (table V) Although such larger amounts are usually well tolerated a few infants may show toxic effects, as there is wide individual variation in the response to vitamin D (Anning et al 1948, Bicknell and Prescott 1953) We suggest that the spontaneous improvement of idiopathic hypercalcæmia may be due to diminishing consumption of foods fortified with vitamin D in later childhood, as well as to a possible increase in individual tolerance

In the United Kingdom the question may well be posed whether more illness may now be due to vitamin D than to the rickets it is given to prevent As long ago as 1936, Thatcher expressed alarm at the potentialities then existing for the development of vitamin D intoxication in infancy, these have vastly increased in the succeeding twenty years We agree with Creery and Neill (1954b) that there is a need for reassessment of the degree of fortification of all infant foods and we feel that there should be warning labels on potent preparations of vitamin D, since few mothers are aware of the many ways in which their children may receive this vitamin

Summary

Descriptions are given of 2 infants with idiopathic hypercalcæmia, of whom 1 died Balance studies showed a large absorption of calcium This was probably due to overaction of vitamin D, although it is impossible to distinguish between the effects of overdosage and those of hypersensitivity

The symptoms are attributed to the hypercalcæmia, which may also damage the kidneys The plasma-calcium level can be reduced by a low-calcium diet without added vitamin D, and more rapidly by giving cortisone in addition

Cortisone increases the proportion of fæcal to dietary calcium and phosphorus and may also redistribute calcium within the body

Disodium E D T A will also reduce the plasma calcium level but has toxic effects

The considerable fortification of many infant foods in the United Kingdom undoubtedly increases the risk of hypervitaminosis D

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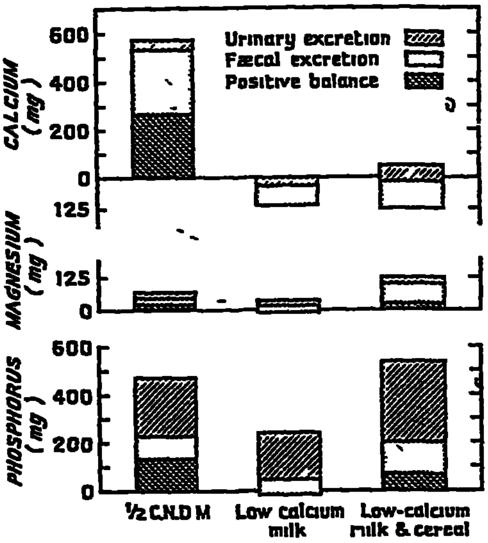

Fig 2—Treatment related to daily calcium, magnesium and phosphorus balances, which are averages of four-day collections Symbols as in table.

Before the low calcium diet was started and when the patient was taking half cream National dried milk (average daily intake of calcium 580 mg vitamin D not less than 600 I U daily) a four day balance study was done (fig 1) The balance was repeated (1) when the patient was taking Locasol,' a low-calcium milk (average daily intake of calcium less than 50 mg , no vitamin D) , and (2) when a low calcium cereal was added to the low-calcium milk (average daily intake of calcium less than 50 mg , no vitamin D) This cereal increased the caloric intake , it also had a high inorganic phosphate and phytate content

The clinical and biochemical progress of the infant is recorded in the table and fig 2 There was a steady weight-gain dating from the change in diet Vomiting ceased abruptly and he became less constipated Within a month the systolic murmur became inaudible and the blood pressure fell

After treatment for two months when he was aged 7 months vegetables cooked in distilled water and egg yolks, were added to the low calcium diet A further six weeks later the use of distilled water in preparing the feeds was discontinued and a milk mixture consisting of whole cow's milk and low-calcium milk in equal amounts was given The range of solid foods was increased, avoiding only those fortified with vitamin D

The child continued to improve skeletal and skull growth progressed at normal rates , muscle tone became normal and activity vigorous At the age of 9 months he was attempting to sit up , his mental development appeared normal , the changes in the tarsal bones shown on previous radiological examination had diminished. At the age of 11 months he weighed 15 lb 4 oz

Discussion

The Balance Studies

The balance studies were carried out (1) before treatment was started , (2) after one week on a low-calcium milk , and (3) after a further three weeks during which time a calcium-free cereal had been added to the diet (fig 1) The balances of calcium, phosphorus, magnesium, sodium, potassium, chloride, and nitrogen were measured over four-day periods Except for the calcium and phosphorus balances, no significant difference was found between the balances in the three periods, those for magnesium, sodium potassium, chloride, and nitrogen being approximately in equilibrium It was felt that these balances not only demonstrated that there was no overt upset in the metabolism of these substances, but also confirmed the accuracy of the collections during the four-day periods

The calcium balance was strongly positive during the active stage of the condition before treatment started It became negative when the infant was on low-calcium milk but there was a slightly greater fæcal excretion when the low-calcium cereal was also being taken

Management

Although some infants with hypercalcæmia recover slowly without special treatment recovery can be accelerated by giving a diet low in calcium or by administering cortisone Thus three aspects of the management call for comment the choice between a low-calcium diet or cortisone to reduce the calcium absorption and hence the serum calcium level , the advantages of a low-calcium cereal in addition to a low calcium milk , and the criteria for deciding when the child can safely return to a normal diet Our conclusions are based on the results in nine cases treated at St Mary's Hospital during the past two years

Low calcium diet or cortisone —The disadvantages of cortisone are that it has other effects than those required, in particular increasing the dangers of intercurrent infections and that short courses of treatment with cortisone are not satisfactory because, on discontinuing the cortisone the serum calcium rebounds to a high level (Macdonald and Stapleton 1955) The merit of the cortisone method of treatment is that it is simple and does not require the use of distilled water for the preparation of the feeds Small doses of cortisone are probably adequate if they are given over long periods (Creery and Neill 1954, Morgan et al 1956) It may sometimes be advisable to give a short course of cortisone at the start of a low-calcium diet if the serum calcium is very high since cortisone may cause a more rapid fall in serum-calcium than diet alone

The disadvantage of the low calcium diet is that the preparation of the low-calcium milk and cereal requires the use of distilled water It is not yet known whether using low-calcium dried milk and cereal, prepared with ordinary tap-water which may contain considerable amounts of calcium, would be satisfactory during the initial stages of treatment The advantage of the low-calcium diet is that so far as is known it is adequate in all other respects and does not have the hazards which are associated with the use of cortisone

Low-calcium cereal —The advantages of adding the low-calcium cereal to the diet of low-calcium milk are that it has a higher caloric value so that weight gain is better (and this may be an important factor in accelerating cure if calcium utilisation improves) that the high phytate and inorganic phosphorus contents may increase the loss of calcium in the fæces by binding calcium in the intestinal secretions (Bonham Carter et al 1955, Macdonald and Stapleton 1955), and that it provides a food suitable for older infants For infants who are entirely bottle-fed, it can be added to the milk in small amounts (up to a drachm per ounce has been found satisfactory)

Duration of treatment —The criteria used to decide when it is wise to return to a normal diet are a return of the serum calcium to normal , a fall in the blood-urea to normal (unless this occurs it is probable that the previous high serum-calcium has led to irreparable kidney damage [Lowe et al 1954, Schlesinger et al 1956]) , a rise in the serum alkaline-phosphatase , and a steady gain in weight None of these criteria is reliable by itself

The disappearance of the cardiac murmur and the lowering of the raised blood-pressure are of great interest, since these signs are usually found only in the more severely affected infants (Lightwood and Stapleton 1953, Lowe et al 1954, Schlesinger et al 1956) Some observers do not consider that the severe and the simple forms of the condition are distinct because their experience includes many cases intermediate between the simple and the severe ones showing only a few of the features of the severe cases (Lightwood 1955, Lightwood et al).

The nature of the cardiac murmur is not clear In some instances it may be due to actual calcification in the

If the initial condition of the patient was very severe, or if the case was of long duration a further course of 20 tablets in four days was given eight days after the first course If an acute liver abscess was present with serious symptoms, chloroquine was given in addition to resotren for the first two or three days

SIDE EFFECTS

Resotren was well tolerated The blood-count erythrocyte-sedimentation rate, and analysis of urine in all the cases showed no deviation from normal during treatment No alteration of the buccal or intestinal flora, such as is seen with the antibiotics, was noted during treatment with resotren The commonest side effect was initial diarrhœa This may not be a disadvantage, for some workers recommend an initial purge to remove the amœbæ from the lacunæ of the bowels If the diarrhœa was severe, the dose was reduced for a few days, and this was sufficient to stop this side effect

Discussion

The liver is involved in more cases of amœbic dysentery than is generally realised 10–20% has been given as the prevalence of amœbic hepatitis, and more than half the cases of chronic amœbic dysentery give abnormal liver-function tests (Mazzitelli 1954) Any treatment of amœbic dysentery which ignores this fact is not sound The development of amœbic hepatitis or liver abscess either during or after treatment of amœbic dysentery with a broad-spectrum antibiotic has already been reported by McHardy and Frye (1954) and Scaffidi and Sangiorgi (1952) The fact that 14 of the present cases had relapsed with hepatic amœbiasis after treatment elsewhere of amœbic dysentery with either aureomycin or oxytetracycline emphasises that treatment of the dysenteric symptoms alone is insufficient

The requisite drug should act both intestinally and extra-intestinally This means that it must be absorbed high in the intestine and concentrate in the liver, yet remain in the lumen of the gut and act against the trophozoites in the lacunæ of the large intestine Resotren seems to be able to do this Clinically it is effective in acute amœbic dysentery, chronic dysentery, and the hepatic manifestations of amœbiasis Its effect on liver abscess is dramatic, and none of the cases reported here required surgery, even though they were severe One case was "needled" to free about 5 oz of pus

Summary

42 cases of amœbiasis, including 31 of hepatitis and 6 of liver abscess, were treated with resotren

All forms of amœbiasis responded to resotren Clinical cure was achieved in all the cases, and at the end of treatment the stools were negative for both cysts and vegetative forms in 40 of the 42 cases

In cases of severe liver abscess chloroquine was given in addition to resotren on the first two or three days

Treatment with broad-spectrum antibiotics does not appear suitable in 14 of the present cases amœbic hepatitis had developed after treatment elsewhere with such antibiotics

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OSTEOMALACIA FOLLOWING GASTRECTOMY

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Although steatorrhœa may follow gastrectomy and steatorrhœa may lead to osteomalacia, in clinical practice osteomalacia must be very rare as a complication of gastrectomy, so the present case is worth recording

Case-report

A married woman, aged 52, attended the General Infirmary at Leeds on April 24, 1954, with recent severe backache Later, as a result of investigations and the discovery of a previous breast biopsy report, she was referred to one of us (L N P) for advice about bilateral adrenalectomy for supposed bone metastases complicating a possible carcinoma of the breast This diagnosis was not accepted, and the patient was readmitted to hospital on Oct 4, 1954, for review and further investigation By this time she had been taking stilbœstrol 5 mg thrice daily for three months

History—Her childhood had been healthy, with no suggestion of rickets, cœliac disease, or other serious illness At the age of 18 she began to have indigestion with epigastric pain and vomiting, from which she obtained partial relief by the use of a suitable diet, olive oil, and alkalis Eight years later she made a rapid recovery from an operation for acute appendicitis with pelvic peritonitis When she was aged 33 (in 1935), a perforated chronic gastric ulcer was sutured A month after this a biopsy specimen of a lump in her left breast was reported to show "chronic mastitis with evidence of considerable epithelial proliferation producing small papillomata in some ducts, but no definite evidence of malignancy" While taking the prescribed diet she remained fairly well for the next five years, but in 1940 severe epigastric pain developed, and a barium meal showed a chronic gastric ulcer with an hour glass deformity On March 11, 1940, Mr E R Flint did a partial gastrectomy with a Polya Moynihan anastomosis, the patient recovered well and was not seen again for seven years When questioned later, she admitted that she usually had two rather loose stools daily In 1947, at the age of 45, she was readmitted to hospital with severe microcytic anæmia (Hb 28%, red cells 2,380,000 per c mm, colour index 0 5) She had complete achlorhydria, and her bowels were loose but not unduly active After treatment with iron and hog's stomach, her Hb increased slowly to 86% At this time she first noticed pain in her left shoulder, and radiography of her cervical spine was reported to show minimal osteo arthritis During the next two years her shoulder pain grew worse, she began to complain of increasing backache, and the anæmia reappeared By 1950, just after the menopause, she had almost continuous severe backache with much tenderness over her vertebral column, she began to drag her right leg, and her husband had to help her into and out of chairs and bed In 1951 her symptoms grew worse, and pain radiated from her back to her right loin and thigh, she had dorsal kyphosis, and radiography of her chest showed several fractured ribs, her anæmia had also recurred In April, 1954, while walking, she was suddenly immobilised by very severe backache and was taken home by ambulance, the pain now radiated round both sides of her trunk and was made worse by coughing

Physical examination in May, 1954, showed a small frail woman, 4 ft 8 in tall and weighing 5 st 6 lb, she had once been 4 ft 11 in tall and had weighed 7 st 2 lb She had pallor, koilonychia, well marked dorsal kyphosis, and tenderness over many ribs and her wrists and ankles, which were not swollen Her breasts showed no evidence of carcinoma Nothing abnormal was found in her abdomen, pelvis, or nervous system

Investigations

Blood examination showed Hb 51%, red cells 3,000,000 per c.mm, colour index 0 85, white cells 7200 per c mm, and erythrocyte sedimentation rate 3 mm in 1st hour (Wintrobe)

Biopsy of right eleventh rib (Oct 12, 1954).—Histologically this was a healing fracture which showed remodelling of well formed bony trabeculæ. The spaces between the trabeculæ contained loose fibrous tissue in which there were some osteoclasts. A few small areas of necrosis were present in the bone. The rib structure on either side of the fracture appeared normal, and no evidence of carcinoma or myelomatosis was seen in the marrow spaces. The appearances were not pathognomonic but were consistent with pre-existing osteomalacia in the fracture area although there was no evidence of bone disease or osteitis fibrosa cystica.

Diagnosis

The radiographic appearance of the skeleton, showing generalised decalcification, deformity of the bony pelvis, and symmetrical false fractures, suggested osteomalacia, particularly since a review of old films showed that pathological fractures of the ribs had been present at least 5½ years before, with evidence of healing. This diagnosis was supported by the history of loss of height, indicating bone softening, and by the raised serum alkaline phosphatase level, normal serum-calcium level, and low urinary excretion of calcium. The bone biopsy added further support, though by the time this biopsy was made, the patient had already spent several weeks in hospital on a good mixed diet, stilbœstrol, and vitamin tablets, and this regime may explain the healing which by then was apparent. The finding of only 63% absorption of fat established the diagnosis of steatorrhœa, but its ætiology was not obvious at first. The absence of a history of cœliac disease was against a diagnosis of idiopathic steatorrhœa. Moreover, the general shape of the chest, which was of the adult type, did not suggest the shrunken under-developed bony thorax seen in osteomalacia secondary to steatorrhœa dating from infancy. The presence of pancreatic enzymes excluded serious disease of the pancreas. The rapid absorption of glucose did not suggest disease of the jejunum as a cause of malabsorption but conformed rather to the typical post-gastrectomy type of curve characterised by a rapid rise of the blood sugar level to a high value with attendant glycosuria, followed by an equally rapid fall even to a subnormal value, which in some cases results in late postprandial hypoglycæmia. Moreover the patient also showed other deficiency phenomena which are now recognised as late complications of gastrectomy: failure to gain weight, recurring severe microcytic anæmia, and a low serum protein level suggesting a negative nitrogen balance. It therefore seems likely that the osteomalacia was caused by steatorrhœa which in turn was attributable to the previous gastrectomy. In our hospital partial gastrectomy became the standard operation for chronic duodenal ulcer in the middle of the war period, probably about 1942; gastrectomy had been the standard operation for chronic gastric ulcer for many years before that, but such cases were less common than those of chronic duodenal ulcer. The fact, therefore, that gastrectomy had been in wide use for the past fourteen years only, may explain why no other cases of this slowly developing syndrome were noted.

Treatment and Progress

On Nov 16, 1954, the patient was placed on a daily dose of calcium lactate gr. 90 and vitamin D 150,000 units and encouraged to take extra fat contained in additional frequent small feeds throughout the day. After a month's treatment most of her backache had disappeared and her legs felt better, though she was still slow to get about. Her serum-alkaline-phosphatase level had risen to a peak of 87 units, indicating active repair of bone. After three months' treatment she could get about just as she wished, felt better in herself than she had for many years, still had a little low backache and aching ankles, and was still taking the same dose of calcium and vitamin D. Her alkaline-phosphatase level had fallen to 18 units suggesting that the bone was almost completely healed. After six months she was hard at work lifting clothes in a cleaner's shop; she was quite free from pain and was surprised to find that she could run and catch a bus. Two months later she began to complain of nausea after her tablets. Although her serum calcium level was only 9 mg. per 100 ml., the dosage was reduced to 50,000 units of vitamin D and gr. 30 of calcium lactate daily; the nausea disappeared, and she has since remained well.

Comments

Osteomalacia

Except in time of war osteomalacia is rare in civilised communities and is hardly ever due to a simple lack of vitamin D (Winston and Pendergrass 1954). It is not only usually due to steatorrhœa but also one of the most significant complications thereof. Steatorrhœa is common after gastrectomy, especially after total resection. Bone changes have been seen in gastrectomised young animals. Such changes are rare in man, presumably because gastrectomy is not usually done in adolescence. A case of osteomalacia seventeen years after gastrectomy was described by Groult (1945). The patient was a nun aged 42, with advanced skeletal changes, including extensive decalcification, codfish vertebræ, heart-shaped deformity of the pelvis, and numerous symmetrical fractures. Five years after her gastrectomy she developed arthritis with swollen painful toes, feet, and ankles. As bone and joint pains increased, kyphosis developed with loss of height, and after twelve years she was driven to bed. There is no mention of her diet or of steatorrhœa, but Groult attributed her disease to malnutrition, hypovitaminosis D, and calcium deficiency resulting from her ascetic life, her previous gastrectomy, and war-time rations. Her disabilities rapidly improved under treatment with calciferol, extra calcium, and ultraviolet light.

The present case strongly suggests that the steatorrhœa which sometimes follows gastrectomy can be bad enough to cause hypovitaminosis D with bone changes. As regards practical management, it is necessary only to implement the recommendations of Brain and Stammers (1951) that gastrectomised patients should take extra fat in frequent small meals, especially if the whole stomach has been removed. Additional calcium, vitamin D, and other fat-soluble vitamins should be given by mouth if the steatorrhœa resists treatment. If gastrectomy has to be done on a child or an adolescent, these particular hazards to general and skeletal development should be remembered.

Summary

A case is described in which steatorrhœa and severe osteomalacia developed fourteen years after partial gastrectomy.

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DEATH FROM APIOL USED AS ABORTIFACIENT

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WE describe here a case in which a patient apparently ingested apiol, in order to procure abortion. Coma and convulsions with flaccid paraplegia ensued, and the patient died. This outcome may have been due to contamination of the apiol with triorthocresyl phosphate. The case is reported since further such cases may arise from the sale, without medical prescription, of contaminated apiol as "female pills."

and toxic effects on liver, kidneys, and heart All apiol preparations which had caused damage to the nervous system of pregnant women were found to contain tri-orthocresyl phosphate Polyneuritis and spinal cord damage was produced in animals which had been fed with triorthocresyl phosphate The neurological signs in these animals did not appear until ten to twenty days after the toxic substance had been ingested

These findings resulted in restrictions on the sale of apiol to the public, and in certain parts of Germany the pharmacist was required to ensure that his supply of apiol contained no triorthocresyl phosphate

Because there have been numerous cases in different European countries, it is unlikely that triorthocresyl phosphate was an accidental admixture in apiol preparations, possibly it was deliberately included without realisation of its dangers Triorthocresyl phosphate is not unlike yellow apiol in appearance and it is a plasticiser Liquid yellow apiol is liable to give a deposit of white crystalline apiol and to become thick and pasty in consistency An addition of triorthocresyl phosphate would serve a twofold purpose it would give added bulk where this was necessary (e g , in filling a capsule without altering the dose of apiol or affecting its appearance) and, both in the capsule and in bulk it would tend to preserve the appearance and consistency of the apiol by preventing precipitation and conversion into a paste

Most women who have had peripheral neuritis as the result of triorthocresyl-phosphate poisoning have recovered One of us (K H) recalls survival of a case of ascending myelopathy with permanent paraplegia, and a death from respiratory failure in a similar syndrome (Neither of these cases was published) Most of the victims of Jamaica-ginger paralysis—a motor neuronitis proven to be due to adulteration of ginger extract with triorthocresyl phosphate (Smith and Elvove 1930, Smith and Lillie 1931, Smith et al 1932, Ahring 1942)—have also recovered Cases of acute poisoning leading to sudden coma and convulsions with severe diffuse cerebral lesions appear to be rare Lowenberg (1938) described such a case, but he described no post-mortem examination of the spinal cord, nor was it known what dose of apiol the patient had taken

The circumstances in which our patient was found suggest that she may have taken the drug more than once, since undigested capsules were found in the vomitus when she was overcome by coma Moderate doses taken earlier than the dose which produced coma might account for the presence of well-developed flaccid paraplegia a few hours after she had brought up still undigested capsules We suggest that moderate doses of the poison produce delayed effects on the peripheral nerves and spinal cord, while large doses cause immediate cerebral damage

This is the first case of damage to the nervous system from ingestion of an apiol preparation that we have seen in twenty years of neurological practice in Edinburgh We have been unable to find any references to this subject in the British literature, and only a few American reports deal with apiol poisoning although there are many accounts of the affection of the nervous system caused by triorthocresyl phosphate as impurity of ginger extract Probably apiol has in the past been used as an abortifacient in this country, but possibly previous preparations did not contain the dangerous impurity

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PROTECTION OF OVARIES FROM RADIATION

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THE sensitivity of the gonads to X rays often complicates radiotherapy, especially in the treatment of malignant disease in children In boys it is easy to protect the gonads by shielding the scrotum with lead, as is usually done in radiotherapy departments In girls it is more difficult to protect the ovaries We describe here a method of doing this

Case-report

A girl, aged 8 years, was referred to the Hospital for Sick Children, Great Ormond Street, London, in August, 1952, with twelve months history of intermittent enuresis

On examination her bladder was found to be enlarged to the umbilicus, and per rectum a soft but solid mass was felt, filling the pelvis and fixed to the sacrum There was an anæsthetic area around the anus, but no other abnormality was found She was admitted under the care of Mr Twistington Higgins with a provisional diagnosis of pelvic neuroblastoma

Treatment —Surgical removal of the tumour was planned , but, since this might be incompatible with the child s survival, plans were also made to treat the tumour with X rays Dr W M Levitt pointed out that the dose of X rays necessary to do this would probably sterilise her Therefore since laparotomy was going to be done, it was planned to protect the ovaries by moving them out of the direct beam of X rays and ensheathing them in lead For this purpose, lead 2 mm thick was shaped to resemble the two halves of a walnut shell The ovaries were expected to measure 2 0–3 0 cm long and 1 0–1 5 cm in the greatest width Two complete sets of shells were made one 2 25 × 1 25 cm the other 3 5 × 2 0 cm (internal dimensions) Each pair had a hole for the fallopian tube and broad ligament, and two small holes in each side of the half shells to enable the shells to be secured together and sutured to the abdominal wall Each part was then dipped several times in liquid latex to produce an innocuous coating for the lead

At laparotomy on Aug 15, 1952, Mr Twistington Higgins found that the neoplasm filled the pelvis , it was retroperitoneal, fixed, and very vascular, apparently a typical neuroblastoma The attempt to enucleate the tumour was eventually abandoned, a piece excised for section, and the peritoneal covering repaired The ovaries being unexpectedly large, a pair of shields had to be fashioned on the spot from sheets of lead of the same thickness shaped manually and covered with rubber finger cots The ensheathed ovaries were then sutured together and attached to the anterior parietal peritoneum as high as possible

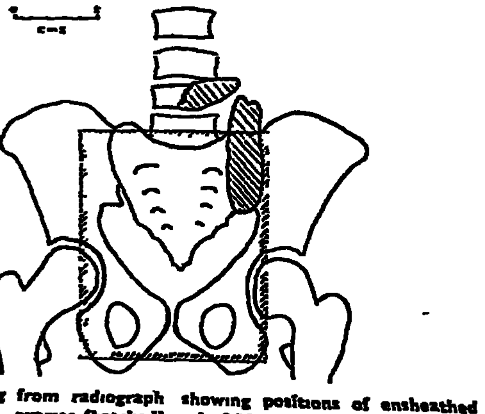

Fig 1—Tracing from radiograph showing positions of ensheathed ovaries (hatched) and of X-ray field